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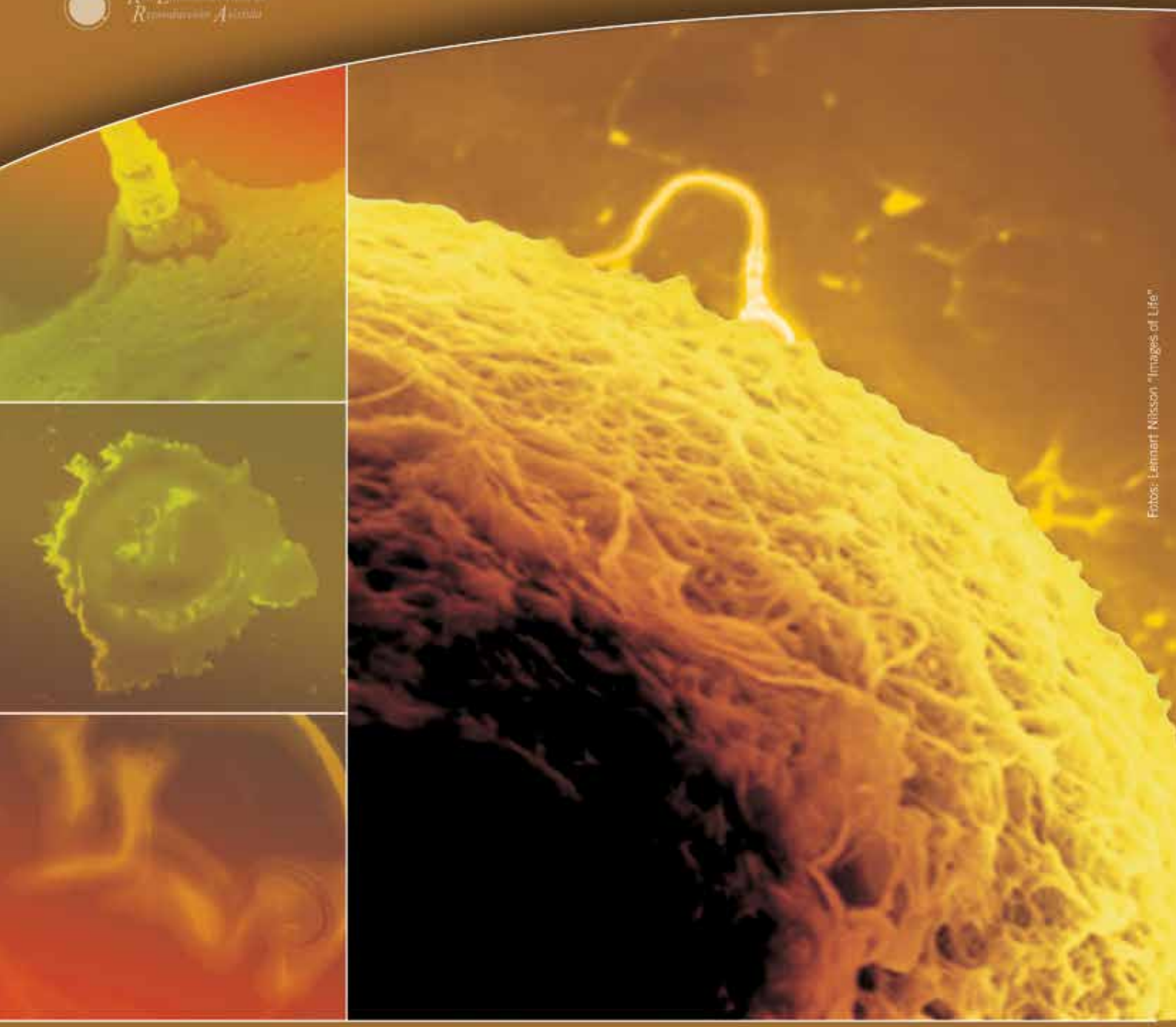
JBRA Assisted Reproduction

JORNAL BRASILEIRO DE REPRODUÇÃO ASSISTIDA



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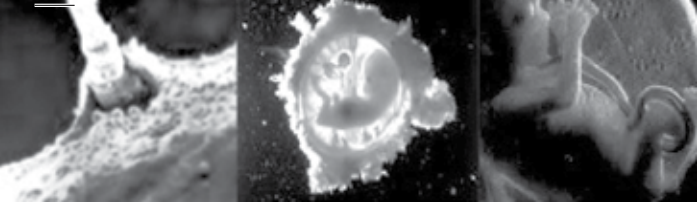
SAC Merck Serono: **0800.113320**

Anúncio veiculado em Maio de 2011.



Edição Especial - Dados de Registro Latinoamericano

JBRA Assisted Reproduction

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Inovação Recombinante.

Pergoveris

(alfafolitropina e alfalutropina)

Precisão, pureza e consistência na associação das duas gonadotrofinas[1,2]

Referências bibliográficas: 1. Basset R.M. et al. Continued improvements in the quality and consistency of follitropin alfa, recombinant human FSH. Reproductive BioMedicine Online. 2005; 10(2): 169-177(9). **2.** Gervais A, et al. Glycosylation of recombinant gonadotrophins: characterization and batch-to-batch consistency. Glycobiology 2003; 13(3):179-189.

Bula do produto no interior desta publicação. Destinado exclusivamente à classe médica. Veiculado em junho de 2012.

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Inovação Recombinante.

Pergoveris
(alfafolitropina e alfalutropina)

Pergoveris® alfafolitropina (r-hFSH) 150UI (11µg) alfalutropina (r-hLH) 75UI (3µg). USO SUBCUTÂNEO USO ADULTO **Indicações:** Pergoveris® é indicado para a estimulação do desenvolvimento folicular em mulheres com insuficiência grave de LH e FSH. Nos ensaios clínicos, estas pacientes foram definidas por um nível sérico de LH <1,2 UI/L. **Contra-indicações:** Hipersensibilidade à alfafolitropina, alfalutropina ou a qualquer dos excipientes; tumores do hipotálamo ou da hipófise; hipertrofia ou cistos ovarianos não originados por doença do ovário policístico; hemorragias ginecológicas de etiologia desconhecida; carcinoma do útero, ovário ou mama e nas situações em que não é possível a obtenção de uma resposta efetiva (insuficiência ovariana primária, malformações dos órgãos sexuais incompatíveis com gravidez e fibromiomas uterinos incompatíveis com gravidez). **Cuidados e Advertências:** Na mulher, a utilização segura e eficaz de Pergoveris® requer monitorização ecográfica regular da resposta ovariana, de preferência em conjunto com a determinação dos níveis séricos de estradiol. Deve ser utilizada em mulheres a dose mínima eficaz em relação ao objetivo do tratamento. As pacientes devem ser avaliadas para as seguintes situações, devendo ser instituído um tratamento específico apropriado: hipotiroidismo; insuficiência da supra-renal; hiperprolactinemia; tumores do hipotálamo ou da hipófise. A síndrome de hiperestimulação ovariana (OHSS) é uma situação clínica distinta da hipertrofia ovariana assintomática, podendo se manifestar em graus crescentes de gravidade. Uma resposta excessiva ovariana ao tratamento com gonatropinas raramente origina uma OHSS, exceto quando se administra hCG para induzir a ovulação. Portanto, em casos de hiperestimulação ovariana é prudente não administrar hCG e recomendar à paciente que se abstenha de ter relações sexuais ou utilize métodos anticoncepcionais de barreira, durante pelo menos 4 dias. Em mulheres submetidas à indução da ovulação, a incidência de gravidez e nascimentos múltiplos é aumentada quando comparada à concepção natural. A maioria das concepções múltiplas é de gêmeos. Gravidez e aleitamento: Pergoveris® não deve ser administrado durante a gravidez ou o aleitamento. **Reações adversas:** Cefaléia, exacerbação de asma, dor abdominal e sintomas gastro-intestinais, tromboembolismo normalmente associado com síndrome de hiperestimulação ovariana grave (OHSS), reações no local da injeção. Reações alérgicas sistêmicas leves (eritema cutâneo, edema, urticária, dificuldades respiratórias) e graves (reações anafiláticas). Cistos ovarianos, dor mamária, dor pélvica, OHSS, torção do ovário. **Interações medicamentosas:** Pergoveris® não deve ser administrado com outros medicamentos na mesma seringa, exceto com alfafolitropina. **Posologia:** O tratamento deve ser adaptado à resposta individual da paciente. Um regime posológico recomendado inicia-se com a administração diária de um frasco de Pergoveris®. Caso um aumento da dose de FSH seja considerado apropriado, o ajuste da dose deve ser efetuado preferencialmente após intervalos de 7-14 dias e com incrementos de 37,5 a 75 UI, utilizando um medicamento contendo alfafolitropina. Pode ser aceitável prolongar a duração da estimulação em qualquer um dos ciclos por até 5 semanas. Quando se obtém uma resposta ótima, deve ser administrada uma única injeção de 5.000 UI a 10.000 UI de hCG, 24 a 48 horas após a última injeção de Pergoveris®. Recomenda-se que a paciente tenha relações sexuais no dia da administração de hCG e no dia seguinte. Caso se obtenha uma resposta excessiva, o tratamento deve ser interrompido e hCG não deve ser administrado. O tratamento deve ser reiniciado no ciclo seguinte, com uma dose de FSH inferior à do ciclo anterior. **Cuidados de conservação:** Prazo de validade: 24 meses. Este medicamento é de uso único e deve ser utilizado imediatamente após abertura e reconstituição. Conservar em temperatura entre 15 e 30°C. Conservar na embalagem original para proteger da luz. VENDA SOB PRESCRIÇÃO MÉDICA. SAC Merck Serono: 0800-113320. Registro MS: 1.0089.0360.

Contraindicação: carcinoma do útero, ovário ou mama. **Interação medicamentosa**: Pergoveris® não deve ser administrado com outros medicamentos na mesma seringa, exceto com alfafolitropina.

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Destinado exclusivamente à classe médica. **Veiculado em junho de 2012.**

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Utilize preferencialmente o processador de texto Microsoft Word®. Os trabalhos devem ser digitados em fonte Times New Roman tamanho 12, espaço simples, alinhados à esquerda, iniciando cada seção em página nova, na seguinte ordem: página de rosto, resumo e palavras-chave, abstract e keywords, texto, agradecimentos, lista de referências, tabelas, legendas de figuras e figuras. Todas as páginas devem ser numeradas.

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2. Livro
Wolf DP, Quigley MM, eds. Human in vitro fertilization and embryo transfer. New York: Plenum Press; 1984.

3. Capítulo de livro
Simpson JL. Gonadal dysgenesial and sex abnormalities: phenotypic-karyotypic correlations. In: Vallet HL, Porter IH, eds. Genetic mechanisms of sexual development. New York: Academic Press; 1979. p. 365-77.

4. Artigo de revista eletrônica
Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [revista eletrônica]. 2002 Jun [citado 2002 ago 12];102(6):[aproximadamente 3 p.]. Disponível em: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm.

5. Artigo publicado na Internet:
Wantland DJ, Portillo CJ, Holzemer WL, Slaughter R, McGhee EM. The effectiveness of web-based vs. non-web-based interventions: a meta-analysis of behavioral change outcomes. J Med Internet Res. 2004;6(4):e40. Disponível em: http://www.jmir.org/2004/4/e40/. Acessado: 29/11/2004.

6. Site
OncoLink [site na Internet]. Philadelphia: University of Pennsylvania; c1994-2006. [atualizado 2004 set 24; citado 2006 mar 14]. Disponível em: http://cancer.med.upenn.edu/.

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5. The number of authors for each manuscript is limited to six. The co-authorship concept connotes substantial contribution in the creation and planning of the paper, analysis and interpretation of data not to mention the writing and critical revision of the text. Significant contributions given to the study which do not fit these criteria may be cited in the acknowledgements section.

6. Clinical trials articles should be registered in the Clinical Trials Registry validated by the criteria established by the World Health Organization and by the International Committee of Medical Journal Editors (for instance, www.actr.org.au, www.clinicaltrials.gov, www.ISRCTN.org, www.umin.ac.jp/ctr/index/htm and www.trialregister.nl). The study identification number shall be presented at the end of the abstract.

7. For texts accepted for publication, a statement signed by all authors shall be sent to the journal, including the following information: a) the manuscript is original; b) the manuscript has not been previously published nor submitted to any other journal, and will not be published in case it is accepted by JBRA Assisted Reproduction; c) all authors have actively taken part in the preparation of the study and have approved of the final version of the text; d) situations on potential conflict of interests (either financial or of any other nature) are being informed; e) an approval of the study by the Ethics Committee of the institution to which the paper is linked was obtained (for articles reporting experimental research data; f) an informed consent by the patients included in the study was obtained (when applicable) . All information on the approval of the study by the Ethics Committee and the possession of an informed consent should also be mentioned in the Methods section of the article.

8. Before the publication of accepted articles, the corresponding authors will receive the published article via e-mail attachment in a PDF archive for approval. At this point, corrections should be limited to typographic mistakes, without altering the content of the study. Authors should return approved papers by e-mail or fax 48 hours after receiving the message.

TYPES OF PUBLISHED ARTICLES

Original articles. Pieces of work resulting from scientific research presenting original data about experimental or observational aspects of medical, biological, biochemical and psychosocial character and including descriptive statistical analysis and/or inferences of own data. These articles have priority for publication. They must be composed of: title page, resumo e palavras-chave (in Portuguese)abstract and keywords, text (divided in Introduction, Methods, Results, Discussion or equivalent, Conclusion), acknowledgments (if applicable), references (40 at the most), tables (if available) figure legends (if available) and figures (if available).

Reviews. Papers whose aim is to summarize, analyze, evaluate or synthesize investigative papers already published in scientific journals. They must include a synthesis and critical analysis of the researched literature and cannot be confused with update articles. They must be composed of: title page, resumo e palavras-chave (in Portuguese), abstract and keywords, text, references, tables (if available) ,figure legends (if available) and figures (if available).

Update or opinion articles. Papers reporting usually current information on themes of interest to certain specialties (such as a new technique or method). They have different characteristics from reviews , since they do not display critical analysis of the literature. They must be composed of: title page, resumo e palavras-chave (in Portuguese), abstract and keywords, text, references, tables (if available) ,figure legends (if available) and figures (if available).

Case reports. Articles representing descriptive data of one or more cases, exploiting a method or problem through example(s). The selected cases should be of great interest, with unusual disease or evolution or submitted to unexpected or alternative treatments. They may involve humans or animals and should present the studied individual's characteristics (gender, age, etc.). They must be composed of: title page, resumo e palavras-chave (in Portuguese), abstract and keywords, text (divided in: Introduction, Case Description and Discussion or equivalent), references, figure legends (if available) and figures (if available).

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PREPARATION OF ORIGINAL PAPERS

Preferably use Microsoft Word® processor. Papers should be typed in Times New Roman font sized 12, single-spaced and aligned to the left. Every section should be started on a new page in the following order: title page, resumo e palavras-chave (in Portuguese), abstract and keywords, text, acknowledgements, references, tables, figure legends and figures. All of the pages should be numbered consecutively.

Abbreviations should be spelled out in the first mention in the text; and after the first appearance, only the abbreviation should be used. In the abstract, the use of abbreviations should be avoided.

Chemicals should be presented by their generic name. If relevant, commercial name of the substance and the manufacturer's name may be informed in parentheses.

The presentation of units of measurements should follow the International System (IS).
Genes of animals should be presented in italics with capital letter initials (example: Sox2); genes of human beings should also be presented in italics; however, with all capital letters (example: SOX2). Proteins should follow the same pattern: capital/small, without italics, though.

TITLE PAGE

The title page should carry the following information:
- Concise and comprehensive title, representing the content of the article, both in Portuguese and English
- Short running head (no more than 40 characters including letters and spaces)
- Authors' names
- Authors' institutional affiliation, showing department/unit, institution and geographic region
- Name of the institution where the work was carried
- Information about support given in the form of loan, equipment or drugs
- Congresses where the study was presented
- Name, mailing address, telephone and fax numbers, and e-mail address of the corresponding author

RESUMO AND ABSTRACT

All articles should present an abstract both in Portuguese and in English. Papers written in Spanish should present, besides their abstracts in the original language, one abstract in Portuguese and another one in English. The content of both texts should be identical, and should not exceed 250 words. For original articles, the abstract should be structured as follows: Objective, Methods, Results and Conclusion. For case reports, reviews and update articles, the abstract should not be structured. The use of abbreviations should be avoided in the abstract, and references should not be cited.
Right after the resumo/abstract/resumen, three to six keywords belonging to the list of Health Sciences Descriptors (http://decs.bvs.br) should be presented.

ACKNOWLEDGEMENTS

This part is dedicated to acknowledging the work of those who have helped intellectually, but whose contribution does not justify co-authorship or those people or institutions who have given material support.

REFERENCES

In the text, the citations will be identified by the author's last name in parentheses followed by the publication year. Examples: one author (Steptoe, 1978), two authors (Edwards & Steptoe, 1980), and more than two authors (Van Steirteghem et al., 1988).
The references should be presented in alphabetical order (each author's surname followed by his/her first two initials), and should not be numbered. Papers by the same author should be chronologically organized; papers by the same author in the same year should be identified with letters after each year (2000a, 2000b, etc.). The presentation of references will follow the format proposed in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (see examples below). All references cited in the list should be mentioned in the text and vice-versa.

1. Journal Article
Edwards RG, Steptoe PC, Purdy JM. Establishing full-term human pregnancies using cleaving embryos grown in vitro. Br J Obstet Gynaecol. 1980;87:737-56.

2. Book
Wolf DP, Quigley MM, eds. Human in vitro fertilization and embryo transfer. New York: Plenum Press; 1984.

3. Book Chapter
Simpson JL. Gonadal dysgenesial and sex abnormalities: phenotypic-karyotypic correlations. In: Vallet HL, Porter IH, eds. Genetic mechanisms of sexual development. New York: Academic Press; 1979. p. 365-77.

4. Electronic Journal Article
Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [electronic journal]. 2002 June [cited 2002 aug 12];102(6):[approximately 3 p.]. Available at: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm.

5. Article published in the Internet:
Wantland DJ, Portillo CJ, Holzemer WL, Slaughter R, McGhee EM. The effectiveness of web-based vs. non-web-based interventions: a meta-analysis of behavioral change outcomes. J Med Internet Res. 2004;6(4):e40. Available at: http://www.jmir.org/2004/4/e40/. Accessed: 29/11/2004.

6. Site
OncoLink [site in the Internet]. Philadelphia: University of Pennsylvania; c1994-2006. [updated 2004 Sept 24; cited 2006 March 14]. Available at: http://cancer.med.upenn.edu/.

7. Software
Smallwaters Corporation. Analysis of moment structures: AMOS [software]. Version 5.0.1. Chicago: Smallwaters; 2003.

TABLES AND FIGURES

Tables and figures (graphs, photographs, etc.) should be numbered in Arabic numerals according to the order in which they appear in the text and should have individual legends, presented at the end of the paper. Each table and figure should be submitted on a separate sheet of paper.
In the tables, use horizontal lines only, and each piece of information should be in an independent cell. Explanations about items in the tables should be presented in footnotes identified by the following symbols, in this sequence: *,†, ‡, §, ||,¶,**,††,‡‡.
Figures in general (graphs, photographs, etc.) will be published in black and white. Expenses due to the eventual reproduction of photographs in color will be the author's responsibility.
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Graphs should be two-dimensional only.
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5. Se limita a seis el número de autores de cada manuscrito. El concepto de coautoría implica contribución substancial en la concepción y planeamiento del trabajo, análisis e interpretación de los datos y redacción o revisión crítica del texto. Contribuciones significativas hechas al estudio, pero que no se cuadran en esos criterios, pueden ser descritas en la sección de agradecimientos.

6. Artículos de investigaciones clínicas (*clinical trials*) deben ser registrados en uno de los Registros de Ensayos Clínicos validados por los criterios establecidos por la Organización Mundial de la Salud y por el International Committee of Medical Journal Editors (por ejemplo, www.actr.org.au, www.clinicaltrials.gov, www.ISRCTN.org, www.umin.ac.jp/ctr/index/htm y www.trialregister.nl). El número de identificación del estudio deberá ser presentado al final del resumen.

7. Caso se acepte su trabajo para publicación, débese enviar al JBRA una declaración firmada por todos los autores, con la siguiente información: a) el manuscrito es original; b) el manuscrito no fue publicado ni sometido a otra revista, ni será, en el caso de su publicación por el JBRA Assisted Reproduction; c) todos los autores participaron activamente en la elaboración del estudio y aprobaron la versión final del texto; d) situaciones de potencial conflicto de interés (financiero o de otra naturaleza) serán informadas; e) se obtuvo aprobación del estudio por el comité de ética de la institución a la cual el trabajo está vinculado (para artículos que relatan datos de pesquisa experimental); f) se obtuvo consentimiento informado de los pacientes incluidos en el estudio (cuando se aplica). Se debe informar en la sección Métodos del artículo los datos sobre la aprobación del estudio por el comité de ética y la obtención de consentimiento informado.

8. Antes de la publicación de los artículos aprobados, los autores correspondientes recibirán, por e-mail, en documento PDF, el artículo listo para publicación, para aprobación. En esta etapa, las correcciones deben limitarse a errores tipográficos, sin cambios de contenido del estudio. Los autores deberán devolver las pruebas aprobadas por e-mail o fax antes de 48 horas después de haberlo recibido.

TIPOS DE ARTÍCULOS PUBLICADOS

Artículos originales. Trabajos resultantes de pesquisa científica que presentan datos originales sobre aspectos experimentales u observacionales de carácter médico, biológico, bioquímico y psicosocial e incluyen análisis estadística descriptiva y/o inferencias de datos propios. Estos artículos tienen prioridad para publicación. Deben contener: hoja frontal, resumen y palabras-llave, *abstract* y *keywords*, texto (dividido en las secciones Introducción, Métodos, Resultados, Discusión o equivalentes, Conclusiones), agradecimientos (si se aplica), listado de referencias (máximo de 40), tablas (si hay), notas al pié de imágenes (si hay) e imágenes (si hay).
Artículos de revisión. Trabajos que tienen por objetivo resumir, analizar, evaluar o sintetizar trabajos de investigación ya publicados en revistas científicas. Deben incluir síntesis y análisis crítica de la literatura levantada y no ser confundidos con artículos de actualización. Deben contener: hoja frontal, resumen y palabras-llave, *abstract* y *keywords,* texto, listado de referencias, tablas (si hay), notas al pié de imágenes (si hay) e imágenes (si hay).
Artículos de actualización u opinión. Trabajos que reportan informaciones generalmente actuales sobre tema de interés para determinadas especialidades (por ejemplo, una nueva técnica o método). Tienen características diferentes de un artículo de revisión, pues no presenta análisis crítica de la literatura. Deben contener: hoja frontal, resumen y palabras-llave, *abstract* y *keywords*, texto, listado de referencias, tablas (si hay), notas al pié de imágenes (si hay) e imágenes (si hay).
Relatos de caso. Artículos que representan datos descriptivos de uno o más casos, explorando un método o problema a través de ejemplo(s). Los casos elegidos deben ser de gran interés, con enfermedad o evolución anormal o sometidos a tratamientos inusitados o alternativos. Pueden involucrar humanos o animales y deben presentar las características del individuo en estudio (sexo, edad, etc.). Deben contener: hoja frontal, resumen y palabras-llave, *abstract* y *keywords*, texto (dividido en las sesiones Introducción, Descripción del caso y Discusión o equivalentes), listado de referencias, notas al pié de imágenes (si hay) e imágenes (si hay).
Cartas al lector. Con gusto recibiremos cartas al editor comentando, discutiendo o criticando los artículos publicados en el JBRA Assisted Reproduction; estas serán publicadas desde que el Consejo Editorial las apruebe. Deben contener: título, nombre del autor, identificación de la publicación que se comenta y listado de referencias (si hay). Recomendase un máximo de 500 palabras, incluyendo referencias. Siempre que posible, se publicará una respuesta de los autores junto a la carta.

PREPARO DE LOS ORIGINALES

Utilice preferentemente Microsoft Word®. Los trabajos deben ser tecleados en Times New Roman tamaño 12, espacio sencillo, alineados a la izquierda, iniciando cada sección en página nueva, en el siguiente orden: hoja frontal, resumen y palabras-llave, *abstract* y *keywords*, texto, agradecimientos, listado de referencias, tablas, notas al pié de imágenes e imágenes. Todas las páginas deben de ser numeradas.
Siglas deben ser definidas por extenso en la primera ocurrencia en el texto; después de la primera ocurrencia, solamente la sigla deberá ser utilizada. En el resumen, el uso de siglas debe ser evitado.

Substancias deben ser presentadas utilizando su nombre genérico. Si es relevante, el nombre comercial de la substancia y el fabricante pueden ser informados entre paréntesis.
La presentación de unidades de medida debe seguir el sistema internacional (SI).
Genes de animales deben ser presentados en itálico con inicial mayúscula (ejemplo: *Sox2*); genes de seres humanos también deben ser presentados en itálico, pero con todas las letras mayúsculas (ejemplo: *SOX2*). Proteínas deben seguir el mismo patrón de mayúsculas / minúsculas, pero sin itálico.

HOJA FRONTAL

La hoja frontal debe contener:
- Título conciso y explicativo, representando el contenido del trabajo, en portugués e inglés. (no seria: portugués, inglés y español ¿)
- Título resumido (máximo de 40 caracteres).
- Nombres de los autores.
- Afiliación de los autores, indicando departamento/unidad, institución y región geográfica.
- Nombre de la institución donde el trabajo fue ejecutado.
- Informaciones sobre ayudas recibidas bajo la forma de financiamiento, equipamientos o medicamentos.
- Congresos donde el estudio fue presentado.
- Nombre, dirección, teléfono, fax y e-mail del autor correspondiente.

RESUMEN Y *ABSTRACT*

Todos los trabajos deben presentar un resumen en portugués y un *abstract* en inglés. Trabajos escritos en español deben presentar, además del resumen en su idioma original, también un resumen en portugués y un *abstract* en inglés. El contenido de los textos debe ser idéntico, y no debe sobrepasar 250 palabras. Para artículos originales, el resumen debe ser estructurado como detallamos a continuación: Objetivo, Métodos, Resultados y Conclusiones. Para relatos de caso, artículos de revisión y artículos de actualización, el resumen no debe ser estructurado. Débese evitar el uso de abreviaciones en el resumen, y no deben ser mencionadas referencias.
Luego después del *resumo*/*abstract*/resumen, deberán ser presentadas de tres a seis palabras-llave que sean integrantes de la lista de Descriptores en Ciencias de la Salud (http://decs.bvs.br).

AGRADECIMIENTOS

Esta sección es dedicada a reconocer el trabajo de personas que hayan colaborado intelectualmente, pero cuya contribución no justifica coautoría, o personas o instituciones que hayan dado apoyo material.

REFERENCIAS

En el texto, las citaciones serán identificadas entre paréntesis, por el apellido del autor seguido del año de publicación. Ejemplos: un autor (Steptoe, 1978), dos autores (Edwards & Steptoe, 1980), más de dos autores (Van Steirteghem et al., 1988).
El listado de referencias debe ser presentado en orden alfabética (último apellido de cada autor seguido de las dos primeras iniciales), y no debe ser numerada. Trabajos del mismo autor deben ser ordenados cronológicamente; trabajos del mismo autor y año deben ser identificados con letras después el año (2000a, 2000b, etc.). La presentación de las referencias seguirá los modelos propuestos en los *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* (ver ejemplos a continuación). Todas las referencias citadas en la lista deben ser mencionadas en el texto y viceversa.

1. Artículo de periódico
Edwards RG, Steptoe PC, Purdy JM. Establishing full-term human pregnancies using cleaving embryos grown in vitro. Br J Obstet Gynaecol. 1980;87:737-56.

2. Libro
Wolf DP, Quigley MM, eds. Human in vitro fertilization and embryo transfer. New York: Plenum Press; 1984.

3. Capítulo de libro
Simpson JL. Gonadal dysgenesial and sex abnormalities: phenotypic-karyotypic correlations. In: Vallet HL, Porter IH, eds. Genetic mechanisms of sexual development. New York: Academic Press; 1979. p. 365-77.

4. Artículo de revista electrónica
Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs [revista electrónica]. 2002 Jun [citado 2002 ago 12];102(6):[aproximadamente 3 p.]. Disponíble en: http://www.nursingworld.org/AJN/2002/june/Wawatch.htm.

5. Artículo publicado en Internet:
Wantland DJ, Portillo CJ, Holzemer WL, Slaughter R, McGhee EM. The effectiveness of web-based vs. non-web-based interventions: a meta-analysis of behavioral change outcomes. J Med Internet Res. 2004;6(4):e40. Disponible en: http://www.jmir.org/2004/4/e40/. Acceso en: 29/11/2004.

6. Sitio web
OncoLink [sitio web en Internet]. Philadelphia: University of Pennsylvania; c1994-2006. [actualizado 2004 set 24; citado 2006 mar 14]. Disponible en: http://cancer.med.upenn.edu/.

7. Software
Smallwaters Corporation. Analysis of moment structures: AMOS [software]. Versión 5.0.1. Chicago: Smallwaters; 2003.

Tablas y figuras
Tablas y figuras (gráficos, fotografías, etc.) deben ser numeradas en arábigo conforme el orden que aparezca en el texto y deben tener explicaciones individuales, presentadas al final del trabajo. Cada tabla y figura debe ser sometida en hoja separada.
En las tablas, deben ser utilizadas solamente lineas horizontales, y cada dato deberá de tener una celda independiente. Explicaciones sobre ítems de las tablas deben ser presentadas en notas de rodapié identificadas por los siguientes símbolos, en esa secuencia: *,†, ‡, §, ||,¶,**,††,‡‡.
Figuras en general (gráficos, fotografías, etc.) serán publicadas en negro y blanco. Gastos con eventual reproducción de fotografías en color serán de responsabilidad del autor.
Figuras pueden ser sometidas electrónicamente, en las extensiones .jpg, .gif ou .tif, con resolución mínima de 300 dpi (para hacer posible una impresión nítida), o por correo (ver instrucciones de envío más adelante). Todas las figuras enviadas por correo deben ser identificadas en el anverso con el uso de etiqueta que contenga el nombre del primero autor, el número de la figura y una flecha que indique el lado para arriba.
No se aceptan fotografías escaneados; fotografías en papel deben ser enviadas por correo. Fotografías de pacientes no deben permitir su identificación.
Gráficos deben ser presentados solamente en dos dimensiones.
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Sumário

Editorial

Meet the RLA 2010

This edition of JBRA presents part of the twenty first edition of the Latin American Registry of Assisted Reproductive Technology (RLA). One hundred and forty centers from thirteen countries reported data involving ART procedures performed from January to December 2010. These data also represent the first multinational registry of published in a case-by-case report by RLA.

Last year we began this tradition of presenting the main data in the official journal of REDLARA. It was a wise decision that brings all the centers to be aware of the strength of RLA, and the possibilities to research we have. At the same time, it enables others groups that still are not within RED to understand the importance in joining this Registry.

Reports from 1990 through 1998 are available as printed copies; from 1999 through 2009 are available as PDF files to be downloaded from the web page of Red Latino Americana de Reproducción Asistida (REDLARA) at www.redlara.com. As always, data from 2011 will also be there and with a free-access.

We wish a Happy 2013 to all in LA,

May the New Year come with Justice, Peace, Health , Friendship and Love to all of us.

Maria do Carmo B Souza
Paulo F Taitson
Editors

Assisted reproductive technologies in Latin America: The Latin American Registry, 2010

Latin American Registry, 2010

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ABSTRACT

Background: This 21st report represents the results of ART procedures performed during 2010 by 140 centers from 13 countries in Latin America. Furthermore, this is the first time, a multinational registry is performed on a case-by-case bases.

Methods: All centers reported their ART procedures electronically and their data was accepted after consistency checks were performed and the institution, certified by an accreditation team. A total of 37,853 initiated ART cycles included 3,731 IVF cycles; 22,637 ICSI cycles; 5,157 FET and 6,320 OD embryo transfers, plus 8 cases of GIFT, which are not described in this report.

Results: The majority (39%) of ET in IVF/ICSI cycles were performed in women age 35-39 years. The delivery rate (DR) per OPU in ICSI and IVF cycles were 28.8% and 30.9%, respectively. The multiple delivery rates in IVF/ICSI cycles were 23.9% (22.1% twins and 1.8% triples). When ≥ 2 embryos were transferred, neither the CPR nor the proportion of twins increased significantly. However, the proportion of triplet increased significantly when ≥3 embryos were transferred. In OD cycles, twin and triplet deliveries were 25.4% and 2.2%, respectively. In FET cycles, twin and triplet deliveries were 17.6% and 1.5%, respectively. Multiple deliveries were associated with a significant increase in preterm delivery and perinatal mortality. The CPR was 18% with eSET and 43% with eDET. In women aged ≤34 years, CPR with eSET was 30% and 52% with eDET. In OD cycles, the CPR with eSET was 29%, and 52% with eDET.

Conclusions: Overall, delivery rates are comparable to most developed countries in the world. However, REDLARA has to enforce the reduction in the number of embryos transferred in IVF/ICSI and OD cycles, in order to prevent multiple births and decrease the corresponding perinatal complications.

RESUMO

Objetivo: Este 21º relato representa os resultados de procedimentos de RA realizados em 2010 por 140 centros de 13 países na América Latina. Pela primeira vez, um registro multinacional é realizado caso-a-caso.

Métodos: Todos os centros registraram seus procedimentos eletronicamente e os dados foram aceitos após checagem de consistência, cada instituição certificada por acreditadores. Do total de 37,853 ciclos iniciados de RA , foram 3,731 ciclos de FIV, 22,637de ICSI, 5,157 transferências de embriões congelados e 6,320 transferências em ciclos de Ovo-Doação(OD), além de 8 casos de GIFT.

Resultados: A maioria (39%) das TE nos ciclos de FIV/ICSI foram realizadas em mulheres de 35-39 anos. A taxa de partos por aspiração (OPU) nos ciclos de ICSI e FIV foi de 28.8% e 30.9%, respectivamente. Os nascimentos múltiplos em FIV/ICSI foram de 23.9% (22.1% duplos e 1.8% triplos). Quando transferidos ≥ 2 embriões, nem a taxa de gestação clínica (CPR) ou a proporção de duplos aumentou significativamente. Todavia, a proporção de triplos aumentou significativamente quando ≥3 embriões transferidos. Nos ciclos de OD, nascimentos duplos e triplos foram 25.4% e 2.2%, respectivamente. Nas transferências de embriões congelados (FET), relatos de duplos e triplos foram 17.6% e 1.5%. Partos múltiplos foram associados a aumento significativo de nascimentos pré-termo e mortalidade perinatal. A taxa de gravidez clínica foi de 18% com a transferência seletiva de 01 embrião (eSET) e 43% na dupla (eDET). Nas mulheres ≤34 anos, a CPR com eSET foi 30% e 52% com eDET. Nos ciclos de OD, estas taxas de gravidez clínica foram de 29% com e-SET , e 52% com eDET.

Conclusões: Em geral, as taxas de nascimentos são comparáveis aos países mais desenvolvidos. Todavia, a REDE deve reforçar a necessidade de transferir menor número de embriões nos ciclos de RA, a fim de prevenir nascimentos múltiplos e diminuir as consequentes complicações perinatais.

INTRODUCTION

This report corresponds to the twenty first edition of the Latin American Registry of Assisted Reproductive Technology (RLA). Reports from 1990 through 1998 are available as printed copies; from 1999 through 2009 are available as PDF files to be downloaded from the web page of Red Latino Americana de Reproducción Asistida (REDLARA) at *www.redlara.com .*

The main objectives of RLA include: to register the number and characteristics of assisted reproductive techniques (ART) procedures performed in Latin America (LA); to register their outcomes, including controlled ovarian hyperstimulation, pregnancies and perinatal outcomes; to register the complications associated with ART procedures and the frequency and characteristics of congenital malformations; and to evaluate trends in multiple pregnancy and delivery, preterm birth, perinatal mortality and others.

MATERIAL AND METHODS

Data collection:One hundred and forty centers from thirteen countries reported data involving ART procedures performed from January to December 2010. ART procedures included in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), gamete intrafallopian transfer and similar techniques (GIFT), oocyte donation (OD), frozen/thawed embryo transfer (FET), prenatal genetic diagnosis and screening (PGD), and assisted hatching (AH). The main methodological

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characteristic of the current report is that for the first time the data of each treatment cycle was recorded independently, instead of a summary of cases, as it was reported until now, thus, this is the first multinational case by case registry. This way of collecting data has two main advantages. First, it reduced the work of those responsible for reporting data from each center, and second, a case-by-case multinational register, allows for more sophisticated biostatistics and epidemiological analysis. As in the past, each center provided their data on voluntary bases. Furthermore, before the data is accepted, each center has to undergo periodical accreditation visits, where a clinician and an embryologist from a different country, evaluate the professionals, the infrastructure and equipment of the center, together with their quality control programs and their consent forms. Furthermore, the data provided by the center to the RLA is carefully and thoroughly analyzed. Each center has an individual password in order to access the RLA-server, where the center can upload the data of each cycle. The data can be uploaded either by filling a specially designed page each time a new case is performed, or by uploading an Excel file whenever possible. The central office of RLA gains immediately access to the data, and checks for inconsistencies and resolve any further question with the center.

Data validation: The data provided by each centers is checked for inconsistency by the program; and any error is discussed with the center, and the data is rectified if necessary. The truthfulness of the data reported by each institution is checked as part of the periodic accreditation process conducted by a biologist and a clinician from different countries.

Limitations of data collection: Some centers do not have complete follow-up of each pregnancy. This is especially so in institutions not associated with obstetric units. Our calculations are that missing data is in the order of 5% of pregnancies. From a different perspective, not all centers performing ART belong to REDLARA. We estimate that the RLA registers more than 80% of ART procedures performed in Latin America.

Statistical analysis: Chi square test was used to analyze independence of categorical variables. When multiple variable analyses were performed, i.e. logistic regression or lineal regression, the dependent variables were considered significant if the confidence interval of the odd ratio (OR), or regression coefficient did not cross the non-significant value. A p-value <0.05 was considered as statistically significant. When comparing two outcomes, the risk ratio (RR), and its corresponding 95% confidence interval (95%CI) are presented.

RESULTS

Participating centers: One hundred and forty (140) centers belonging to 13 countries reported their ART procedures performed during 2010 (Annex I). These represent five more centers than those reporting in 2009. The new institutions belong to Argentina, Brazil, Ecuador and Mexico.

Size of participating institutions: The number of initiated cycles corresponds to the sum of initiated cycles of IVF/ICSI/GIFT, and embryo transfers, both FET and OD. The average number of initiated cycles registered by the clinics was 268. More than half of the centers registered less than 150 cycles, whereas only three centers registered more than one thousand cycles. The distribution of the clinics according to the number of cycles registered is as follows: 27%, ≤ 100 cycles; 36% between 100 and 250 cycles; 24% between 251 and 500 cycles; 11% between 500 and 1,000 cycles; and only 2%, ≥ 1,000 cycles.

ART procedure and access: The total number of ART procedures registered by the RLA was 37,853. Of these, 47% (n=17,673) were reported by Brazil; 22% (n=8,336) by Argentina; and 12% (n=4,433) by Mexico (table 1). Out of 26,3736 initiated autologous--cycles, 3,731 (14%) corresponded to IVF, and 22,637 (86%) to ICSI cycles. One hundred and twenty six clinics registered 5,157 FET cycles. And one 127 clinics reported 6,320 OD cycles. In 56% of TABELA these cycles, the eggs were donated from pure donors, i.e. women that underwent controlled ovarian hyperstimulation (COS) and oocyte pick up with the only purpose of donating their oocytes; and 44% were egg-sharing, i.e. patients undergoing COS and oocyte pick-up, for an autologous treatment and simultaneously donated a proportion of their gametes. Table 1 also shows access to ART procedures in LA, expressed as the total number of initiated cycles per million women aged 15 to 45 years.

Table 1. RT procedures and access in 2010

Country	Number of clinics	Assisted reproductive techniques					Access (***)
		IVF(*)	ICSI(*)	FET	OD(**)	Total	
Argentina	22	810	4,462	1,231	1,832	8,336	921.2
Brazil	56	542	12,913	2,515	1,703	17,673	372.2
Chile	7	143	1,088	255	159	1,652	426.4
Colombia	8	358	420	127	284	1,189	112.5
Ecuador	5	61	248	79	104	492	139.2
Guatemala	1	42	43	12	17	114	35.9
Mexico	25	828	1,991	637	977	4,433	160.2
Nicaragua	1	66	25	0	5	96	66.1
Panama	2	38	163	27	50	278	354.8
Peru	4	436	713	104	805	2,058	289.6
Dominican R.	1	55	15	2	5	77	34.2
Uruguay	2	32	226	46	48	352	501.8
Venezuela	6	320	330	122	331	1,103	168.7
Total	140	3,731	22,637	5,157	6,320	37,853	304.8

include 7 cycles of GIFT/TOMI in Chile and 1 in Argentina
(*) initiated cycles; (**) includes the transfer of fresh and frozen embryos ; (***) number of cycles/million of women 15-45 years

Pregnancies and deliveries: Tables 2a and 2b show the clinical pregnancy rate (CPR) and delivery rate (DR) of ART procedures performed in 2010. In the case of ICSI cycles, the overall CPR and DR per oocyte pick-up were 28.8% and 22.1%, respectively. These rates were marginally better in the case of IVF cycles: 30.97% and 25.63%, respectively (table 2a).

Table 2a. Clinical pregnancy rate and delivery rate IVF/ICSI, 2010

ART procedure	Oocyte pick up (OPU)	Clinical pregnancy rate per OPU	Delivery rate per OPU
ICSI	21,763	28.8%	23.1%
IVF	3,526	30.9%	25.6%

In both instances, the difference reached statistical significance, however the lack of random distribution of subject in each treatment category, does not allow for conclusions to be obtained. The RR for clinical pregnancy per OPU was 1.07 (95% CI 1.01-1.13); and for delivery rate per OPU was 1.10 (95% CI 1.03-1-17). In OD cycles, the clinical pregnancy rate and delivery rate were 47.0% and 38.6%, respectively. In FET cycles, the clinical pregnancy rate and delivery rate were 29.3% and 22.5%, respectively. These rates were higher in FET with OD: 32.4% and 24.7%, respectively (table 2b).

Table 2b. Clinical pregnancy rate and delivery rate OD, FET, FET(OD); 2010

ART procedure	Embryo transfer (ET)	Clinical pregnancy rate per ET	Delivery rate per ET
OD	4,763	47.0%	38.6%
FET	5,157	29.3%	22.5%
OD (FET)	1,557	32.4%	24.7%

Age of women undergoing ART procedures: The mean age of women undergoing IVF/ICSI/GIFT was 36 years (SD 4.7). Figure 1 shows the age distribution of women undergoing IVF/ICSI/GIFT. 37% of initiated cycles were in women aged ≤34 years; 39% in women aged 35 through 39 years; 16% in women aged 40 through 42 years; and 7% in women aged ≥43 years. This accounts for 23% of women ≥ 40 years.

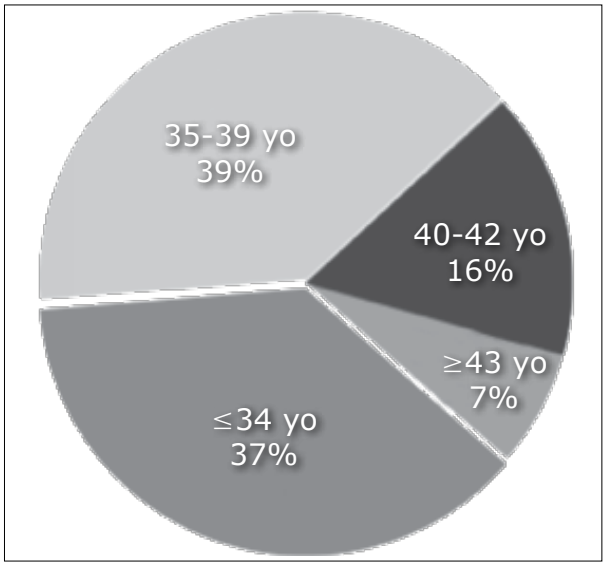

Figure 1. Age distribution of women undergoing IVF/ICSI, 2010

As expected, the delivery rate per embryo transfer was significantly influenced by the age of the female partner. We analyzed DR/ET in the following age categories: women aged ≤34 years; women aged 35 through 39 years; women aged 40 through 42 years; and women aged ≥43 years. DR decreased in all age groups, from 35.5% in the younger women to 8.5% in the oldest group (p<0.001). The eldest women that deliver a baby with autologous oocytes was 49 years at the time of the procedure (Fig. 2a and 2b).

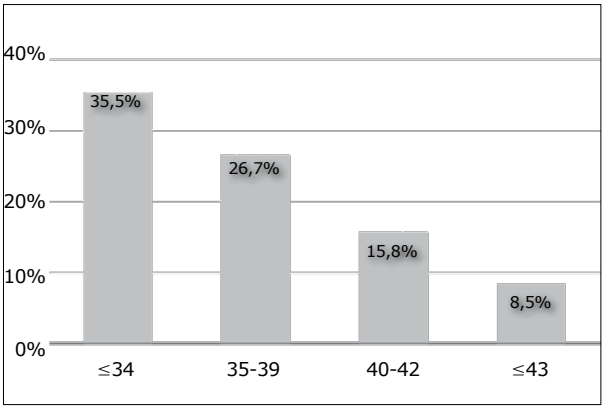

Figure 2. Delivery rate per embryo transfer in different age categories of women undergoing IVF/ICSI, 2010

In cases of OD, DR/ET in oocyte recipients aged ≤34 years (n=523 ET) was 40.2%. In women aged 35 through 42 (n=2,155 ET), was 40.0%; and 37.1% (ET=2672), in women ≥43 years. These differences did not reach mathematical significance.

In cases of FET with OD, women aged ≤34 years had a delivery rate per ET of 28.8%; compared with 23.8% in women aged 35 to 39, and 22.4% in women ≥43 years (p=0.321).

NUMBER OF EMBRYOS TRANSFERRED AND MULTIPLE DELIVERIES

Autologous reproduction: Table 3 shows the outcome of 21, 526 IVF/ICSI embryo transfers. The mean number of embryos transferred was 2.4, identical to the previous report. In 45.2% of cases, two embryos were transferred, and the transfer of 3 and ≥4 embryos represented 34.6% and 7.2% respectively. The overall frequency of multiple delivery was 23.9%, of which, 22.1% were twins and 1.8% triplets and higher, compared with 21.5% and 2.1% respectively in 2009.

The risk of twin delivery increased with the transfer of ≥2 embryos. The risk of twin deliveries was 21.8% when two embryos were transferred, and the transfer of three embryos increased the risk to 1.1 (95%CI 1.0-1.3). The transfer of ≥ four embryos also increased the risk to 1.1 (95% CI 0.9-1.3). The risk of triplet-and-higher delivery also increased significantly with the number of embryos transferred. When only one embryo was transferred, there were no triplets or higher order deliveries; when two embryos were transferred the rate of triplets-and-higher delivery was 0.5%; when three embryos were transferred, the rate of triplets-and-higher delivery increased to 3.3%; with a further increase to 3.9% (p<0.001), when ≥ 4 embryos were transferred.

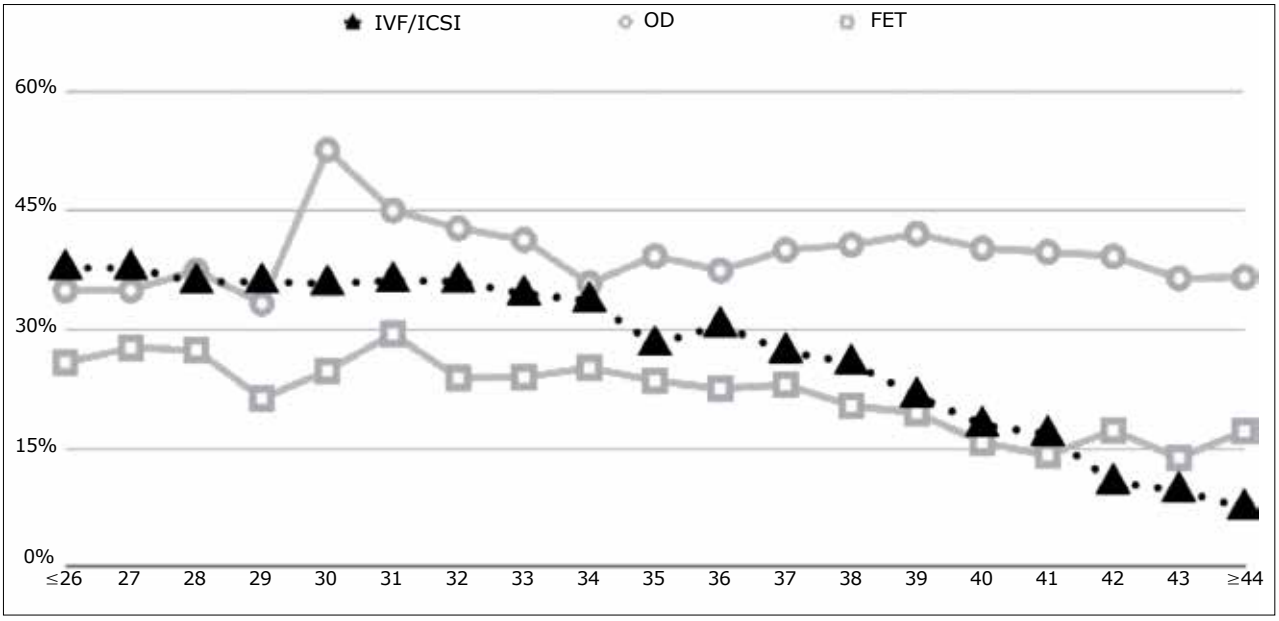

Figure 2b. Delivery rate per embryo transfer according to age of woman, 2010

Table 3. Clinical pregnancy rate, delivery rate and gestational order according to the number of embryos transferred, IVF/ICSI 2010

Number of transferred embryos	Total ET		CPR/ET	Deliveries			
	number	%		Total (number)	Singleton	Twin	≥Triplets
1	2,795	13.0%	15.3%	314	97.0%	3.0%	0.0%
2	9,726	45.2%	36.5%	2905	77.7%	21.8%	0.5%
3	7,452	34.6%	37.9%	2281	72.0%	24.8%	3.3%
≥4	1,553	7.2%	36.1%	434	72.3%	23.9%	3.9%
Total	21,526	100.0%	34.2%	5,934	76.1%	22.1%	1.8%

ET= embryo transfers
CPR=clinical pregnancy rate

HETEROLOGOUS REPRODUCTION (OD)

Table 4 shows the outcome of 4,763 OD cycles. The mean number of embryos transferred was 2.4, identical to the previous report. In the majority of cases, two embryos were transferred (58%), and the transfer of ≥3-embryos represented 38% of the cases. The overall frequency of multiple birth was 27.6%; 25.4% were twin delivery, and 2.2% triplets and higher, compared with 23% and 2% respectively in 2009. When compared with the transfer of two embryos, the transfer of three or four embryos increased the relative risk for twins by 1.2 (95%CI 1.00-1.40); and by 1.1 (95%CI 0.8-1.6) respectively. However, the risk of triplet and higher order delivery increased significantly with the transfer of more than two embryos. The rate of triplets increased from nil when one embryo was transferred to 0.5%, 4.8% y 6.8% (p<0.001), when 2, 3 and ≥4 embryos were transferred.

FROZEN/THAWED EMBRYO TRANSFERS(FET)

Table 5 shows 5,157 cases of FET. The mean number of embryos transferred was also 2.4. Two embryos were transferred in 46% of cases. The rate of multiple births was 19.5%; 17.6% were twin delivery (13.1% in 2009); and 1.5% triplets-and-higher delivery (2.7% in 2009). The increase in the rate of multiple-delivery was less profound than in the previous techniques. The rate of triplets-and-higher delivery when one, two,

Table 4. Clinical pregnancy rate, delivery rate and gestational order according to the number of embryos transferred, OD 2010

Number of transferred embryos	Total ET		CPR/ET	Deliveries			
	number	%		Total (number)	Singleton	Twin	≥Triplets
1	164	3.4%	25.0%	33	100.0%	0.0%	0.0%
2	2,779	58.3%	48.5%	1,113	75.2%	24.3%	0.5%
3	1,606	33.7%	47.0%	620	66.6%	28.5%	4.8%
≥4	214	4.5%	44.9%	74	66.2%	27.0%	6.8%
Total	4,763	100.0%	47.0%	1,840	72.4%	25.4%	2.2%

ET= embryo transfers
CPR=clinical pregnancy rate

Table 5. Clinical pregnancy rate, delivery rate and gestational order according to the number of embryos transferred, FET 2010

Number of transferred embryos	Total ET	CPR/ET	Deliveries			
			Total (number)	Singleton	Twin	≥Triplets
1	692	17.9%	90	100.0%	0.0%	0.0%
2	2,368	31.3%	559	81.2%	17.5%	1.3%
3	1,775	30.3%	424	77.4%	20.8%	1.9%
≥4	322	33.5%	86	76.7%	20.9%	2.3%
Total	5,157	29.3%	1,159	80.9%	17.6%	1.5%

ET= embryo transfers
CPR = clinical pregnancy rate

three and ≥four embryos were transferred was 0.0%, 1.3%, 1.9% and 2.3% respectively (p<0.001). Table 6 shows 1,557 cases of FET with donated oocytes. The mean number of embryos transferred was 2.4. Multiple-delivery rate was 23.2%: 21.8% twins and 1.4% triplets. The risk of multiple-pregnancy also increased with the number of transferred embryos, however, this was less accentuated than in the case of fresh transfers (p=0.557).

ELECTIVE SINGE AND DUAL EMBRYO TRANSFER (ESET & EDET)

Elective single embryo transfer (eSET) and elective dual embryo transfer (eDET) accounted for 3.8% (n=810) and 23.6% (n=5,081) respectively, of embryo transfers performed in 2010. This represents an important increase to the previous register, when they represented only 1.0% and 14.2% respectively. The CPR/ET was 18% with eSET and 43% with eDET. Elective SET and DET had higher CPR than non-elective transfers (table 3). The CPR/ET was higher in younger women. In women aged ≤34 years the CPR of eSET and eDET were 30% and 52%, respectively..In OD cycles, the CPR/ET, with eSET was 29% (OR 0.95 95%CI 0.5-1.8), and 52% with eDET (OR 1.2 95%CI 1.0-1.4).

Perinatal outcome: The duration of gestation was reported in 7,126 deliveries (5,281 singletons, 1,704 twins, and 141 ≥triplets). Among singletons, the mean gestational age at delivery was 38 weeks amenorrhea (WA); among twin it was 35 WA; and among ≥triplets it was 32 WA.The risk of preterm birth, (before completing 37 WA), among singletons was 17% (n=898). The relative risk of preterm birth among twin deliveries was 3.9 (95% CI 3.7-4.2), and among triplets-and-higher was 5.7 (95% CI 5.3-6.1). The risk of very-preterm birth among singletons was 3.6% (n=190); among twins it was 13.2 % (n=225) and among ≥triplets it was 51.8% (n=73) (p<0.0001). We explored whether embryo cryopreservation affected neonatal weight.

For this, we compared the neonatal weight between singletons born after IVF/ICSI with those born after FET, both with autologous oocytes. The mean gestational age of singletons after FET differs considerably from that of fresh embryo transfers, 37.9 and 37.6 WA respectively (p=0.001). Although the difference reached statistical significance, it has no clinical significance, since it only few days. We performed a multivariate lineal regression to determine the effect on neonatal weight. After correcting for gestational age, neonatal weight was not affected by the type of embryo (FET or fresh IVF/ICSI), (coef. -38.8; 95% CI -130.9-53.2, p=0.408). Table 7 shows that perinatal mortality increased significantly with gestational order. Singletons had a perinatal mortality of 6.7 per thousand, compared with 18.5 per thousand in twins and 19.1 per thousands in ≥ triplets (p<0.0001). The RR of perinatal mortality among twins was 2.8 (95% CI 1.9-4.0), and among triplets-and-higher was 2.9 (95% CI 1.4-6.1).

PRE IMPLANTATION GENETIC DIAGNOSIS (PGD)

Clinics located in Argentina, Brazil, Chile, Colombia, Ecuador, México, Panama, Peru, Uruguay and Venezuela reported cycles where PGD and genetic screening (PGS) were performed. Overall, 740 cycles were initiated, and only 480 embryo transfer cycles. The major contributors to 480 transfer cycles were Brazil (55%), Peru (27%) and Argentina (11%). The mean age of women undergoing embryo transfer after PGD was 37 years (21 to 47 years). A mean of six embryos were analyzed in each cycle, and a mean of two of each were reported as normal. 152 clinical pregnancies were registered and 117 deliveries (92 singletons, 24 twins y 1 quadruplet). A total of 144 babies were born after PGD, none of which were reported with any birth defect. After correcting for age of woman, we found no significant effect of PGD on the odds of pregnancy, OR 0.89 (95% CI 0.78-1.02).

Table 6. Clinical pregnancy rate, delivery rate and gestational order according to the number of embryos transferred, FET(OD) 2010

Number of transferred embryos	Total ET		CPR/ET	Deliveries			
	Number	%		Total (number)	Singleton	Twin	≥Triplets
1	141	9.1%	22.7%	22	95.5%	4.5%	0.0%
2	701	45.0%	31.8%	158	75.3%	23.4%	1.3%
3	629	40.4%	34.3%	160	76.9%	21.3%	1.9%
≥4	86	5.5%	39.5%	18	66.7%	33.3%	0.0%
Total	1,557	100.0%	32.4%	358	76.8%	21.8%	1.4%

ET= embryo transfers
CPR = clinical pregnancy rate

Table 7. Perinatal mortality according to gestational order, 2010

	Singleton			Twin			≥Triplets		
	LB	SB	ND	LB	SB	ND	LB	SB	ND
IVF/ICSI	4,093	12	17	2,375	9	38	274	4	1
FET	815	2	1	412	0	3	0	0	0
OD	1,072	1	8	937	5	17	124	0	1
FET(OD)	271	0	1	153	0	1	13	0	2
Total	6,251	15	27	3,877	14	59	411	4	4
Perinatal mortality	6.7 per thousand				18.5 per thousand			19.1 per thousand	

LB= live borns; SB= still borns; ND=neonatal death

MISCARRIAGE RATE

The miscarriage rate in women undergoing IVF/ICSI was 17%, which increased significantly as women age. 13% in women aged ≤34; 18% in women aged 35 through 39 years; 32% in women aged 40 through 42 and 39% in women aged 43 years (p<0.001). The miscarriage rate in women undergoing FET was 22%, and there were no significant differences according to age categories. 21% in women aged ≤34; 23%; in women aged 35 through 39 years; 29% in women aged 40-42 years and 26% in women aged ≥43 (p=0.447). The miscarriage rate in women undergoing OD was 17%, and there were no significant differences according to age categories. 12% in women aged ≤34 years; 17% in women aged 35 through 39 years; 16% in women aged 40-42 and 18% in women aged ≥43 years (p=0.341).

Within each age category, the miscarriage rate did not differ significantly in women having PGD, however, the characteristic of women in each category might be different and therefore, not comparable.

ASSISTED HATCHING (AH)

Clinics in Argentina, Brazil, Mexico, Panama, Peru and Uruguay reported AH in 3,556 embryo transfer cycles, generating 1,162 clinical pregnancies and 892 deliveries (25.1%). Of these, 668 were reported as singletons, 216 twins and 8 triplets. The mean age of the women undergoing assisted hatching was 35 years. After correcting for age, the OR for delivery rate after embryo transfer for AH compared with regular ICSI (no AH), was 1.1 (95% CI 0.98-1.16).

INTRAUTERINE INSEMINATION

Table 8 shows the results of IUI cycles, either with semen of the husband (IIU-H) or donor (IIU-D), reported by clinics located in eight different countries. Forty nine clinics reported 4,874 cycles of IIU-H. The delivery rate per cycles was 15%. The multiple-delivery rate was 14%: 12% twin and 2% triplets-and-higher. Thirty seven clinics reported 876 cycles of IIU-D. The delivery rate per cycles was higher, 20%. The multiple-delivery rate was 13%: 11% twin and 2% triplets-and-higher.

Table 8. Intrauterine insemination 2010

IUI	Cycles	Deliveries/ cycles	Gestational order		
			Singleton	Twin	≥Triplets
Husband	4,874	15%	87%	12%	2%
Donor	876	20%	88%	11%	2%

CUMULATIVE/TOTAL DELIVERY RATE

The cumulative delivery rate corresponds to the number of deliveries resulting from one initiated or aspirated ART cycle including the cycle when fresh embryos are transferred, and subsequent frozen/thawed ART cycles. This rate is used when less than the total numbers of embryos fresh and/or frozen/thawed have been utilized from one ART cycles. If all embryos are used, it is referred to as total delivery rate. Because this is the first year of a case-by-case registry, cumulative deliveries are calculated by adding deliveries derived from fresh plus frozen transfers. In future years, it will be possible to calculate cumulative events by each person. So far, cumulative delivery rates in Latin America is 28% (Table 9).

Table 9. Cumulative delivery rate IVF/ICSI, 2010

	(n)	Delivery rate per OPU
Total OPU	25,289	NA
Deliveries IVF/ICSI	5,934	23.5%
Deliveries FET	1,159	4.6%
Cumulative delivery	7,093	28.0%

COMPLICATIONS

Clinics reported 90 cases of ovarian hyper stimulation syndrome, corresponding to a rate of 0.4%. Other less frequent complications included six cases of hemorrhage and one case of infection. It is likely that there is a sub-registry of complications.

DISCUSSION

This is the twenty-first version of the Latin American registry of ART. The RLA has published continuously since 1990, covering ART procedures reported by institutions in Latin America since 1990. Over the years, the RLA has evolved, including the recollection and analysis of more complex information, and allowing the readers to download the resultant in PDF file from our web page (*www.redlara.com*).

This is the first time we implement a case-by-case register and is the only multinational case-by-case registry. The software used was developed by personnel from the RLA and field-tested in several institutions in the region. In order to implement this new method, workshops were carried out in different countries, and we believe, that the program is still in a developmental phase and continuous check-in systems are being incorporated as problems arise during its implementation. This modification in the reporting system has represented huge demands to all clinics and to personnel working in RLA.

The case-by-case register allowed to simplify the recollection of data, and also, to perform more precise and sophisticated analysis.

Another strength of this register is the uniformity of terminology. All clinics reporting to RLA, use the glossary defined in 2009 by the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) and the World Health Organization (WHO) [1; 2]. In 2010, 140 clinics from thirteen countries reported the data of 37,853 ART cycles. This represents a small drop of 0.5 % compared to 2009. In 2010 the mean number of cycles registered by each clinic reached 268 cycles, whereas in 2009 it was 281. This drop in the mean number of cycles performed by each clinic can in part result from the lack of public support for infertile couples and therefore, low access to ART procedures [3]. Only one center from Argentina, which reported 500 cycles in 2009 and one center from Venezuela, which reported 700 cycles in 2009, did not report this year. The rest of centers, which having reported in 2009, did not report in 2010 had only 30 and 150 initiated in 2009. Therefore, it is likely that the number of procedures per center is not increasing as much as new centers reporting.

The use of ICSI instead of conventional IVF continues to increase. In 2010 represented 86% of oocyte pick-ups, while in 2009 and 2008, ICSI represented 85%; and in 2007 the 83% (*www.redlara.com*). This tendency is also seen in Europe, where in the last report, 69% of autologous cycles were ICSI [4].

The age of women undergoing IVF/ICSI cycles continues to increase. In 2009, the proportion of IVF/ICSI cycles performed in women aged 35 through 39, represented 40%; and 18% of women were ≥40 years. In 2010, women age ≥40 years represent 23% of fresh IVF/ICSI cycles. Furthermore, 7% of IVF/ICSI cycles were performed in women aged ≥43 years. Since the age of the woman is one of the most important prognosis factors, this demographic reality is important to consider when analyzing regional outcomes.

The delivery rate per oocyte pick-up in IVF/ICSI reached 23.4%, and the cumulative delivery rate reached 28%. These results are higher than the data published by ESHRE, where cumulative delivery rate reached 22% [5]. Part of this difference is explained by the higher mean number of embryos transferred in Latin America compared with the majority of Europe.

The mean number of transferred embryos in IVF/ICSI did not decrease in comparison with previous years. However, the frequency of eSET and eDET did increase significantly. This might be due to a more accurate and thorough register of cases. In spite of this encouraging news, it is worrisome that in 42% of embryo transfers more than three embryos were transferred, and in 7% of cases, more than four embryos were transferred. According to ESHRE´s last report, only 24% of their embryo transfers corresponded to three and more embryos [5].

Both in IVF/ICSI and OD cycles, the transfer of more embryos resulted in an increase in the risk of triplets--and-higher order deliveries. Interestingly, the increase in the risk of twin-deliveries was marginal, and barely reached statistical significance. Thus, 24% of deliveries in IVF/ICSI cycles were multiple (2% triplets-and-higher), and 28% deliveries in OD cycles were multiple (2% triplets and higher). Increasing the number of ET above two, does not significantly impact delivery rates nor twin rates. What it does, is increase the high order multiples which are so detrimental for perinatal mortality and morbidity.

As shown in this as well as previous reports, even twin deliveries increase the risk of preterm birth and perinatal mortality. And as discussed previously, the transfer of ≥two embryos is associated to an increase in the risk of multiple delivery. Probably, the main reason to transfer more embryos is the desire of both clinicians and patients to improve the outcome of each ART cycle, without considering the risk of multiple deliveries and associated prematurity. The data showed in this report is quite reassuring, since the results associated with eSET and eDET, especially in younger patients undergoing IVF/ICSI, and OD cycles-are higher than reported in previous reports.

Since the present report correspond to the analysis of observational data, and not the results of randomized controlled trials, the results cannot be considered as a evidence or support for a decreased benefit in some procedures. For example, PGD was not associated with neither a significant increase in the delivery rate nor a reduction in the miscarriage rate. This might be explained by the fact, that the number of procedures is still low and RLA does not register differently pre-natal genetic diagnosis and pre-natal screening. Furthermore, the selection of women having PGD can be very different to the rest of the population, even when stratified by age. On the other hand, assisted hatching does not increase delivery rate, since no statistical significance was reached, however, caution must be expressed when analyzing this data.

The frequency of complications associated to ART procedures was rather low, only 90 cases of OHSS were reported, which represented a risk of 0.3% of initiated cycles. Furthermore, only 6 cases of genital hemorrhage and 1 case of infections were reported. This might represent a recollection bias, that needs to be improved.

This is the fourth report of IUI cycles. Clinics reported 4,874 IUI with husband´s semen, and 876 cycles with donor´s semen. This represent a clear drop compared to 2009, when 13,410 IIU-H and 2,430 IIU-D cycles were reported. This might be explained by the labor--consuming work that represented the change into a case-by-case register.

In summary, this is the first case-by-case register published by the RLA.

It is reassuring for patients and clinics that the results of ART procedures performed in the region are similar or even better than in most European and Asian countries [6,5]. However, REDLARA has to enforce the reduction in the number of embryos transferred in IVF/ICSI and OD cycles, in order to prevent multiple births, or at least, high order multiples and decrease the corresponding perinatal complications.

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ANNEX I

Participating Institutions

ARGENTINA

Buenos Aires
1. Centro de estudios en Ginecología y Reproducción (CEGYR)
2. Centro de Salud Reproductiva (CER)
3. Centro de Investigaciones en Medicina Reproductiva –CIMER
4. FECUNDITAS
5. Centro especializado en tratamientos para la mujer-GENS
6. Hospital de Clínicas
7. Centro de Reproducción-Servicio de Ginecología-Hospital Italiano
8. HALITUS, Instituto Médico
9. PREGNA, Medicina reproductiva
10. Procrearte
11. Fertilidad San Isidro
12. SEREMAS
13. FERTILAB

Córdova
1. Centro Integral de Ginecología, Obstetricia y Reproducción (CIGOR)
2. FECUNDART

La Plata
1. Centro de Reproducción

Mar del Plata
1. Centro de estudios en Reproducción y Procedimientos de Fertilización Asistida (CRECER)

Mendoza
1. Centro de estudios en Reproducción Humana (CERH)
2. Instituto de Medicina Reproductiva

Salta
1. MATER Medicina Reproductiva
2. SARESA, Salud Reproductiva Salta

Bahía blanca
1. AMERIS, Centro de Fertilidad, Ginecología y Urología (nuevo reportó sólo 13 casos)

BRASIL

Belo Horizonte
1. Instituto de Saúde Mulher
2. Clínica ORIGEN
3. Clínica Pro-criar/Mater Dei

Brasilia
1. Instituto Verhum - Video Endoscopia e Reproduçao Humana
2. GÊNESIS – Centro de Assistência em Reproduçao Humana Ltda.
3. Centro de Ensino e Pesquisa em Reproducao Assistida

Campo Grande-Mato Grosso
1. Fertility Centro de Fertilização Humana Assistida de Campo Grande

Campinas-SP
1. Centro de Reprodução Humana de Campinas
2. Clínica Androfert

Cuiabá-Mato Grosso
1. Instituto Pérola de Reprodução Humana
2. LIFE Reproducción Humana

Curitiba
1. ANDROLAB – Clínica e Laboratorio de Andrología
2. CONCEBER, Centro de Medicina Reproductiva
3. Clínica FERTWAY

Florianópolis
1. CLINIFERT – Centro de Reprodução Humana-Fortaleza
2. BIOS - Centro de Medicina Reprodutiva
3. FERTVIDA (anteriormente "CRIAR - Centro de Reproducao Humana")
4. CONCEPTUS – Centro de Reprodução Humana do Ceará

Goiania Goiás
1. Fértile Diagnósticos - Reprodução Humana

Juiz de Fora-Minas Gerais
1. Pro-criar, Monte Sinai, Clinica de Reprodução Humana

Londrina-Paraná
1. CEDILON Serviços Médicos S.C. Ltda.

Paso Fundo
1. GÉNESIS – Clínica de Reprodução Humana

Porto Alegre
1. Centro de Reprodução Humana Nilo Frantz
2. FERTILITAT – Centro de Medicina Reprodutiva
3. INSEMINE - Centro de Reprodução Humana
4. Núcleo de Reprodução Humana do Hospital Moínhos de Vento GERAR
5. PROGEST
6. SEGIR – Servicio de Ecografía, Genética e Reprodução Humana

Recife-Pernambuco
1. NASCER Medicina Reprodutiva
2. Clínica de Fertilidade GERAR

Ribeirao Preto-SP
1. Centro de Reprodução Humana Prof. Franco Junior
2. Clinica Matrix
3. Laboratorio de Reprodução Humana, Hospital das Clínicas de Ribeirao Preto

Rio de Janeiro-RJ
1. Centro de Medicina da Reprodução Ltda.
2. Centro de Fertilidade Rede D´Or
3. Clínica Origen
4. Clinica Pró Nascer
5. G&O Ginecología e Obstetricia da Barra (now Fertipraxis)
6. HUNTINGTON – Centro de Medicina Reproductiva (now Primordia)

Salvador Bahía
1. Centro de Reprodução Humana, Endoscopia e Medicina Fetal

Sao José Dos Campos-SP
1. Clínica REPROFERTY
2. Embryolife-Instituto de Medicina Reprodutiva

Sao José do Rio Preto
1. IMR - Centro Instituto de Medicina Reprodutiva e Fetal

Sao Paulo-SP
1. Centro de Reprodução Humana FERTIVITRO Ltda.
2. ORIGINARE, Centro de Investigação em Reprodução Humana
3. Centro de Reprodução Humana Monteleone
4. CEERH – Centro Especializado em Reprodução Humana
5. FERTILITY – Centro de Fertilização Assistida
6. FERTICLIN – Clínica de Fertilidade Humana
7. Chedid Grieco Medicina Reprodutiva
8. HUNTINGTON – Centro de Medicina Reprodutiva
9. Serviço de Reprodução Humana, Hospital e Maternidade Santa Joana

Uberlandia –Minas Gerais
10. FECUNDA - Instituto de Reprodução Humana

Vitória
11. Jules White Medicina Reproductiva (anteriormente, "HUNTINGTON - Centro de Medicina Reproductiva")

Santos
1. Clínica PRO GENESIS (new)

Presidente Prudente
1. REPRODUCTION, Clínica Urológica e Centro de Reproducao Humana LTDA. (new)

CHILE

Santiago
1. Centro de estudios Reproductivos (CER)
2. Unidad de Medicina reproductiva, Clinica Alemana
3. Unidad de Medicina Reproductiva, Clinica las Condes
4. Unidad de Medicina Reproductiva, Clinica las Nieves
5. Programa de Fertilización Asistida I.D.I.M.I.

Viña del Mar
1. Unidad de Medicina reproductiva, Clinica de la Mujer

Concepción
1. Centro de Fertilidad y Medicina Reproductiva CONCEPCION S.A.

COLOMBIA

Cali
1. Centro FECUNDAR Cali
2. Centro Médico IMBANACO

Bogotá
1. Unidad de Fertilidad del Couytry Ltda
2. Asociados en Fertilidad Humana
3. PROFAMILIA-Fertil
4. Unidad de Fertilidad, Procreación Médicamente Asistida

Medellín
1. IN SER, Instituto Antioqueño de Reproducción

Barranquilla
1. PROCREAR

ECUADOR

Quito
1. Centro Ecuatoriano de Reproducción Humana
2. CONCEBIR, Unidad de Fertilidad y esterilidad

Guayaquil
1. Instituto Nacional de Investigación de Fertilidad Esterilidad (INNAIFEST) (new)
2. Unidad de Fertilidad Hospital Alcivar Cuenca
3. Clinica de Medicina Reproductiva BIOGEPA

GUATEMALA
1. Centro de Reproducción humana S.A.

MEXICO

Ciudad de Juarez-Chihuahua
1. Unidad de Reproducción Humana y Genética

Guadalajara-Jalisco
1. Centro de Reproducción Asistida del Occidente
2. Instituto de Ciencias en Reproducción Humana – VIDA
3. Instituto de Medicina Reproductiva del Bajío (IMER)

Hermosillo
1. Clínica de Biología de la Reproducción, Hospital CIMA - León –Guanajuato
1. Instituto de Ciencias en Reproducción Humana – VIDA

Matamoros
1. Instituto de Ciencias en Reproducción Humana – VIDA

México DF
1. Centro Especializado en Esterilidad y Reproducción Humana
2. INGENES
3. Centro Médico Nacional 20 de Noviembre
4. Centro de Reproducción Asistida del Hospital Español
5. Instituto Médico de la Mujer
6. Instituto Mexicano de alta tecnología reproductiva S.C. (new)
7. Centro especializado para la atención de la mujer
8. Instituto Valenciano de Infertilidad (IVI) (new)

Monterrey
1. Centro Universitario de Medicina Reproductiva, Universidad Autónoma de Nuevo León
2. Instituto para el Estudio de la Concepción Humana

Puebla
1. Centro de Ginecología y Reproducción Asistida S.C. GYRA

Querétaro
1. Médica Fértil

San Luis de Potosí
1. Médica Fértil
2. Filius (anteriormente, OBGIN S.C., SLP) Tijuana Baja California
1. Instituto de Medicina Reproductiva del Bajío – IMER

Veracruz
1. Centro de Diagnóstico Ginecológico Saltillo
1. Centro de Reproducción asistida de Saltillo (new)

NICARAGUA

Managua
1. Centro de Fertilidad de Nicaragua, NICFERT

PANAMA
1. IVI, Panamá S.A.
2. Women´s Health in IVF

PERÚ

Lima
1. Clínica CEFRA, Centro de fertilidad y Reproducción Asistida
2. Clínica Miraflores, Instituto de Ginecología y Fertilidad
3. Grupo PRANOR, Clinica Concebir
4. Grupo PRANOR, Instituto de Ginecología y reproducción.

REPUBLICA DOMINICANA

Santo Domingo
1. 1.-PROFERT, Programa de Fertilización Asistida y Medicina Perinatal.

URUGUAY

Montevideo
1. Centro de Esterilidad Montevideo (CEM)
2. Centro de Reproducción Humana del Interior

VENEZUELA

Caracas
1. FERTILAB, Clinica el Avila
2. UNIFERTES, Clínica el Avila
3. EMBRIOS, Centro de Fertilidad y Reproducción humana, Hospital de Clínicas Caracas
4. GENESIS, Unidad de Fertilidad y Reproducción

Valencia
1. Instituto Venezolano de Fertilidad

Maracaibo
1. Laboratorios In Vitro de Venezuela

Elective embryo transfer

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ABSTRACT

Multiple birth, due the transfer of more than one embryo, constitutes the most serious complication for both mother and children after assisted reproductive technology. Embryo cryopreservation allows the sequential transfer of the whole cohort of embryos generated in one ART cycle, either by electively transferring one embryo (eSET) or two embryos (eDET). We reviewed the database of ART procedures reported to the Latin American Network of ART (REDLARA) by 140 institutions in 2010. We identify eSET, eDET, and 3ET and 4ET when three and four or more embryos were transferred, respectively, and none was cryopreserved. We analysed the outcome of 808 eSET, 5,978 eDET, 4,398 3ET and 968 4ET. Women that underwent eSET and 4ET were older than women that underwent eDET and 3ET ($p<0.0001$). The mean number of oocytes recovered was higher in women undergoing eDET (12.3) than in women undergoing eSET (6.7); 3ET (9.0); and 4ET (9.8) ($p<0.0001$). The clinical pregnancy rate reached 18% with eSET; 43% with eDET; 34% with 3ET; and 35% with 4ET. the proportion of twin delivery was 0.9% with eSET; when more than one embryo were transferred, the twin rate did not differ significantly: 22% with eDET; 21% with 3ET and 23% with 4ET. However, high order multiple births (≥3newborns) increased significantly with both 3ET (3.0%) and 4ET (4.4%). that neither the weight nor gestational age at delivery of singletons were associated to the number of embryos transferred. With the proper counselling regarding cumulative pregnancy rate and risks associated with twin pregnancy, and a fixed payment for all ET performed, we expect more couples -and physicians- would undergo eSET.

INTRODUCTION

Multiple birth constitute the most serious complication for both mother and children after Assisted Reproductive Technology (ART). For the mother, multiple pregnancies are associated with higher risks of hypertensive disorders, anaemia and haemorrhage during pregnancy [1;2]. For the foetuses, multiple pregnancy increases significantly the risk of preterm birth and perinatal morbidity and mortality[3].

Since our ability to predict the capacity of the embryo to implant is limited, the transfer of more than one embryo increases the possibility of transferring one normal embryo, and thus obtaining a pregnancy. It is for this reason that clinicians, many times, influenced by couples, transfer more than one embryo, hoping to maximise the outcome of a single cycle. Couples in countries with little or no reimbursement for infertility-related procedures are even more prone to such attitude [4].

Embryo cryopreservation allows the sequential transfer of the whole cohort of embryos generated in one ART cycle, either by electively transferring one embryo (eSET) or two embryos (eDET). Elective SET has been shown to be an effective strategy to minimise the risk of twins without compromising IVF cumulative success rates[5], while eDET have shown to maintain a higher pregnancy rate by exposing women to high twin-pregnancy rates [6-8].

The objective of this study is to compare the outcome of elective single embryo transfer (eSET); elective dual embryo transfer (eDET); three-embryo transfer (3ET); and four-and-more embryo transfer (4ET).

MATERIALS AND METHODS

We reviewed the database of ART procedures reported to the Latin American Network of ART (REDLARA) by 140 institutions in 2010. We identify eSET and eDET, when one or two embryos were transferred, and the rest of the cohort of embryos were cryopreserved; an 3ET and 4ET when three and four or more embryos were transferred, respectively, and none was cryopreserved. The data analysed included age of the female partner, number of oocytes recovered, number of embryos transferred, stage of development at embryo transfer (ET), and clinical outcome. Clinical outcome was defined as clinical pregnancy rate per ET (CPR/ET), abortion rate, newborn weight in grams, and gestational age in completed weeks at the time of delivery. Precise definitions can be found in the ICMART glossary (ref).

STATISTICAL ANALYSIS

Categorical variables were compared with Fisher´s exact test. Interval variables were compared either with Student´s t-test or one-way ANOVA, depending on the number of strata of the categorical variable. Multiple variable analysis was performed either with lineal regression or logistic regression, depending on the nature of the outcome variable. We considered a p-value les than 0.05 to be statistical significant.

RESULTS

We analysed the outcome of 808 eSET, 5,978 eDET, 4,398 3ET and 968 4ET. Table 1 shows the demographic data of these ET. Women that underwent eSET and 4ET were older than women that underwent eDET and 3ET ($p<0.0001$). The mean number of oocytes recovered was higher in women undergoing eDET (12.3) than in women undergoing eSET (6.7); 3ET (9.0); and 4ET (9.8) ($p<0.0001$). Also, the mean number of embryos cryopreserved was higher in cases of eSET (4.4) than in eDET (4.0) ($p=0.0468$)- The majority of embryos were cryopreserved at cleaving stage, both in eSET (56%) and eDET (63%).

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Aceito em 17-12-12

Table 1. Demographics

	eSET	eDET	3ET	4ET
Age	36.9 (4.7)	34.0 (4.3)	35.8 (4.4)	37.0 (4.4)
Number of oocytes retrieved	6.7 (6.7)	12.3 (7.0)	9.0 (5.0)	9.8 (4.8)
Embryos cryopreseved	4.4 (3.1)	4.0 (2.7)	0	0

average (SD)
eSET= elective single embryo transfer; eDET= elective dual-embryo transfers; 3ET= triple-embryo transfer; 4ET four or more embryo transfer

In both, eSET and eDET, only 14% of ET were performed at blastocyst-stage, while 2% of 3ET and 4ET were performed at blastocyst-stage. Table 2 shows the outcome of ET. The miscarriage rate was the highest when eSET was performed (21%), and the lowest when eDET was performed (14%). However, after correcting for age, we found that the number of embryos transferred was not associated to the odds of miscarriage. The CPR/ET reached 43% when eDET was performed. When more than two embryos were transferred, the CPR reached 34% (3ET) and 35% (4ET). The CPR/ET was significantly lower when eSET was performed (18%). Nevertheless, in women aged less than 35 years, the CPR/ET when eSET was performed reached 30%. Multiple variable logistic regression showed, that after correcting for the age of woman and embryonic developmental stage, the OR for CPR/ET was significantly higher only when eDET was performed (OR 3.0, 95% 2.5-3.6). Table 3 shows perinatal outcome. As expected, the proportion of twin delivery was the lowest when eSET was performed (0.9%). When more than one embryo were transferred, the twin rate did not differ significantly. Twin delivery reached 22% when eDET was performed, 21% when 3ET and 23% when 4ET was performed. However, high order multiple births (≥3newborns) increased significantly with both 3ET (3.0%) and 4ET (4.4%). We analysed the perinatal outcome as expressed by the mean weight and mean gestational age at birth of singletons and compared them, after eSET, eDET, 3ET and ≥4ET. We did not find any significant difference neither in the weight (p=0.118) nor in the gestational age at delivery (p=0.336). Multiple variable lineal regression, after correcting for woman´s age and gestational age at delivery, demonstrated that neither the weight nor gestational age at delivery of singletons were associated to the number of embryos transferred.

DISCUSSION

A multiple pregnancy is a clinical risk to both infant and mother following IVF treatment. Children born after IVF had a poorer obstetric outcome compared with children from the general population. Singletons, when analysed as one group, irrespective of whether the children were born after eSET, non-eSET or DET, also had a poorer obstetric outcome with higher rates of preterm and LBW compared with singletons in the general population [9].

We found that eSET was significantly associated with a lower frequency of multiple delivery and abortion rate. We were not able to prove a difference in perinatal outcome of singletons, expressed as the mean weight and gestational age at delivery.

It is interesting that the transfer of ≥2 embryos yielded similar twin-delivery rate, around 20%, among eDET, TET and FET. However, the transfer of ≥3 embryos was significantly associated with an increase in the proportion of triple-deliveries.

Thus, the only way to reduce the risk of multiple gestation and delivery is to enforce eSET. Since eSET is significantly associated with a reduction in the CPR, many clinicians and patients might be reluctant to undergo eSET and might prefer to undergo at least eDET. At least, this have been the experience in different countries. Per example, Murray et al found that maintaining existing rates of pregnancy and offering a fixed charge for all embryo transfers resulting from an oocyte recovery may encourage more couples to consider eSET[10].

In general, patients' preferences for a singleton or twins are not definitive during IVF treatment. Possible explanations of a shift in preference are that pregnant patients attuned their preferences to what they expect their pregnancy to result in, whereas non-pregnant patients shifted towards a preference for twins in order to be able to fulfil their ultimate child wish[11]. Furthermore, when exposed to the risks of multiple births and the option of selecting elective single-embryo transfer, the use of complex persuasive communication techniques on a student population to promote eSET preferences is more successful at promoting eSET than merely reporting educational content [12].

On the other hand, physicians are reluctant to perform eSET. In a study published by Van Peperstraten a total of 107 professionals participated. The most frequently mentioned barriers to eSET use were suboptimal success rates associated with cryopreservation (96%) and not seeing twin pregnancies as a complication (79%) [13].

Table 2. Embryo transfer

	eSET	eDET	3ET	4ET
Embryo transfers	808	5078	4398	968
Transfers at blastocyst stage	14%	14%	2%	2%
CPR	18.2%	43.3%	34.0%	34.9%
abortion rate	21%	14%	17%	18%

eSET= elective single embryo transfer; eDET= elective dual-embryo transfers; 3ET= triple-embryo transfer; 4ET four or more embryo transfer

Table 3. Perinatal outcome

	eSET	eDET	3ET	≥4ET
twin delivery (%)	0.9	22.4	20.8	22.7
≥ triple delivery (%)	0	1.5	3.0	4.4
perinatal mortality (*)	0	7.9	6.3	0
mean weight of singletons (SD)	2671 (1274)	2666 (1118)	2768 (1797)	2913 (749)
mean gestational age of singletons	38 (2)	38 (2)	38 (2)	38 (2)

eSET= elective single embryo transfer; eDET= elective dual-embryo transfers; 3ET= triple-embryo transfer; 4ET four or more embryo transfer (*) among singletons, per 1,000

We found that patients undergoing eSET cryopreserved in average 4 embryos, thus they have four further intents of eSET. Thus, the outcome that should be discussed with the patient is the cumulative CPR, rather than the CPR after a fresh transfer. Probably, a main barrier to do this is the oeconomical, since in Latin America most of the couples must pay for the treatments by themselves, with little or no governmental support.

The present study has the strength that corresponds to the analysis of a robust database. The RLA keeps the data of ca. of 80% of ART procedures performed in Latin America since 1990. The clinics are used and trained in providing such data, and the data is periodically verified by an independent committee. However, an important weakness of this study is that it corresponds to an observational study. As such, the intervention i.e. the number of embryos transferred were not randomised, and no causality can be inferred. Furthermore, some unmeasured variables such as the experience of the clinician or laboratory, may influence the outcome of the procedure.

With the proper counselling regarding cumulative pregnancy rate and risks associated with twin pregnancy, and a fixed payment for all ET performed, more couples -and physicians- would undergo eSET.

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Trends in the number of transferred embryos, clinical pregnancy rate and multiple pregnancy rate in Latin America: 1998 through 2008

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ABSTRACT

Background. Reducing the rate in IVF of multiple births and associated perinatal complications has become the major challenge in Latin America, due to is association with a significant increase in the prematurity, and perinatal mortality.

Methods. We selected all procedures involving the transfer of IVF embryos, reported to the Latin America Registry of ART, initiated between January 1998 and December 2008. A Poisson regression analysis was performed, stratified by woman´s age to analyse the trend in the transfer of 2, 3 and ≥4-embryos and ≥triple-pregnancy rate.

Results. A total of 164,874 IVF/ICSI transfers were considered. Overall, there was a decline in the proportion of procedures performed in women aged ≤34 years old from 51% to 43%; and an increase of ICSI procedures from 61% to 86%. All age groups experienced a reduction in the proportion of ≥4-embryos transfers and an increase in that of 2-embryo transfers. Overall, the clinical pregnancy rate improved from 29% to 35% (p=0.01); and the incidence of ≥triple-pregnancy decreased from 8% to 3% in 2008 (p<0.001), while twin pregnancy remained stable (~20%)

Conclusions. Our data support the policy of transferring less embryos. It shows a decline in the mean number of embryos transferred and proportion ≥ 4-embryos transfers. Moreover, it reports a clinical pregnancy rate which instead of being reduced, has shown an increase over the 10-year period.

INTRODUCTION

The first IVF-baby in Latin America was born in Colombia in 1984. This technology spread rapidly all over Latin America generating a substantial increase in the number of patients gaining access to Assisted Reproductive Technologies (ART). The current need for ART procedures, however, is by far underserved, and great disparity persists in the access to such technology[1].

The latest report by the International Committee Monitoring Assisted Reproductive Technology presents worldwide information about ART procedures performed in 2003[2]. At that time, the number of cycles reported by Latin-American centers represented only 2.3% of the 932,415 cycles performed worldwide. Expressed as the ratio of ART cycles per million inhabitants, the disparity in access to ART is even more striking: countries like Sweden, Denmark and Belgium perform between 1,000 to 2,000 cycles per million inhabitants, whilst countries in Latin America perform between 33 and 109 cycles per million inhabitants[2]. In countries where ART is reimbursed or covered by public health insurance, the mean number of embryos transferred is much smaller than the number of embryos transferred in countries where ART is funded by each couple[3].

Current economic policies in Latin America cause that only a small percentage of the gross domestic product is allocated to health related expenditures. Furthermore, the majority is diverted to private health expenditure such as insurance companies, who do not cover infertility-related procedures[4]. Thus couples have to rely on their own resources to fund their treatments which limits the number of infertile couples with access to treatment and the number of opportunities that couples have to receive ART treatments.

In order to achieve successful outcomes while minimising the number of ART procedures attempts, multiple embryos are transferred into the uterus which in term increases the chances of pregnancy[5]. However, this strategy also increases in the rate of twin and high order multiple pregnancies[6].

At a regional level, Latin America shows comparable clinical outcomes to those of developed countries. Similar clinical pregnancy rates and delivery rates, are reported, although with a larger number of embryos transferred, and regardless of the age of the female partner[2].

Reducing the number of embryos transferred with a reduction in the rate of multiple births and associated perinatal complications has become the major challenge in Latin America, since multiple pregnancies are associated with a significant increase in the prematurity, and perinatal mortality[1]. Furthermore, the increase in family disorders mainly absorbed by women, and high individual and insurance costs to cover neonatal expenses are also issues that need to be addressed.

This study examines trends in embryo transfer practices and clinical and multiple pregnancy rates for assisted reproductive technologies performed in Latin America between 1998 and 2008. Given the strong association between number of embryos transferred and multiple birth risk[7,8], assessment of embryo transfer practices is essential to understanding the multiple gestation and birth risk associated with assisted reproduction. Our aim is to document the decline in the number of embryos transferred, and the impact such shift might have had on clinical pregnancy and multiple gestation rates.

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Table 1. Characteristics of IVF/ICSI embryo transfers performed 2000-2008 in Latin America

	Year											
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
Number of ET	9,054	10,187	11,063	12,601	12,704	14,129	16,053	17,744	18,843	21,285	21,211	164,874
Patient age, years (%)												
≤34	51%	52%	51%	50%	48%	49%	47%	46%	46%	44%	43%	46%
35-39	36%	34%	34%	35%	35%	35%	37%	36%	37%	38%	39%	36%
≥40	14%	14%	15%	15%	17%	16%	16%	18%	17%	18%	18%	17%
IVF procedure (%)												
IVF	39%	32%	29%	28%	23%	25%	23%	19%	18%	15%	14%	22%
ICSI	61%	68%	71%	72%	77%	75%	77%	81%	82%	85%	86%	78%

Numbers may not add up to 100% due to rounding.

MATERIAL AND METHODS

Study population

The Latin American Registry of Assisted Reproductive Technologies (RLA) was established in 1990 as the first multinational registry in the world. Today, it registers more than 80% of the cycles performed in the region, including countries such as Mexico in the North and Argentina/Chile in the South.

It corresponds to a registry of summary cases, in which every year each centre voluntarily summarises the characteristics and outcomes of the cycles performed, and uploads said information in a web page maintained by RLA. The administrative office in Santiago, Chile, periodically recovers and analyses this data for consistency. Once all the information is cleared, and the centre is checked as accredited by the RED, the data is included and published by the RLA as part of yearly report, available on the web.

For analysis we selected all procedures involving the transcervical transfer of IVF embryos (either through ICSI or standard IVF) into the uterus, with the woman's own eggs, initiated between January 1998 and December 2008. A total of 164,874 IVF/ICSI transfers were considered.

We focus in the proportion of embryo transfers in which 1, 2, 3 and ≥4 embryos were transferred. The transfer of 5 and 6 embryos represented a minor proportion, thus we preferred to categorised them under the transfer of ≥4 embryos.

Data analysis

The number of embryo transfers in IVF/ICSI cycles, in which 1, 2, 3, and ≥4 embryos were transferred; the number of clinical pregnancies; and the number of multiple pregnancies were analysed. Clinical pregnancy was defined as the identification of at least one gestational sac by ultrasound, whereas multiple pregnancy was defined as the identification of one or more gestational sac(s)[9].

The annual proportion of transfers with 1, 2, 3 and ≥4 embryos embryos transferred, and clinical pregnancy rate and multiple pregnancy rate were investigated stratified by woman's age category: ≤34 years old, between 35 and 39 years old, and ≥40 years old.

Statistical analysis

We performed a Poisson regression analysis, stratified by woman´s age to analyse the trend in the transfer of 2, 3 and ≥4-embryos and ≥triple-pregnancy rate, using Stata Software package, version 11,0 (Texas, USA).

RESULTS

Embryo transfers

Table 1 shows the number of IVF/ICSI embryo transfers performed between 1998 through 2008, according to the woman's age category and type of fertilisation. Overall, there was a two-fold increase in the number of procedures registered; a decline in the proportion of procedures performed in women aged ≤34 years old from 51% to 43%; and an increase of ICSI procedures from 61% to 86%

Number of embryos transferred

Figure 1 shows the decline in the mean number of embryos transferred between 1998 and 2008. The mean number decline from 3.3 in 1998 to 2.5 2008, which was statically significant ($p<0.001$). Table 2 shows the distribution of IVF/ICSI embryo transfers according to the number of embryos transferred in each age category. All age groups experienced a reduction in the frequency of ≥4-embryos transfers, and an increase in the proportion of 2-embryo transfers.

Women aged ≤34 years old experienced an increase in the proportion of 2-embryo transfers from 15% in 1998 to 45% in 2008 ($p<0.001$) and a decrease in the

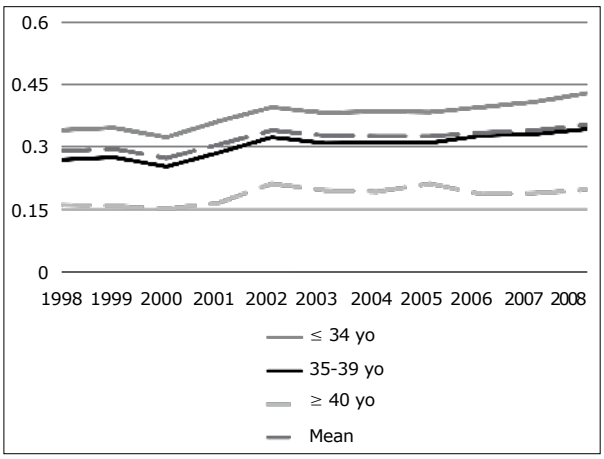

Figure 1. Clinical pregnancy rate per embryo transfer in women undergoing IVF/ICSI cycles according to woman's age category RLA 1998-2008

Table 2. Distribution of embryo transfers according to the number of embryos transferred in each age category. RLA 1998-2008

IVF/ICSI embryo transfers in women aged ≤34 years old												
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
n	4,600	5,325	5,610	6,273	6,146	6,951	7,509	8,148	8,668	9,418	9,180	77,828
Number of embryos transferred (%)												
1	8%	7%	8%	7%	7%	6%	7%	7%	8%	8%	8%	7%
2	15%	17%	18%	17%	19%	23%	27%	29%	35%	40%	45%	29%
3	28%	33%	30%	35%	37%	39%	40%	43%	43%	40%	37%	38%
≥4	49%	43%	44%	41%	37%	32%	26%	20%	15%	13%	10%	26%
IVF/ICSI embryo transfers in women aged 35 to 39 years old												
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
n	3,223	3,430	3,807	4,428	4,444	4,945	5,923	6,377	6,925	8,064	8,219	59,785
Number of embryos transferred (%)												
1	12%	11%	12%	11%	9%	11%	10%	11%	12%	11%	12%	11%
2	16%	17%	18%	19%	20%	20%	21%	24%	29%	32%	38%	26%
3	23%	27%	26%	28%	31%	33%	39%	39%	39%	41%	38%	35%
≥4	49%	44%	44%	42%	39%	35%	30%	25%	20%	16%	12%	28%
IVF/ICSI embryo transfers in women aged ≥40 years old												
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	Total
n	1,231	1,432	1,646	1,900	2,114	2,233	2,621	3,219	3,250	3,803	3,812	27,261
Number of embryos transferred (%)												
1	22%	20%	17%	18%	17%	18%	19%	17%	19%	21%	21%	19%
2	22%	21%	23%	24%	21%	21%	21%	23%	24%	25%	30%	24%
3	20%	21%	21%	22%	25%	23%	27%	28%	30%	31%	33%	27%
≥4	37%	38%	39%	36%	38%	37%	34%	32%	27%	24%	16%	30%

Numbers may not add up to 100% due to rounding.

proportion of ≥4-embryo transfers from 49% to 10% (p=0.006). Similar findings were reported by women aged 35 to 39 years with an increase in the proportion of 2-embryo transfers from 16% to 38% (p=0.001) and a decline in the proportion of ≥4-embryo transfer (p<0.001). This trend was less pronounced in women aged ≥40 years experienced the proportion of 2-embryo transfers increased from 22% to 30% (p=0.075) and the proportion of ≥4-embryo transfers decreased from 37% to 16% (p=0.01).

Clinical Pregnancy

Figure 1 shows the clinical pregnancy rate per embryo transfer in each age category between 1998 and 2008. Overall, the clinical pregnancy rate improved from 29% in 1998 to 35% in 2008 (p=0.01). In women aged ≤34 years this improvement was from 34% to 43% (p<0.001); in women aged 35 to 39 years it was from 27% to 34% (p<0.001); and in women aged ≥40 years it was from 16% to 20% (p=0.047).

Multiple Pregnancy

Figure 2 shows the distribution of clinical pregnancies according to gestational order in women who underwent IVF/ICSI between 1998-2008. Overall, the incidence of ≥triple-pregnancy decreased from 8% in 1998 to 3% in 2008 (p<0.001), while the proportion of twin pregnancy remained stable (~20%).

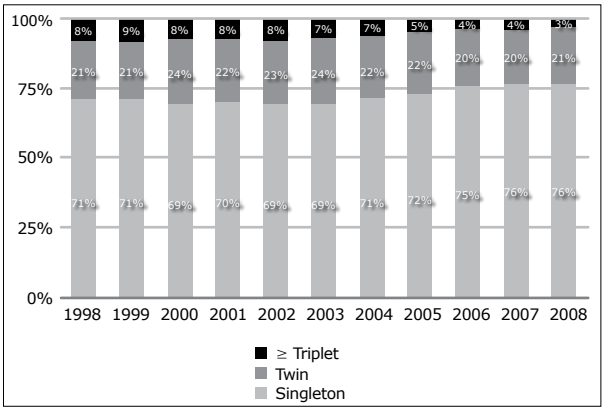

Figure 2. Clinical pregnancies according to gestational order in women undergoing IVF/ICSI. RLA 1998-2008

Table 3 shows the distribution of clinical pregnancies according to gestational order in each woman's age category. The frequency of ≥triple pregnancy, from 1998 to 2008, decreased , from 10% to 5% (p<0.001) in women aged ≤34 years; from 6% to 3% (p<0.001) in women aged 35 through 39 years and 4% to 2% (p=0.058) in women aged ≥40 years.

Table 3. Multiple pregnancy rate according to woman's age category. RLA 1998-2008

Clinical pregnancies according to gestational order in women aged ≤34 years old											
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
n	1,568	1,843	1,815	2,276	2,431	2,659	2,895	3,127	3,434	3,853	3,946
Gestational order (%)											
Single-ton	66%	65%	66%	66%	66%	68%	69%	71%	72%	72%	73%
Twin	23%	23%	26%	24%	25%	26%	25%	24%	24%	24%	22%
≥Triplet	10%	11%	9%	9%	9%	8%	7%	6%	5%	5%	6%

Clinical pregnancies according to gestational order in women aged 35 to 39 years old											
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
n	869	944	963	1,272	1,439	1,531	1,840	1,982	2,268	2,674	2,819
Gestational order (%)											
Single-ton	75%	76%	73%	72%	71%	72%	73%	74%	80%	80%	79%
Twin	19%	19%	21%	21%	21%	22%	20%	22%	18%	17%	18%
≥Triplet	6%	6%	6%	7%	7%	5%	7%	4%	3%	3%	2%

Clinical pregnancies according to gestational order in women aged ≥40 years old											
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
n	197	226	248	315	448	437	504	681	604	720	751
Gestational order (%)											
Single-ton	82%	84%	79%	83%	78%	75%	79%	81%	85%	88%	87%
Twin	14%	14%	18%	14%	18%	18%	16%	16%	14%	10%	11%
≥Triplet	4%	2%	3%	3%	5%	7%	5%	4%	2%	2%	1%

Numbers may not add up to 100% due to rounding.

Table 4 shows the incidence risk ratio for ≥ triple pregnancy adjusted for woman´s age category, stratified by quartile of the mean number of transferred embryos. As seen, the incidence risk ratio for ≥triple pregnancy diminished significantly over time in the groups where less embryos were transferred. In the two groups where more embryos were transferred, the decrease in the incidence risk ratio did not change significantly over time.

Table 5 shows the perinatal outcome of babies born due to FIV/ICSI performed between 1998 and 2008 according to the gestational order. The risk of perinatal mortality increased significantly with higher gestational orders.

Table 4. Incidence Risk Ratio for ≥ triple pregnancy stratified by quartile of mean number of embryos transferred[1]

Quartile (mean number of transferred embryos)	IRR year (95% CI)	*p*
1- (2.47-2-70)	0.87 (0.80-0.969	0.003
2- (2.71-2.97)	0.41 (0.19-0.86)	0.019
3- (2.98-3.13)	0.98 (0.93-1.04)	0.638
4- (3.14-3.42)	0.97 (0.92-1.04)	0.477

[1] Adjusted for age category

Table 5. Perinatal outcome according to gestational order of 73,857 babies born due to IVF/ICSI cycles performed between 1998 and 2008

Gestational Order	Perinatal mortality	RR (95%IC)
single	0.86%	1
twin	2.92%	3.05 (2.69-3.45)
triplets	6.49%	6.79 (5.94-7.76)
≥quadruplets	19.29%	20.19 (17.02-23.95)

DISCUSSION

The number of infertile couple undergoing assisted reproductive technologies increased significantly in the period analysed, as did the clinical pregnancy rate per embryo transfer, regardless of the woman's age-category. When focusing on the success such procedures, attention should also be given to its complications. The most important being that of multiple pregnancy which is significantly associated with preterm delivery and perinatal morbidity and mortality.

In Latin America, the frequency of ≥triple pregnancy rate has halved in all woman's age categories over this 10-year period, while the proportion of twin pregnancy

remained stable. Multivariate analysis showed that the most important factor that accounted for this decline is the significant decrease in the mean number of embryos transferred. The constant, yet minor, decrease in the mean number of embryos transferred significantly lowered the frequency of ≥triple pregnancy, but showed no significant effect in the proportion of twin pregnancies. The increase seen in the proportion of three-embryo transfers may have countered,the effect caused by the reduction in the proportion of ≥four--embryo transfers.

Importantly, this decline in the number of embryos transferred was not associated with a decline in the clinical pregnancy rate, on the contrary, the clinical pregnancy rate per embryo transfer improved significantly between 1998-2008 in all age categories. This suggests that other unmeasured factors improved over time. One of these might be the transfer of embryos in later stages of development, allowing for a better selection and improved implantation rates.

In an attempt to diminish the ART-related multiple pregnancies epidemic, countries like Sweden, Belgium and Japan have implemented strict policies and support the elective transfer of one embryo, with a clear reduction in the multiple pregnancy rate (10-14). This is feasible in countries where ART procedures are covered by health insurance and thus have some control over ART practice. This is difficult in Latin America, where ART procedures are mainly covered by infertile couples, and the open market economy dictates strong competition between different ART centres, which have the tendency to maximise results, regardless of multiple pregnancy rate.

Nevertheless, we found that practice in the region is moving towards the right direction with more work needed for reducing the number of embryos transferred. Our data support the policy of transferring less embryos. It shows a decline in the mean number of embryos transferred and proportion ≥ 4-embryos transfers. Moreover, it reports a clinical pregnancy rate which instead of being reduced, has shown an increase over the 10-year period.

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Experimental evaluation of bovine pericardium efficacy on adhesion pelvic prevention in the dog model.

Avaliação experimental da eficácia do pericardio bovino na prevenção de aderências pélvicas em modelo canino.

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RESUMO

Objetivo: avaliar a eficácia do pericárdio bovino (PB) na prevenção de aderências em cães submetidos a duas lesões indutoras de aderências no grupo controle (GC) e no grupo experimental (GE). Métodos: dezessete cadelas, sem raça definida e não prenhas, foram anestesiadas e submetidas a lesões indutoras de aderências, sendo a primeira a miometrectomia anterior com sutura isquêmica, e a segunda, o fechamento do peritônio com sutura ancorada isquêmica. No GE, com nove cadelas, colocou-se o PB recobrindo integralmente a primeira lesão; na segunda lesão, recobriu-se a área de sutura isquêmica na extremidade inferior. Após seis dias, no mínimo, as cadelas foram sacrificadas e as aderências quantificadas, segundo a sistematização sugerida pela Adhesion Sudy Group denominada MCASM*(more comprehensive adhesion score method), e pela avaliação do percentual de área aderida, excluindo a força da aderência, denominada AEEL*(adhesion extension experimental lesion). **Resultados:** O GC e GE não tiveram diferenças significativas na média de peso (kg) e tempo cirúrgico em minutos (12,62/15,66 *p*= 0, 3868) e (78,25/77, 88, *p*= 0, 9086). Lesão 1: o GC apresentou escore médio 6,50 versus 6,00 no GE, *p*= 0,718 (MCASM) e 4,87/4,33 com *p*= 0,615 (AEEL), diferenças não significativas. Lesão 2: o GC teve escore médio 4,62 versus 7,55 no GE e *p*= 0,005 (MCASM) e 2,75/4,77 com *p*= 0,015 (AEEL), diferenças significantes.

Conclusões: As lesões foram fortes indutoras de aderências, e o PB não preveniu a formação de aderências. Além disso, o PB produziu mais aderências na lesão 2.

Palavras-chave: aderências pós-operatorias, métodos de barreira cirúrgicos, pericárdio bovino, lesões experimentais de aderências, prevenção de aderências.

ABSTRACT

Purpose: to investigate the efficacy of bovine pericardium to prevent pelvic adhesion in dogs.

Methods: Seventeen female non pregnant dogs were anesthetized and submitted to two adhesion-inducing lesions – the first lesion was performed in the anterior portion of uterus (elliptical incision) and sutured with an ischemic line of chromic catgut and the second, when closing the peritoneum, also with an ischemic suture. BP was used as the barrier agent in nine dogs, fully covering the first lesion and applied on the inferior part of the second lesion. Six days later, the dogs were sacrificed and the adhesions were examined according to the ¨More Comprehensive Adhesion Score Method¨ (MCASM, Adhesion Study Group-EUA) and to the score developed by the author in which only the percentage of the adhesion is examined, ¨Adhesion Extension in Experimental Lesion¨ (AEEL).

Results: There were no significant differences between the two groups regarding weight and surgical time in minutes . No significant differences were observed between the MCASM scores of the two groups (6.50 vs. 6.00, *p*= 0.718) and the AEEL (4.87 vs. 4.33, *p*= 0.615) for lesion 1. There were significant differences in the second lesion in the two groups, regarding the mean scores given by the MCASM system (4.62 vs.7.55, *p*=0.005) and the adhesion extension score (2.75 vs. 4.77, *p*=0.015).

Conclusions: BP did not prevent the formation of adhesions caused by the lesions performed. Furthermore, BP enhanced the formation of adhesions in lesion 2.

Key words: Postoperative adhesion prevention, surgical barriers, bovine pericardium, experimental lesions of adhesion, prevention of adhesion.

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INTRODUCTION

Over the past years abdominopelvic adhesion has been studied in a very detailed and professional way. These studies analyze the importance of adhesion formation to the human being once it is related to chronic pelvic pain, infertility, surgery complication in reoperation and the relevant costs in the health care systems.
Ellis *et al.*, 1999 studied the percentage of hospital admittance caused directly or indirectly by abdominopelvic adhesion in Scotland in the year of 1994. The studied population consisted of patients that underwent surgery in 1986 who had no record of abdominopelvic surgery in the preceding 5 years. Among 27.790 patients 34.6% were readmitted to hospital on an average of 2.1 times in ten years of observation; 22.1% of patients were readmitted in the first year after the surgery. In developed countries the main cause of bowel obstruction can be attributed to abdominopelvic surgery (Beck *et al.*, 2000).
Svanes Fevang *et al.*, 2004 studied 500 patients in Norway between 1961 and 1995 . They underwent surgery because of bowel occlusion related to adhesion and they were followed for an average of ten years, but some patients were followed for fourty years. The cumulative recurrence rate was 18% at ten years and 29% at thirty years. Patients with high recidivism rate showed higher recurrence rate and for those who underwent four previous surgeries, for example, the recidive rate was 81%. Wilson *et al.*, 2002 estimated that in Scotland the re-admission cost for post-surgical abdominal adhesion, mainly colon-rectal, during ten years follow-up observation was about 569 million pounds. Scientists speculate that if adhesion prevention products costing 50 pounds per patient were used, the hospital re-admittance would diminish 16% and if the cost was 200 pounds the hospital re-admittance would diminish 64% in three years.
The barrier method presents preventive properties against adhesion and this method is the most well researched over the past years. Among the common barrier methods, apparently effective, there is the polytetrafluoroethylene membrane (PTFE) commercialized by Gore Tex Surgical Membrane, Interceed and Seprafilm. Many multicentre studies were published about Interceed (oxidized regenerated cellulose and Absorbable Adhesion Barrier) after studies in animals (Interceed Adhesion Study Group, 1998; Nordic Adhesion Prevention Study Group, 1996; Franklin, 1995). Such studies showed a reduction in the incidence, extension and severity of post-surgery adhesion in human patients but, on the other hand, some negative results were showed by different researches (Saravielos & Li, 1996; Reid *et al.*,1997; Baysal, 2001). Diamond & The Seprafilm Adhesion Study Group., 1996 showed positive results of Seprafilm (sodium hyaluronate-carboxymethylcellulose membrane) against pelvic adhesion.
Boyers *et al.*, 1988 studying the effect of the expanded membrane (PTFE) in rabbits achieved a positive result. This result motivated a multicentre study in humans which was published in 1992 by The Surgical Membrane Study Group. They tested the effectiveness of the membrane against adhesion reformation. After this study some conclusions could be drawn: a-few training procedures are needed; b-the membrane must be located at least 1cm beyond the cruenta area; c- laparoscopic removal was not a difficult task; d-the product did not cause the death of the user. Studies in animals (Montz *et al.*, 1992; Grow *et al.*, 1994; Hellebrekers *et al.*, 2000) showed the positive adhesion prevention effect of Gore Tex Surgical Membrane. Other authors (Haney *et al.*, 1995; The Miomectomy Adhesion Multicenter Study Group, 1995) confirmed this positive result in humans. Hurst *et al.*, 1999 coordinated an observational multicentre study to determine if permanent implantation of the PTFE membrane in the pelvis caused any adverse effects and they concluded that removal of the barrier was not necessary. The membrane was implanted permanently and no long-term complications occurred in any of the 146 women subjected to the study.
Farquhar *et al.*, 2006 conducted a metanalysis study to assess the effect of mechanical barriers such as PTFE membrane, Interceed and Seprafilm. Their results suggest a positive adhesion prevention effect and Gore-Tex may be slightly superior to Interceed in preventing adhesion.These products are expensive in our country and it has motivated scientists to look out for different options which would be compatible with our environment and less expensive. In our country the bovine pericardium(BP) is intensively used in heart surgery and that could be the right option. Such membrane is stored in formaldehyde and it is thicker than the Surgical Membrane which could be an inconvenience. On the other hand the bovine pericardium is resistant and malleable (Braile *et al.*, 1998). Mavritas *et al.*, 2005 , studied the dynamic mechanical behavior of BP in its native form and under specific enzymatic degradation with chondroitinase ABC. They confirmed the viscoelastic properties of BP.
Gomes *et al.*, 1994 studied the effect of this product in abdominal hernias correction in pigs and there was no adhesion formation. Therefore we decided to evaluate the bovine pericardium in adhesion prevention in female dogs with no specific pedigree. An efficient adhesion inducing model was used and it was previously tested in a pilot project approval by Animal and Human Research Ethics Committee in Clinical Hospital of Federal University of Goiás.

METHODS AND MATERIALS

Twenty non-pregnant female dogs with no specific pedigree were assigned to two groups each containing ten animals – control group (CG) and experimental group (EG). For the CG were used only the lesions described as it follows, no anti-adhesion method was used. For the EG, bovine pericardium was used.
In order to induce adhesion formation two lesions were performed. The first lesion consisted of one elliptic incision of 3 to 4 centimeters (Figure 1) in the anterior portion of uterus sutured with an ischemic line of chromic catgut 00 and associated with obliteration to the bilateral uterine artery branch. The second lesion consisted at the closing of peritoneum also with an ischemic suture of chromic catgut 00 (Figure 2). It was performed after placing the bovine pericardium

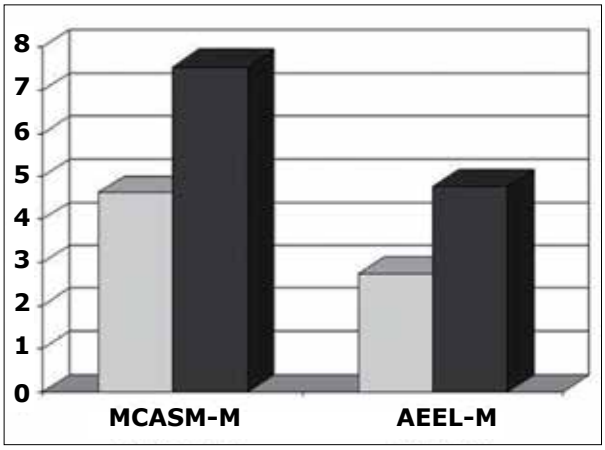

Figure 1. Lesion of the uterus (UL). Elliptical resection and ischemic suture of the anterior uterine portion. Placement of bovine pericardium, covering to the lesion and subsequent fixation of the edges laterally.

in the animals from EG and at the end of the surgery for the CG.

The bovine pericardium was fixed to the anterior portion of uterus with six mononylon 5-0 stitches covering the lesion completely. When closing the abdominal wall, the same membrane was used to protect the inferior part of the incision which was 6 centimeters long. The suture was performed in the paramedian aponeurosis by six stitches, three in each side of the suture.

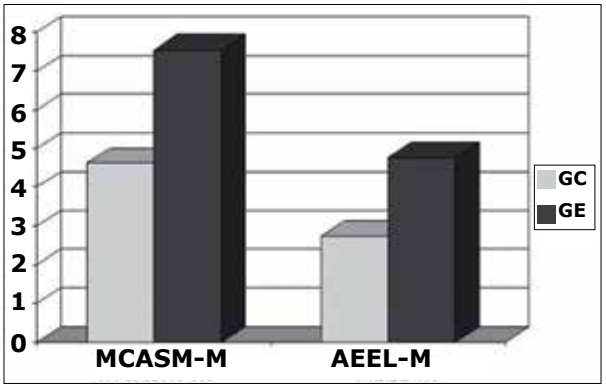

Figure 2. Midline lesion (MLL). Infra umbilical laparotomy showing the placement of bovine pericardium and its laterally fixation to the aponeurosis, covering the midline ischemic peritoneal suture.

Before the surgery the dogs were observed for three days. They were sanitized a day before the surgery which was performed always in the morning. After the weight evaluation, the animals were anesthetized by a veterinarian who is a Surgery Techniques professor. Intramuscular Acepromazine 1% was used as pre-anesthetic (0,2 ml/Kg- 0,5 ml/Kg). Intravenous administration of sodium thiopental 2,5% (25mg/ml) was used as anesthetic with spontaneous breathing. Intramuscular ketoprofene 50mg was used after the surgery every 12 hours for two days. During the surgery days there were an average of five teams with a gynecologist and resident or student as auxiliaries.

Six days after the surgery the animals were sacrificed using an intravenous injection of potassium 10% and then re-operated systematically. The animals that died before the sixth day were evaluated for adhesion prevention according to established criteria. In order to evaluate adhesion, a paramedian pararectal incision was performed and then photographed (Figure 3). This incision was larger than the primary. The bovine pericardium used is a Brazilian one (bovine pericardium Hpbio®).The adhesions were assessed and catalogued according to the Adhesion Scoring Group – EUA, 1994 designated MCASM (more comprehensive adhesion score method). Though progress has been achieved, it is difficult to point out the best method to identify and quantify aspects of focal adhesion. The new method establishes more efficient identification of the place adhesion is formed and also the identification of the adhesion severity. The adhesion fixation grade was classified from 0 to 3 and the adhesion extension grade from 0 to 4. These grades can be summed or multiplied independently. The grades in the present analysis were summed. The abdominal wall suture results were used as control (internal control) because only half of the suture was covered by the bovine pericardium. In the uterus, the inside control was the posterior uterine wall and external control was characterized by the comparison of CG and EG. The other classification utilized was ¨Adhesion Extension in Experimental Lesion¨(AEEL).

Figure 3. Midline lesion (MLL). External paramedian pararectal laparotomy showing adhesions covering the entire suture, omentum and the thin bowel fixation.

The analyzed data were: 1 – a number that characterized each animal; 2 – the measure of the incision extension; 3 – the measure of the adhesion extension; 4 – adhesion intensity; 5 – structures related to the adhesion (if the omentum were adhered to the bladder, and the bladder were adhered to the uterus lesion, the sum of the grades would be done separately, according to MCASM). 6 – percentage of the adhesion area related to the lesion extension or related to the membrane; 7 – animal weight; 8 – surgery time in minutes ; 9 – the date the animal was sacrificed; 10 – complications; 11 – reasons for animal exclusion; 12 – Intravenous Cefazolin dosage in the beginning of the surgery; 13 – MCASM-SUM; 14 – MCASM average/animal; 15 – AEEL-SUM(25); 16 – AEEL average/animal (these two last criteria are from our group research in 1991 in which only the percentage of compromised lesion was used). The same analysis was performed

for the uterus lesion. The force-inducing adhesion was catalogued in the following degrees: Degree I – the adhesion inducing lesion showed an average sum less than or equal to 25% of the possible grade for that lesion. Second Degree – the adhesion inducing lesion showed an average sum between 26% and 50% of the possible grade for that lesion. Third Degree – the adhesion inducing lesion showed an average sum between 51% and 75% of the possible grade for that lesion. Fourth Degree – the adhesion inducing lesion showed an average sum higher than 75% of the possible grade for that lesion.

The animal exclusion criteria for the experimental group were: a- animals that did not survive at least three days after the surgery. b- animals that developed severe post-operative infection at the place where the surgery took place. c- animals that developed intense suture dehiscence after the surgery, with or without infection.

Experimental group exclusion criteria: the experimental group should be excluded if there was animal loss in a rate equal or larger than 60%. Statistical analysis were performed by the Epi Info program. The analyses were based on average weight, surgery time and adhesion grades. ANOVA test and Kruskal Wallis tests were used to assess the data.

The rejection level of the null hypothesis was established in 5% (p<0,05), identified on the table or chart by an asterisk.

RESULTS

Two animals were excluded from the Control Group (CG) and one from the Experimental Group (EG). Animal 1 was excluded because of its death on the first day after the surgery and animals 2 and 3 because of severe infection. Consequently the study was concluded with eight animals in the CG and nine animals in the EG.The average weight of the animals were in 12.50 Kilograms in the CG and 15.66 Kilograms in the EG (p=0.5952). The average time of the surgery was 78.25 minutes in the CG and 77.89 in the EG (p=0.9609). The structures involved in the adhesion were related either to the abdominal wall or to the uterus. They were the omentum, the bladder and the bowel (mainly the thin one) with higher adhesion scores.

Through MCASM for the second lesion (Figure 4) were observed an average of 4.62 in the CG versus 7.55 in the EG (p=0.0055).

Using the AEEL was observed an average of 2.75 in the CG versus 4.77 in the EG (p=0.0155). For the uterine lesion (Figure 5), through MCASM the results were an average of 6.50 in the CG and 6.00 in the EG (p=0.7188) and the AEEL , the results were an average of 4.87 in the CG and 4.33 in the EG (p=0.6155).

DISCUSSION

The abdominopelvic adhesions have been object of a lot of studies over the past years, not only because of the suffering that they cause in patients but also because of the costs for the health care systems. These consequences are well evidenced by bowel occlusion or sub-occlusion, infertility and chronic pelvic pain (Oelsner *et al.*, 1994; Lower *et al.*, 2004; Parker *et al.*, 2004).

As noted in the introduction of this paper, barrier methods, including membranes, gels, viscous solutions or not, have dominated the research in this area. Although researchers have not found the ideal substance yet, there is no doubt that some of these methods are useful in clinical practice. Some authors (Johns, 2001; Ahmad *et al.*, 2008) found pelvic adhesion prevention level 1 in three barrier methods (Interceed®, Seprafilm®, GoreTex®).

Figure 4. Midline lesion: average score for both groups (CG and EG) according the classification used. MCASM-M = average score of the group. AEEL-M = average score of the group. CG= control group. EG= experimental group.

In our country, there is no tradition of research in this field, except for rare cases (Beck *et al.*, 2000). Another factor that complicates investigation of barrier methods is the cost of certain membranes. Regardless, one cannot suggest the use of a specific method of adhesion prevention, as research in recent years offers no degree of security. The proposal for studying the pericardium can be attributed to two aspects: first, the apparent similarity to the Gore-Tex, and second, the fact that the pericardium is routinely used in cardiac surgery in Brazil, with relatively low cost (Braile *et al.*, 1998).

The role of the effectiveness of lesion-inducing peritoneal adhesions, as emphasized by several authors (Florencio *et al.*, 1991; diZerega, 1997; Mutsaers, 2002), has been well documented in this paper, in which adhesions occurred in an intense and extensive form. The choice of inducing lesion, can lead to two types of errors: 1-a small inducing lesion force, can overvalue a method of prevention and 2-with an excessive lesion

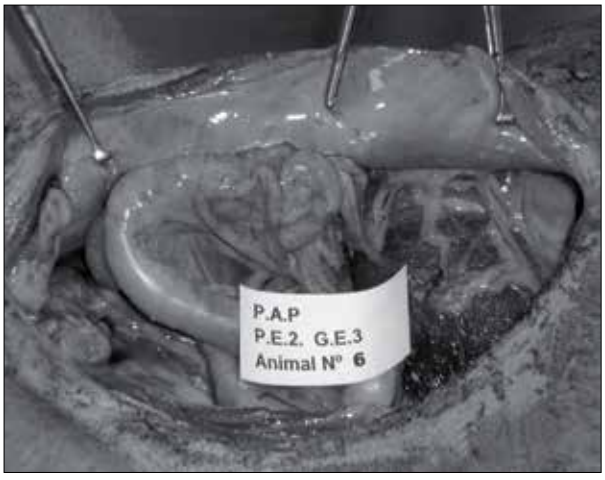

Figure 5. Uterine lesion: average score for the groups (CG and EG) according to the classification used.

inducing force, can assess ineffectively a method that could be effective in humans, in daily practice. In this study we choose strong inducing lesions (adhesions in more than 90% of dogs), independently of the location the majority of adhesions showed a high score on the day of observation (the sixth day after surgery), which allowed this research to be catalogued within the criteria stipulated in the material and methods, such as inductive study with grade IV lesion. Some authors (Hurst, 1999; Rodgers *et al.*, 1998) used in their research, such lesions without binding force, and they reached excellent results in animals but those results were not subsequently confirmed in humans.

In this experiment, some dogs had a score two times greater than the maximum value, also evident in the GE second lesion, in which six of the nine dogs had two structures attached to the lesion site. For example: the dogs that developed omentum adhesion, bowel and omentum adhesion, bladder and bowel adhesion, with a maximum adhesion area, would achieve a score three times greater than the maximum specified. The internal control of the uterus, the posterior uterine wall in such case, showed no adhesion, while the second lesion had high levels of adhesion, mainly in the part that was not used protection in the suture. This fact points out the importance of ischemic injury in the genesis of adhesions.

Once adhesions developed in 100% of the first lesion and in 90% of the second lesion it is possible to claim that the high-strength adhesion of peritoneal sutures are potentially ischemic. Nagele *et al.*, 1996 and Sharma *et al.*, 2002 observed a rate of 10% to 30% of adhesions in non-ischemic conventional sutures in the peritoneum and lower rates in the absence of sutures. In this experiment, the second lesion reached significant levels showing that the BP acted inducing adhesion (Figure 4). However, the examination of adhesion rates in the uterus lesions did not show any difference between CG and EG (Figure 5).According to the results we must emphasize the importance of the classification chosen for this research to be carried out. If we had chosen a simple classification that takes into account only the injured area and not the structures involved and attached to the lesion, as was the case of the classification used in previous studies (Florencio *et al.*, 1991; Rodgers *et al.*, 1998), the results could be totally different and probably would not show that the bovine pericardium caused more adhesions instead of preventing them in the second lesion. Some considerations should be made about the pericardium regarding to its preservation and preparation in order to be used in humans. The product is conserved in a formaldehyde solution and it is valid up to four years. In this experiment, we removed the formaldehyde in five saline washes though only two to four washes are normally necessary. Handling of bovine pericardium is easy and non-absorbable suture does not break the membrane. Up to the present we are not able to assess the impact of the pericardium preservative on the abdominal cavity.

ADDRESS

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CORTE INTERAMERICANA DE DERECHOS HUMANOS
COUR INTERAMERICAINE DES DROITS DE L´HOMME
CÔRTE INTERAMERICANA DE DIREITOS HUMANOS
INTER-AMERICAN COURT OF HUMAN RIGHTS

SECRETARIA DE LA CORTE

San José, 20 de diciembre de 2012
REF.: CDH-12.361/177

Señores Delegados:

Tengo el honor de dirigirles la presente, de conformidad con el artículo 67.1 del Reglamento de la Corte Interamericana de Derechos Humanos, con el propósito de notificarles la Sentencia de fondo, reparaciones y costas dictada por el Tribunal el 28 de noviembre de 2012, en relación con el caso *Artavia Murillo y otros (Fecundación In Vitro)*.

Asimismo, adjunto encontrarán el resumen oficial de la Sentencia para dar cumplimiento a lo señalado en el punto dispositivo sexto de la misma.

Al respecto, me permito informarles que los plazos establecidos en la referida Sentencia para su cumplimiento, así como cualquier otro plazo, empezarán a correr a partir de la notificación del texto íntegro de la misma.

Aprovecho la oportunidad para reiterarles las muestras de mi más alta y distinguida consideración.

Aprovecho la oportunidad para reiterarles las muestras de mi más alta y distinguida consideración.

Pablo Saavedra Alessandri
Secretario

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COSTA RICA, again part of the Latin American Community of ART.

Maria do Carmo Borges de Souza[1] and Roberto Coco[2]

[1] President of Redlara
[2] Vice President of Redlara

It was with great pleasure and enthusiasm that we received the result of the judgment of the Court of Human Rights with regard to the question that was in force in Costa Rica. In the judgment of the Court on November 28 last, won the reason, the desire to provide an offspring when not possible by natural means.
We recognize the efforts of all who participated in this fight, in order to welcome the feelings of a population that suffered the limitation of both their human and reproductive rights.
Carlos Valerio Monge and his fellow public defenders were valiant in Costa Rica and there has been an extraordinary effort in unity uttering opinions of experts, directly participating in public events in Costa Rica, producing opinions and subsidizing the Court with scientific data, giving us all one dimension of what we can do when together and united.
Thanks Fernando Zegers, impeccable referee appointed by WHO and thank you Maria Teresa Urbina, Director of Redlara Region of Venezuela, Colombia and the Caribbean, for their tireless work. Thanks to Ian Cooke, Sheryl Vanderpoel, Santiago Munné, Klaus Wiemer, Vera Raposo and many others who have pledged and glowed, full of enthusiasm to cooperate.
As points Fernando Zegers, the recent decision of the Court of Human Rights requires Costa Rica to re-establish the practice of assisted reproduction and make it enforceable to infertile people. Moreover, it forces the government to provide this service to individuals by a national health program, the latter on the basis of protecting the right to non-discrimination.
Perhaps most relevant to this resounding failure is that explicitly states:

1 - Reproductive rights are part of human rights and the right to found a family and the right to live autonomy privacy must be protected by the countries.
2 - Recognize infertility as a disease of the reproductive system (WHO) that generates a disability. In this context, the prohibition to perform IVF constitute discrimination against persons with a disability
3 - States that the embryo is not subject to the right to life as are the people. That protecting the embryo is exercised through the protection they are entitled to pregnant women (Article 4.1 of the Convention). Explicitly recognizes that conception begins at implantation of the embryo and not the moment of fertilization. The owner of the right to life is the pregnant woman and not the embryo.
4 - Sets that the pre implantation embryos, ie generated by in vitro fertilization techniques, are not subject to current law as individuals. Moreover, explicitly recognizes that the acquisition of status of person, is established through a gradual process and not set immediately with fertilization.
5 – Provides that the right of women to be protected by international right, cannot be affected by laws protecting embryos. That is, explicitly states the woman as head of law and not the embryo.

The ruling also requires the government to pay the costs of the victims and to provide them with psychological support for four years. A complete disclosure in the media and in the Official Journal must be provided and it forces Costa Rica to train and educate the legal persons regarding reproductive rights.
We are at a crucial moment in the history of the fight for reproductive rights, especially to women in the Americas. The Presidency and Board of Directors of REDLARA are very proud of our institution's effective participation in this process as an active part of a moment in history.

RED 11° 2013 CONGRESSO GERAL

Westin Playa Bonita Hotel
Panamá
May 02-04, 2013

Simposia

Merck Serono
Panamanian Society of Gynecology and Obstetrics
IFFS
Genetics

Round tables

Ovarian Stimulation
Andrology
Implantation

Practical Demonstration
IVM
Blastocyst Biopsy

Conferences

And much more!!!

Registration: www.redlara.com/congresso_panama_ing/default.asp

Red Latinoamericana de Reproducción Asistida

2012

FEVEREIRO

04 de fevereiro

Simpósio: Avanços na Medicina Reprodutiva - Interações da clínica com o laboratório
Local: Hotel Windsor Barra - Rio de Janeiro - RJ
Apoio: SGORJ E SBRA
e-mail: ginecologista@cmb.com.br

ABRIL

11 a 14 de abril

V Congresso Mineiro de Ginecologia e Obstetrícia/ XVII Congresso de Ginecologia e Obstetrícia da Região Sudeste/ III Colpominas
Realização: SOGIMIG
Local: Centro de Convenções Expominas – Belo Horizonte/MG
Informações e inscrições:
(31) 3291-9899
www.cmgo2012.com.br

21 a 24 de abril

ASA 37th Annual Meeting - American Society of Andrology
Hilton Tucson El Conquistador / Tucson, Arizona
www.asa.org

MAIO

17 a 20 de maio

The 2nd International Congress on Cardiac Problems in Pregnancy (CPP 2012)
Local: Berlin - Germany
www.cppcongress.com

23 a 25 de maio

38° Congresso Pernambucano de Ginecologia e Obstetrícia
Local: Centro de Convenções - Olinda - PE
Realização: SOGOPE
secretaria@sogope.com.br
http://www.sogope.com.br

24 a 26 de maio

VII Congresso Brasileiro de Climatério e Menopausa
Realização: SOBRAC – Associação Brasileira de Climatério
Local: São Paulo – SP (Centro de Convenções Frei Caneca)
www.menopausa.org.br

30 de maio a 01 de junho

19° Congresso Espírito Santense de Ginecologia e Obstetrícia
Realização: SOGOES
www.sogoes.com.br

JUNHO

07 a 09 de junho

XXXVI Congresso de Ginecologia e Obstetrícia do Rio de Janeiro
Local: Centro de Convenções Sulamérica - Av. Paulo de Frontin, 1 - Cidade Nova - RJ
Realização: SGORJ
sgorj@sgorj.org.br

13 a 16 de junho

I Congresso Goiano de Ginecologia e Obstetrícia
22° Congresso de Ginecologia e Obstetrícia do Brasil Central da FEBRASGO
IV Congresso Internacional de Ginecologia e Obstetrícia de Goiás
37ª Jornada Goiana de Ginecologia e Obstetrícia
Local: Centro de Convenções de Goiânia - Goiás
ginecologia@sggo.com.br

27 a 29 de junho

45º Congresso de Ginecologia e obstetrícia do Distrito Federal,
6º Congresso Internacional de Ginecologia e Obstetrícia do DF e
1º Congresso Internacional de Controvérsias em Ginecologia e Obstetrícia do DF
Local: Centro de Convenções Ulysses Guimarães – Brasília – DF
www.sgob.com.br

28 a 30 de junho

XII Congresso Brasileiro de Ginecologia e Obstetrícia da Infância e Adolescência
Local: Maksoud Plaza Hotel, em São Paulo, SP
http://www.sogorn.com.br

JULHO

1 a 4 de julho

28th Annual Meeting - ESHRE 2012 - Istanbul, Turkey.
European Society of Human Reproduction and Embryology
www.eshre.org

18 a 21 de julho

11º Congresso Brasileiro de Videocirurgia
Local: Windsor Barra Hotel - Rio de Janeiro – RJ
e-mail: congresso@sobracil.org.br
www.sobracil.org.br/congresso

26 a 28 de julho

XI Congresso Sul Brasileiro de Urologia
Hotel Infinity Blue – Recanto das Águas na cidade de Balneário Camboriú – SC.
www.praxis.srv.br

AGOSTO

15 a 18 de agosto de 2012

XXII Congresso Brasileiro de Citopatologia
Local: Mar Hotel - Recife - PE
http://www.xxiicbc2012.com.br/

22 a 25 de agosto

XVI Congresso Brasileiro de Reprodução Assistida Sofitel Jequitimar Guarujá
http://www.sbra2012.com.br/

SETEMBRO

14 a 17 de setembro

63rd Annual Meeting of the German Society of Urology (DGU)
Hamburg – Germany
Organisation:INTERPLAN
E-mail:2011@dgu.de
Website:www.dgu-kongress.de/index.php?id=571

OUTUBRO

7 a 12 de outubro

XX FIGO WORLD CONGRESS OF GYNECOLOGY AND OBSTETRICS
http://www.figo2012.org/fellowship/

10 a 14 de outubro

XIV Simpósio Brasileiro de Patologia do Trato Genital Inferior e Colposcopia e V COLPOVIX
Local: Centro de Convenções de Vitória – ES
Realização: SOGOES
http://www.sogoes.com.br

26 a 26 de outubro

84th Congress of the SIU – Rome – Italy
E-mail:info@siu.it
Website:www.siu.it

25 a 27 de outubro

19º Congresso Baiano de Obstetrícia e Ginecologia
Local: Bahia Pestana Hotel
Realização: SOGIBA
http://www.sogiba.com.br/

28 a 31 de outubro

XVI Congresso Sul-Brasileiro de Ginecologia e Obstetrícia
I Jornada Sul-Brasileira de Mastologia
Costão do Santinho Resort - Florianópolis

Menopur® (menotropina - LH 75 U.I. + FSH 75 U.I.).

USO ADULTO. INDICAÇÕES Mulheres: Esterilidade com insuficiência ovariana hipo – ou normogonadotrófica: estimulação do crescimento folicular, incluindo mulheres com síndrome de ovário policístico que não responderam ao tratamento com citrato de clomifeno. **Homens:** Esterilidade com hipogonadismo hipo – ou normogonadotrófico: em combinação com HCG, para estimular a espermatogênese. **CONTRAINDICAÇÕES Em Mulheres:** tumores na glândula pituitária ou no hipotálamo e no útero, ovários e mamas; gravidez e lactação; sangramento ginecológico de etiologia desconhecida; hipersensibilidade aos componentes da fórmula. aumento dos ovários ou cistos que não tenham sido causados por síndrome de ovário policístico; níveis altos de LH e FSH indicando uma insuficiência ovariana primária. Menopur® não deve ser administrado nos casos de: falência primária ovariana; má-formação de órgãos sexuais incompatíveis com a gravidez; tumor fibroide do útero incompatível com a gravidez. **Em Homens:** câncer de próstata; tumores no testículo. As seguintes condições devem ser tratadas antes do início da terapia: disfunções da glândula tireoide e do córtex da glândula supra-renal; hiperprolactinemia; tumores na glândula pituitária ou no diencéfalo (hipotálamo). **CUIDADOS E ADVERTÊNCIAS** Não deve ser utilizado para induzir a ovulação em mulheres cujos ovários foram involuntariamente hiperestimulados. A terapia requer monitorização da resposta ovariana verificada apenas pela ultrassonografia ou em combinação com a mensuração do nível de estradiol sanguíneo. Alguns pacientes podem apresentar baixa resposta. Pacientes que estão sob estímulo do crescimento folicular para técnicas de reprodução assistida podem apresentar aumento ovariano ou desenvolver hiperestimulação. **Uso em idosos e crianças** Menopur® é um medicamento de uso adulto. **Gravidez e Lactação** Menopur® não deve ser utilizado por mulheres grávidas ou lactentes. **INTERAÇÕES MEDICAMENTOSAS** O uso concomitante de Menopur® com o citrato de clomifeno pode aumentar a resposta folicular. Quando for utilizado um agonista de GnRH, uma dose mais alta de Menopur® deve ser necessária para atingir uma resposta folicular adequada. **REAÇÕES ADVERSAS** dores abdominais, náusea, aumento do abdômen, dor e reação no local da injeção, cefaleia, hiperestimulação dos ovários, dor pélvica, febre, ascite, hidrotórax, oligúria, hipotensão e fenômenos tromboembólicos. Em casos muito raros, pode causar a formação de anticorpos tornando o tratamento ineficaz. **POSOLOGIA** Para indução do crescimento folicular em procedimentos de baixa complexidade (coito programado e inseminação intrauterina) em mulheres normo ou hipogonadotróficas a dose depende da reação ovariana, a qual deve ser definida através de exames ultrassonográficos dos ovários e mensuração dos níveis de estradiol. Se a dosagem de Menopur® for muito alta, podem ocorrer crescimentos foliculares uni e bilaterais múltiplos. Em geral, a terapia é iniciada dentro dos 7 primeiros dias do ciclo menstrual com uma dosagem inicial diária correspondente a 75 - 150 U.I. de FSH. Se os ovários não respondem, a dosagem pode ser gradativamente aumentada até surgirem evidências de aumento da secreção de estradiol e de crescimento folicular. O ajuste na dose não deve ser feito em frequência maior que 7 dias. O tratamento com a mesma dosagem de Menopur® é continuado até atingir-se um nível sérico de estradiol pré-ovulatório. Se o nível aumentar muito rapidamente, a dosagem deve ser reduzida. A dose máxima diária não deve ultrapassar 225 U.I. Caso a paciente não responda após 4 semanas de tratamento, o tratamento deve ser reiniciado com uma dosagem inicial maior do que a do ciclo anterior. Para induzir a ovulação, após uma resposta ótima do tratamento com Menopur®, utiliza-se 5.000 ou 10.000 U.I. de HCG injetado por via intramuscular, 1 dia após a última administração de Menopur®. **Importante:** recomenda-se que a paciente tenha relação sexual no dia e no dia seguinte da administração do HCG. Como alternativa, a inseminação intrauterina pode ser realizada.**OBSERVAÇÃO:** Após a administração de uma dose muito alta de Menopur®, a administração subsequente de HCG pode causar uma hiperestimulação involuntária dos ovários. Neste caso, o tratamento deve ser interrompido tanto com Menopur® ou com HCG e a paciente deverá utilizar um método anticoncepcional ou evitar relações sexuais até o início da próxima menstruação. A dosagem de Menopur® em programas de fertilização assistida (FIV/ICSI) pode variar de pessoa para pessoa. De um modo geral recomendam-se os seguintes esquemas posológicos: Quando for utilizado agonista de GnRH em depósito, a terapia com Menopur® deve ser iniciada aproximadamente 2 semanas após o início do tratamento com o agonista. A dose inicial recomendada de Menopur® é 150 – 225 U.I. por, pelo menos, 5 dias iniciais do tratamento. Baseado na monitorização clínica (ultrassonografia do ovário em combinação ou não com a mensuração do nível de estradiol sanguíneo) as doses subsequentes devem ser ajustadas de acordo com a resposta individual e não devem exceder a quantidade de 150 U.I. por ajuste. A dosagem máxima diária não deve exceder 450 U.I. por dia e na maioria dos casos não é recomendada a utilização acima de 20 dias. Caso não seja utilizado o agonista de GnRH, a terapia com Menopur® deve ser iniciada no 2° ou 3° dia do ciclo menstrual. É recomendada a utilização de esquemas de variação de doses acima citadas. Quando um número adequado de folículos atingir um tamanho apropriado, uma única injeção de 10.000 U.I. de HCG deve ser administrada para induzir a maturação folicular final, na preparação da aspiração de oócitos. As pacientes devem ser cuidadosamente monitoradas por, pelo menos, 2 semanas após a administração de HCG. Caso seja obtida uma resposta em excesso de Menopur®, deve-se interromper o tratamento e descontinuar o uso de HCG e as pacientes devem utilizar um método contraceptivo de barreira (por exemplo: camisinha) ou evitar relações sexuais até iniciar-se a próxima menstruação. **No Homem:** Inicialmente, 1.000 – 3.000 U.I. de HCG são administrados 3 vezes por semana, até atingir-se um nível sérico de testosterona normal. Então, 75 - 150 U.I. de Menopur® são administradas 3 vezes por semana, por alguns meses e de acordo com o critério médico. Orientar a/o paciente quanto ao protocolo de uso, para que não haja comprometimento do sucesso terapêutico. **Venda sob prescrição médica.** Material de uso exclusivo à classe médica. A persistirem os sintomas, o médico deverá ser consultado. Reg. MS: 1.2876.0011 Farm. Resp.: Helena Satie Komatsu - CRF/SP: 19.714 - Laboratórios Ferring Ltda. Praça São Marcos, 624 - 05455-050 - São Paulo – SP / CNPJ: 74.232.034/0001-48 / SAC: 0800 772 4656.

Contraindicação: Para mulheres com tumores no útero, nos ovários e nas mamas. **Interações medicamentosas:** O uso concomitante com o citrato de clomifeno pode aumentar a resposta folicular.

Referências: 1 Ziebe, S. *et al.* Influence of ovarian stimulation with HP-hMG or recombinant FSH on embryo quality parameters in patient undergoing IVF. Human Reproduction, 22(9): 2404-2413, 2007. **2** Weghofer, A. the impact of LH-containing gonadotropin on diploidy rates in preimplantation embryos: long protocol stimulation. Human Reproduction, 23(3): 499-503, 2008. **3** Al-Inany HG, *et al.* Efficacy and safety of human menopausal gonadotrophins versus recombinant FSH: a meta-analysis.Reprod Biomed OnLine.16:81-88, 2008. **4** Coomarasamy, A. Urinary hMG versus recombinant FSH for controlled ovarian hyperstimulation following an agonist long down-regulation protocol in IVf or ICSI treatment: a systematic review and meta-analysis. Human Reproduction, 23(2): 310-315, 2008. **5** Wely, V. *et al.* Recombinant versus urinary gonadotrophin for ovarian stimulation in assisted reproductive technology cycles. Cochrane Database Syst Rev. 16(2):CD005354. Review, 2011. **6** Al-Inany HG. *et al.* Highly purified hMG achieves better pregnancy rates in IVF cycles but not ICSI cycles compared with recombinant FSH: a meta-analysis. Gynecol Endocrinol.25(6):372-8, 2009. **7** Platteau P. *et al.* Highly purified HMG versus recombinant FSH for ovarian stimulation in IVF cycles. Reprod Biomed Online17(2):190-8, 2008. **8** Andersen, AN. *et al.* Clinical outcome following stimulation with highly purified hMG or recombinant FSH in patients undergoing IVF: a randomized assessor-blind controlled trial. Human Reproduction, 21(12): 3217-3227, 2006. **9** Bosch, E. *et al.* Highly purified hMG versus recombinant FSH in ovarian hyperstimulation with GnRH antagonists - a randomized study. Human Reproduction, 23(10): 2346-2351, 2008. **10** Jee BC. *et al.* Clinical efficacy of highly purified hMG versus recombinant FSH in IVF/ICSI cycles: a meta-analysis. Gynecol Obstet Invest., 70(2):132-7, 2010.

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FERRING PHARMACEUTICALS

MEN AN 112 Maio 2012

CONTRIBUINDO PARA MELHORES RESULTADOS[1-7]

Menopur®
menotropina
(FSH 75 U.I. + LH 75 U.I.)

O TRATAMENTO COM MENOPUR® PROMOVE:

- Maior proporção de embriões de alta qualidade quando comparado ao rFSH[1,2]
- Menores níveis de progesterona ao final da estimulação *vs.* rFSH, o que pode resultar em melhor receptividade endometrial para a implantação do embrião[8,9]
- Taxas de gravidez em curso e de nascidos vivos significativamente maiores comparado com rFSH[3-7,10]

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