

Magnesium sulfate is not used for pre-eclampsia and eclampsia in Mexico and Thailand as much as it should be

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Objective In the past ten years effective treatments for pre-eclampsia and eclampsia have been evaluated and identified following large trials and systematic reviews. We investigated the extent of those effective interventions' implementation. **Methods** Descriptive analysis of data collected as part of a cluster randomized trial. The trial was assigned the International Standardised Randomized Controlled Trial Number ISRCTN 14055385. Hospitals with more than 1000 deliveries per year not directly associated with an academic institution in Mexico City municipal area in Mexico ($n=22$) and the north-east region of Thailand ($n=18$) were included. All women delivering at the participating hospitals at two time periods in 2000 and 2002 contributed data on practice rates. The use of magnesium sulfate for pre-eclampsia and eclampsia were the outcomes. **Findings** Eight out of 22 hospitals in Mexico (range 0.8% to 8.5%) and all 18 hospitals in Thailand (range 18.6% to 63.6%) used magnesium sulfate for women with pre-eclampsia. In Mexico, 11 of 22 hospitals used magnesium sulfate for eclampsia (range 9.1% to 60.0%). In Thailand, all 17 hospitals having eclampsia cases used magnesium sulfate (range 25% to 100%). **Conclusion** Despite compelling evidence, magnesium sulfate use is below desired levels. Clinical practices should be audited and implementation of this effective intervention should be taken up as a priority where universal implementation is not in place.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Pre-eclampsia is a multiple organ disorder of unknown etiology usually associated with raised blood pressure and proteinuria. Eclampsia, the occurrence of one or more convulsions (fits), is a rare but serious complication in patients with pre-eclampsia. Pre-eclampsia/eclampsia remains one of the leading problems that threaten safe motherhood, particularly in developing countries. It was estimated that hypertension complicates approximately 5% of all pregnancies and 11% of all first pregnancies.¹ Based on these estimations and case fatality rates, up to 40 000 women could die from pre-eclampsia and eclampsia each year.¹

In a systematic review involving six trials (11 444 women) magnesium sulfate significantly reduced the risk of eclampsia (relative risk, RR 0.41; 95% confidence interval, CI: 0.29–0.58) and the risk of maternal death (RR 0.54; 95% CI: 0.26–1.10) among patients with pre-eclampsia although the latter was not statistically significant.^{2,3} Magnesium sulfate was more

effective than phenytoin for reducing the risk of eclampsia among patients with pre-eclampsia (two trials, 2241 women; RR 0.05; 95% CI: 0.00–0.84).²

Magnesium sulfate appears to be substantially more effective than phenytoin (six trials, 897 women)⁴ or diazepam (seven trials, 1441 women)⁵ for the treatment of eclampsia. Magnesium sulfate is therefore the anticonvulsant of choice for both prevention and treatment of eclampsia.¹

Implementing magnesium sulfate for the prevention and treatment of eclampsia in low- and middle-income countries could potentially benefit hundreds of thousands of women.⁶ This study aims to evaluate the use of magnesium sulfate for women with pre-eclampsia and eclampsia in Mexico and Thailand, where a cluster randomized trial to evaluate an educational strategy to change obstetric practices was conducted. The study methodology was published in detail elsewhere.⁷ The main results related to the effects of the intervention was published separately.⁸

Methods

The study was conducted in two countries: the Mexico City municipal area, Mexico, and the north-east region of Thailand. Maternity units of hospitals with > 1000 deliveries/year that were not associated directly with a university or other academic/research department were eligible to participate. In Mexico, all state and social security hospitals in the Mexico City municipal area were approached. Twenty-two out of 34 hospitals approached were eligible and agreed to participate in the trial. In Thailand, 18 hospitals out of 19 in the north-east region agreed to participate. There were therefore 40 hospitals in this study. The objective of the main trial was to evaluate the improvement in obstetric practices using an active dissemination strategy to promote uptake of recommendations contained in the WHO Reproductive Health Library (RHL).⁹

A multifaceted intervention addressing potential barriers to evidence-based practice was conducted over a

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Discussion

The prevalence of pre-eclampsia and eclampsia in Mexico was 5.5% and 0.6% respectively, which is quite similar to the overall global picture.¹ However, the corresponding rates in Thailand were 1.8% and 0.3%, which are lower. The uses of magnesium sulfate for pre-eclampsia and eclampsia were surprisingly low in Mexico. In Thailand, magnesium sulfate was used more frequently for both pre-eclampsia and eclampsia.

A report on the management of eclampsia from Sweden shows the remarkably increased use of magnesium sulfate: from 8% during 1980–1989 to 83% during 1990–1999.¹⁰ A questionnaire survey of obstetricians in the United Kingdom and Ireland in 1996 indicated that 40% and 60% of respondents would use magnesium sulfate for pre-eclampsia and eclampsia, respectively.¹¹

The very low rate of magnesium use particularly in Mexico is alarming. Magnesium sulfate is reasonably cheap and its effectiveness when used in pre-eclampsia and eclampsia has been clearly shown by evidence from randomized controlled trials and systematic reviews.^{2,12,13} Although magnesium sulfate use for pre-eclampsia and eclampsia in Thailand is much higher than in Mexico, there is

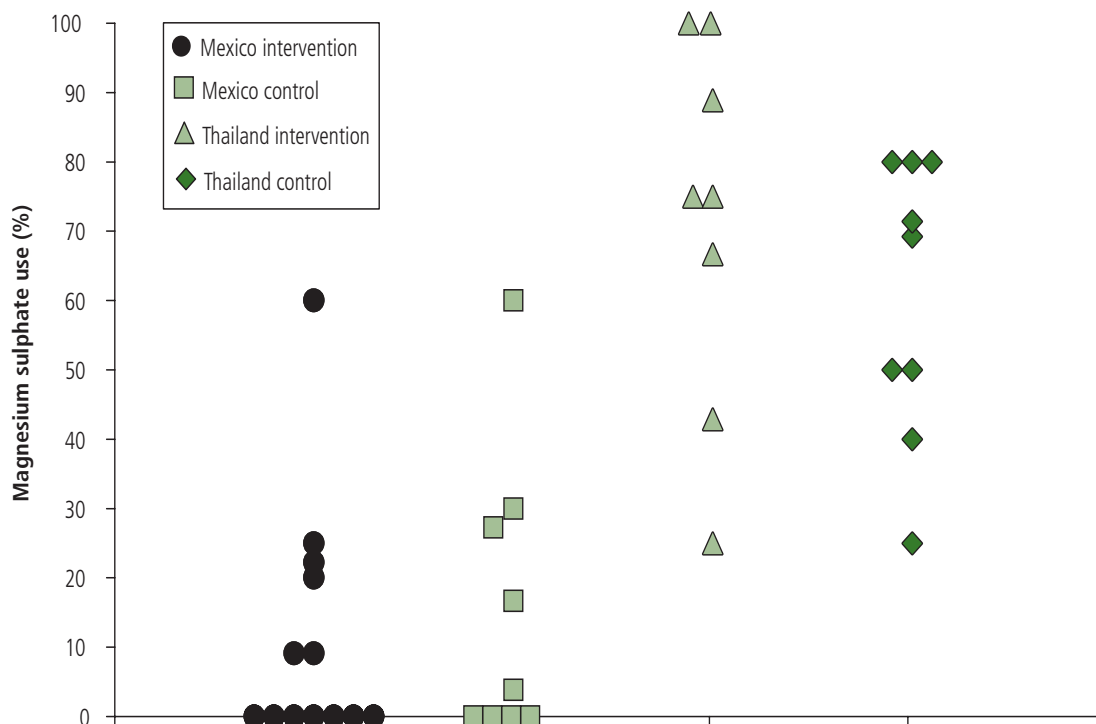
still room for improvement. Magnesium sulfate has been in the National Essential Drug List of Thailand since 1999. As of 2002, there were only 45 countries that had magnesium sulfate in their essential drug list (WHO unpublished data). As of 16 October 2006, the Mexican National Essential Drug List did not include magnesium sulfate (Edición 2005 del Cuadro Básico y Catálogo de Medicamentos, available at: <http://www.salud.gob.mx>). Responsible persons and organizations in these two countries should take immediate actions to ensure wider use of this effective and inexpensive drug for these conditions. Researchers and responsible persons in other low- to middle-income countries should also evaluate the situation regarding this issue and take appropriate actions.

Why has magnesium sulfate not become the treatment of choice particularly for eclampsia throughout the world? There are two possible hypotheses. First, magnesium sulfate is too cheap to motivate mass manufacturing, licensing, production and distribution. Second, health-care providers and administrators may be reluctant to adopt a practice that requires intensive monitoring for a condition (eclampsia) that is relatively infrequent.¹⁴ Not having experience with

magnesium sulfate administration has been proposed as a reason for not using it in the United Kingdom.¹⁵ International organizations have advocated the use of magnesium sulfate in the treatment and prevention of eclampsia.¹⁴ There are often systematic gaps between evidence of effectiveness and what is actually practiced. Failure in the registration, procurement and distribution mechanisms for magnesium sulfate contribute to its poor availability in Mozambique and Zimbabwe.¹⁶ A survey of WHO drug information officers, regulatory officials and obstetricians in 12 countries was undertaken to identify barriers and facilitators to knowledge translation on the use of magnesium sulfate to treat pre-eclampsia. The perceived barriers include drug licensing and availability, inadequate and poorly implemented clinical guidelines, and the lack of political support for policy change.¹⁷ There were significant regional and national differences in the importance of specific barriers.¹⁷

Our report is unique in that we measured actual practices of using magnesium sulfate in pre-eclampsia and eclampsia by extracting data from medical records of a large number of women from 22 hospitals in Mexico and 18 hospitals in Thailand. Based on anecdotal evidence before data collection, we had assumed that mag-

Fig. 2. The rate of magnesium sulfate use for women with eclampsia in Mexico and Thailand (some hospitals did not have any cases)



nesium sulfate would be routinely used in both Mexico and Thailand. For pre-eclampsia we anticipated some variation because the evidence was not strong at the time. The Magpie trial was published in June 2002.¹⁸ However, the use of phenytoin for pre-eclampsia and eclampsia in Mexico was surprising. These data highlight the importance of collecting actual practice data rather than reported behaviour, which can often overestimate the quality of care.

Our data has the limitation of being retrospective. The quality of data might be somewhat limited to the standards of patient records in the two countries. However, both pre-eclampsia and eclampsia are serious conditions where women are hospitalized, and it is unlikely that magnesium sulfate would have been used but not recorded.

We conclude that magnesium sulfate is not as widely used for preventing and treating eclampsia as it should be, in spite of its inexpensiveness and the very clear evidence about its effectiveness. Immediate actions are necessary to promote its use in all countries around the world, including insertion in National Essential Drug Lists. Organizations, such as the International Federation of Gynecology and Obstetrics (FIGO) and the International Confederation of Midwives (ICM), their national counterparts and other professional organizations should advocate for the availability and use of magnesium sulfate, assist in the development of local treatment protocols to follow and training of health-care workers in the use of magnesium sulfate. Given the paucity of evidence to select appropriate strategies for implementation,

research projects to evaluate innovative approaches to implement magnesium sulfate treatment are of high priority in low- and middle-income countries. ■

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Résumé

Dans la municipalité de Mexico et en Thaïlande, le sulfate de magnésium n'est pas utilisé autant qu'il le devrait pour traiter les prééclampsies et les éclampsies

Objectif Au cours de la dernière décennie, des essais de grande ampleur et des revues systématiques de la littérature ont permis d'évaluer et d'identifier des traitements efficaces contre la prééclampsie et l'éclampsie. Nous avons examiné dans quelle mesure ces interventions efficaces étaient appliquées.

Méthodes Analyse descriptive des données recueillies dans le cadre d'un essai randomisé par grappes, ayant reçu le numéro d'essai contrôlé randomisé reconnu au plan international ISRCTN 14055385. Ont participé à l'étude les hôpitaux pratiquant plus de 1000 accouchements par an et non-associés directement à un établissement d'enseignement supérieur de la municipalité de Mexico (Mexique) (n = 22) et de la région nord-est de la Thaïlande (n = 18). Des données sur les fréquences de certaines pratiques ont été recueillies pour toutes les femmes ayant accouché dans les hôpitaux participant à l'étude pendant l'une des deux périodes étudiées, 2000 et 2002. L'étude visait à déterminer les taux d'utilisation

du sulfate de magnésium contre la prééclampsie et l'éclampsie.

Résultats Huit des vingt-deux hôpitaux de Mexico (taux d'utilisation : 0,8 - 8,5 %) et la totalité des 18 hôpitaux thaïlandais (taux d'utilisation : 18,6 - 63,6 %) utilisaient du sulfate de magnésium pour traiter les femmes dans un état prééclamptique. Dans la municipalité de Mexico, 11 des 22 hôpitaux faisaient appel à ce produit contre l'éclampsie (taux d'utilisation : 9,1 - 60,0 %). En Thaïlande, la totalité des 17 hôpitaux accueillant des cas d'éclampsie ont utilisé du sulfate de magnésium (taux d'utilisation : 25 - 100 %).

Conclusion Malgré les preuves éloquentes de son utilité, la fréquence d'administration du sulfate de magnésium est encore inférieure au niveau souhaitable. Une inspection des pratiques cliniques devrait être réalisée et la mise en œuvre de cette intervention efficace devrait être considérée comme une priorité partout où elle n'est pas universelle.

Resumen

El sulfato de magnesio se utiliza menos de lo necesario en los casos de preeclampsia y eclampsia en México y Tailandia

Objetivo En los últimos diez años se han evaluado e identificado los tratamientos más eficaces para la preeclampsia y la eclampsia mediante grandes ensayos y revisiones sistemáticas. Decidimos investigar el grado de aplicación de esas intervenciones eficaces.

Métodos Se llevó a cabo un análisis descriptivo de datos recopilados como parte de un ensayo aleatorizado por conglomerados. Se incluyeron en el ensayo -código ISRCTN (International Standardised Randomized Controlled Trial Number) 14055385- hospitales con más de 1000 partos al año no vinculados directamente a instituciones académicas situados en el término municipal de Ciudad de México (n = 22) y en el noreste de Tailandia (n = 18). Todas las mujeres que dieron a luz en los hospitales participantes en dos periodos de 2000 y 2002 aportaron datos sobre la atención recibida. Los resultados considerados

fueron el uso de sulfato de magnesio contra la preeclampsia y contra la eclampsia.

Resultados Ocho de los 22 hospitales de México (intervalo: 0,8% - 8,5%) y los 18 hospitales de Tailandia (intervalo: 18,6% - 63,6%) trataron con sulfato de magnesio a las mujeres con preeclampsia. En México, 11 de los 22 hospitales utilizaron sulfato de magnesio contra la eclampsia (intervalo: 9,1% - 60,0%). En Tailandia, la totalidad de los 17 hospitales con casos de eclampsia administraron sulfato de magnesio (intervalo: 25% - 100%).

Conclusión Pese a lo contundente de la evidencia, el uso de sulfato de magnesio es inferior a lo deseable. Es necesario revisar la práctica clínica, y la aplicación de esta intervención eficaz debería considerarse una prioridad en los casos en que no se ha implantado de forma universal.

ملخص

نقص كمية سلفات المغنيزيوم المعطاة لمعالجة مقدمات الارتعاج والارتعاج في المكسيك وتايلاند

الغرض: تم في السنوات العشر الماضية تحديد وتقييم عمليات المعالجة الفعّالة لمقدمات الارتعاج والارتعاج، بعد تجارب ودراسات منهجية موسّعة. وقد استهدفت هذه الدراسة تقصي مدى تنفيذ تلك التدخلات الفعّالة.

الطريقة: استُخدم في الدراسة التحليل الوصفي للبيانات التي جُمعت في إطار تجربة عنقودية معشاة. وقد أُعطي لهذه التجربة رقم 14055385 ISRCTN، وهو يمثل الرقم الدولي المعياري للتجارب المعشاة المضبوطة بالشواهد. وقد شملت التجربة المستشفيات التي يزيد عدد الولادات التي تُجرى بها في كل عام على 1000 ولادة، والتي لا ترتبط مباشرة بأي مؤسسة أكاديمية، وذلك في كل من المنطقة البلدية لمدينة مكسيكوسيتي بالمكسيك (وعددتها 22 مستشفى)، ومنطقة شمال شرقي تايلاند (وعددتها 18 مستشفى). وقد قُدّمت جميع السيدات اللاتي ولدن في المستشفيات المشاركة في الدراسة في فترتين زمنيّتين، هما عامي 2000 و2004، بيانات عن معدلات إعطاء سلفات المغنيزيوم. وكان معدل استخدام سلفات المغنيزيوم لمعالجة

الارتعاج ومقدمات الارتعاج هو حصيلة البيانات.

الموجودات: تبين أن 8 مستشفيات من جملة 22 مستشفى في المكسيك (بمجال يتراوح من 0.8% إلى 8.5%)، وأن جميع مستشفيات تايلاند البالغ عددها 18 مستشفى (بمجال يتراوح من 18.6% إلى 63.6%) قد أعطت سلفات المغنيزيوم للسيدات اللاتي عانين من مقدمات الارتعاج. وفي المكسيك، أعطى 11 مستشفى من جملة 22 مستشفى سلفات المغنيزيوم لمعالجة الارتعاج (بمجال يتراوح من 9.1% إلى 60%). وأما في تايلاند، فقد أعطت جميع المستشفيات التي واجهت حالات ارتعاج، والبالغ عددها 17 مستشفى، سلفات المغنيزيوم (بمجال يتراوح من 25% إلى 100%).

الاستنتاج: برغم البيّنات القاطعة، لا يزال استخدام سلفات المغنيزيوم دون المستويات المنشودة. وينبغي مراجعة الممارسات السريرية في هذا الشأن، وإعطاء أولوية لتنفيذ هذه الممارسة الفعّالة في المناطق التي لا تنفذ فيها بشكل شامل.

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