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ФЕНОМЕН ЭКСАЙТОТОКСИЧНОСТИ. МЕХАНИЗМЫ ВОЗНИКНОВЕНИЯ, ЗНАЧЕНИЕ В РАЗВИТИИ НЕЙРОНАЛЬНОГО ПОВРЕЖДЕНИЯ И ВОЗМОЖНОСТИ ЕГО КОРРЕКЦИИ ПРИ ПАТОЛОГИЯХ ЦНС

Резюме. *Проведен аналитический обзор мировой литературы, в которой освещены взгляды на механизмы возникновения феномена эксайтотоксичности, а также его значение в развитии нейронального повреждения при острых патологиях ЦНС. Рассмотрено возможности влияния на феномен эксайтотоксичности при различных патологических состояниях.*

Ключевые слова: *феномен эксайтотоксичности, нейрональное повреждение, лечение.*

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PHENOMENON EXITOTOXICITY. OCCURRENCE MECHANISMS, VALUE IN DEVELOPMENT NEURONAL OF DAMAGE AND POSSIBILITY OF ITS CORRECTION AT PATHOLOGIES CNS

Summary. *The state-of-the-art review of the world literature in which sights mechanisms of occurrence of the phenomenon exitotoxicity, and also its value in development neuronal damage are shined at sharp pathologies CNS. It is considered possibilities of influence on a phenomenon exitotoxicity at various pathological conditions.*

Key words: *a phenomenon exitotoxicity, neuronal damage, treatment.*

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THE MODERN CLINICAL ASPECTS IN OBSTETRICIANS TRAINING

Summary. *This review summarises recent progress in the evaluation of the effectiveness of simulation training for maternity care in the world, and presents a vision for ensuring that practical simulation training for maternity care can become an effective tool to reduce global maternal and perinatal morbidity and mortality.*

Key words: *pregnancy, simulation training for maternity care, shoulder dystocia, eclampsia, postpartum haemorrhage, neonatal resuscitation.*

Improving maternal and perinatal care is a global priority. The World Health Organization (WHO) has estimated that 1000 women die every day from preventable complications of pregnancy and childbirth [World Health Organization, 2010]. Worldwide, there are approximately four million neonatal deaths each year and a similar number of stillbirths [Lawn et al., 2005]. On the basis of these factors, it is not surprising that the maternal mortality rate (MMR) in the US is greater than in countries of comparable socioeconomic resources. In 2005, the MMR was 8 per 100,000 live births in the UK but 11 per 100,000 live births in the US.2 The US government's Healthy People 2010 target is no more than 3.3 maternal deaths per 100 000 live births. In contrast, the rate was 1 per 100,000 live births in Ireland [World Health Organization, 2010]. However, unified curriculum for multidisciplinary teams caring for obstetric patients, which includes strategies to initiate resuscitation, accomplish birth quickly after maternal arrest and coordination of efforts with other resuscitation teams does not exist.

Practical simulation training for maternity care might prevent many of these deaths. Simulation training in obstetrics is not new. In 1748, Madame du Coudray, the King of France's midwife, developed a life-size mannequin from leather and bone to teach the management of childbirth.3 She trained local doctors who, in turn, trained local women. In this way, du Coudray disseminated practical training, enabling hundreds of women in France to experience safer childbirth [Gelbart, 1998]. Over 250 years later, there appeared to have been little progress; a systematic review of obstetric emergencies training published in 2003 concluded that few methods of training had been evaluated, and there was minimal evidence of their effectiveness [Black, 2003]. Medical simulation is an educational method that incorporates mannequins of varying anatomical and physiological fidelity and/or patient actors, to allow individuals and teams to practice clinical situations in an environment that causes no risks or discomfort to patients, and poses less time restrictions and less constrains for the provision of feedback. Several aspects of competence can be targeted in simulation based sessions, including knowledge, skills, and attitudes; as well as teamwork skills such as communication, task distributions, and team support. Establishing the educational objectives of the simulation session and the target audience that it is aimed at, are crucial

aspects of the process, and ones that are profoundly affected by the availability of adequate simulators [Draycott et al., 2006; Scholefield, 2007; Draycott et al., 2008; Maouris et al., 2010; Carlo et al., 2010]. This review summarises the 10 years of progress since 2003 and presents a vision for ensuring that practical simulation training for maternity care can become an effective tool to reduce global maternal and perinatal morbidity and mortality.

One of the first published descriptions of obstetric simulation was an eclampsia drill [Draycott et al., 2000]. The simulation of eclampsia enabled departmental staff to develop and trial an eclampsia box containing the equipment, drugs and guidelines required to manage this rare emergency. A randomized controlled trial comparing the effectiveness of multiprofessional training for eclampsia in local hospitals with training in a regional simulation centre showed marked improvement in all aspects of care after training [Ellis et al., 2008]. Training at local sites involved patient-actors, whereas a high-fidelity, full-body simulator was used at the simulation centre; 140 midwives and obstetricians were randomly allocated to local or simulation centre training. Following training, there were significant improvements in the completion of basic tasks (87%, 100%) and in the administration of magnesium sulphate (61%, 92%) in simulated eclampsia. The time taken to commence the administration of magnesium was, on average, nearly 2 minutes quicker following training. There were equal improvements in both settings; it was the training itself, rather than the location or the simulation equipment used, that appeared to be the key to success [Ellis et al., 2008].

Shoulder dystocia is an unpredictable and therefore unpreventable emergency. A large, multisite, randomised controlled trial demonstrated that the management of shoulder dystocia before training was often poor, with only 43% of staff able to successfully manage severe shoulder dystocia [Crofts et al., 2006]. Following a 40-minute practical training session undertaken in multiprofessional teams, there was a significant improvement in the proportion of participants who successfully achieved simulated delivery (43% pre- and 83% post-training). This improvement was largely sustained at 6 months (84%) and 12 months (85%) after training. Training on a high-fidelity mannequin (which included force-perception teaching) offered additional benefit when compared with training on standard equipment; after training, there was a higher successful delivery rate (72%, 94%) and, on average, the deliveries were completed more quickly with a lower total force applied. S.H. Deering et al. and D. Goffman et al. separately demonstrated improved performance of advanced shoulder dystocia maneuvres following simulation training [Deering et al., 2004; Goffman et al., 2008]. [Deering et al., 2004] found that obstetric trainees who had undergone simulation training scored better for the timeliness of both completion of maneuvres and delivery compared with those who had received conventional training. Of greater importance is the effect of shoulder dystocia training on clinical outcomes. A retrospective review over an 10-year period compared birth outcomes for shoulder dystocia before and after the introduction of a local training program in one UK hospital using a prototype PROMPT Birthing Trainer (Limbs and Things Ltd, Bristol, UK) [Draycott et al., 2008]. Following the introduction of training, there was a significant increase in the use of appropriate management manoeuvres, with at least one appropriate manoeuvre used in 90% of cases after training, compared with <50% before. Moreover, the use of excessive traction fell from 54% to 24%. In conjunction with the improvements in clinical management, there was an associated improvement in clinical outcomes. Obstetric brachial plexus injury (OBPI) and/or bony fracture in cases of shoulder dystocia fell from 9,3% before training to 2,3% afterwards [Draycott et al., 2008]. Similar improvements in neonatal outcomes have also been demonstrated after the introduction of annual multiprofessional simulation training for all staff in an American hospital. The OBPI rate after shoulder dystocia decreased from 30% before training to 10,7% after training [Inglis et al., 2011]. Not all training has been found to be effective; introduction into another UK hospital was associated with a higher rate of OBPI [MacKenzie et al., 2007]. This suggests that not all training is equal in effect.

Postpartum haemorrhage (PPH) contributes to 140 000 deaths worldwide [Abou Zahr, 2003]. Deering et al. studied the simulation of PPH secondary to uterine atony with 40 obstetric trainees [Deering et al., 2009]. Only 45% controlled the haemorrhage within 5 minutes, and 48% made medication errors. Birch et al. compared lecture-based training with simulated drills in the management of PPH. All participants showed increased knowledge following training, but those who had undergone simulation training also improved team working skills when compared with those who had only lectures [Birch et al., 2007]. Maslovitz et al. demonstrated that simulation training for PPH enabled the identification of common errors which allowed targeted teaching and training. This training was associated with an improvement in management, which was still evident 6 months later [Maslovitz et al., 2007]. The common errors identified were a lack of knowledge of medication, delay in transfer to theatre and underestimation of blood loss.

The appropriate and safe use of forceps and vacuum instruments to assist vaginal birth is an essential obstetric skill [Patel et al., 2004]. Dupuis et al. developed a high-fidelity model that allows the trajectory of the application of forceps blades to be tracked using spatial sensors. Senior obstetricians demonstrated a superior technique but, after training, the abilities of junior staff improved [Dupuis et al., 2006]. Other models have been developed to train medical trainees in appropriate traction. After practical training, both the correct forces and successful delivery were achieved more often in simulated instrumental births [Leslie et al., 2005; Moreau et al., 2008].

A systematic review concluded that perinatal mortality might be reduced if birth attendants received practical neonatal resuscitation training, but the evidence of

effectiveness was not strong [Bhutta et al., 2005]. More recent studies have evaluated the effect of the WHO Essential Newborn Care course, a neonatal rather than obstetric training course. One study using a before-and-after implementation design showed that training staff on the course was associated with improvements in midwives' skills and knowledge. There was also a reduction in early neonatal deaths among low risk women who delivered in first-level clinics in Zambia [McClure et al., 2007]. A cluster randomised controlled trial to assess this neonatal resuscitation intervention did not concur with these initial findings, however [Carlo et al., 2010]. Following the introduction of the 3-day Essential Newborn Care course in six countries (Argentina, Democratic Republic of Congo, Guatemala, India, Pakistan and Zambia), there was no significant reduction in the rate of early neonatal deaths or in the rate of perinatal death. Interestingly, there was a significant reduction in the rate of stillbirth (relative risk with training, 0,69). It is plausible that the observed reduction in stillbirths might have been the result of training; before training, infants born without obvious signs of life may have been misidentified as stillbirths. After training, resuscitation was more likely to be attempted, with a consequential reduction in births classified as stillbirths. The decrease in fresh stillbirths, but not in macerated stillbirths, after the introduction of the Essential Newborn Care training program supports this hypothesis [Carlo et al., 2010]. Promising preliminary observations of the effect of the Helping Babies Breathe program have been presented recently [Ersdal, 2011]. This is an educational training program for low-resource countries that aims to improve neonatal resuscitation using basic simulation scenarios. Preliminary analysis of 13 575 births in Tanzania revealed a significant decrease in early neonatal mortality from 13,4 to 6,3 deaths per 1000 live births after the implementation of training [Siassakos et al., 2009].

A review of training programs associated with improvements in clinical outcomes was published in 2009 [Schouten et al., 2008] Common features of clinically effective training programmes were as follows: multiprofessional training; training of all staff in an institution; training staff locally within the unit in which they work; Integrating teamwork training with clinical teaching; use of high-fidelity simulation models; institution-level incentives for training (e.g. reduced hospital insurance premiums); use of self-assessment to direct infrastructural changes.

There has been significant progress in the evaluation of simulation training for maternity care over the last 10 years. Evidence has begun to move from the subjective assessment of participants' experiences towards the objective assessment of clinical outcomes. However, at present, all of the evidence associating training with improvements in clinical outcomes relates to neonatal outcomes. There are no studies that objectively demonstrate improvements in maternal morbidity or mortality. Clearly, more research is required to investigate the clinical effectiveness of simulation training on maternal outcome. Quality improvement programs, including training interventions, have been more successful in some organizations than in others [Dixon-Woods et al., 2011]. This variation might be a consequence of local contextual factors: differences in organisational preconditions, readiness at program onset, interpretation of the intervention and local implementation strategies. A recent review of the Matching-Michigan central venous line project identified six key elements through which the project achieved its effects [Centre for Maternal Child Enquiries, 2011]. These might be equally relevant to simulation training programs.

There have been significant changes in the causality of direct maternal deaths in the UK [Hofmeyr et al., 2009]. Sepsis is now the leading cause of direct maternal death. Severe maternal sepsis is a rare obstetric emergency and, at present, there are no published data on its simulation. With the development of novel, whole-body, computer-controlled mannequins, there is the opportunity for the simulation of more complex clinical conditions, such as severe sepsis. Simulation may be a training tool that can be used to increase the awareness of the presentation and clinical management of sepsis, as well as of other complex clinical situations.

A recent review of training used to improve neonatal and child outcomes in low- and middle-income countries, published by WHO, concluded that:

Where in-service training can be provided at a low cost, it may be worthwhile to do so, given that some improvements in care process can be expected. However, in general, such training may be associated with high cost and therefore for most settings it is difficult to justify the conduct of routine in-service neonatal and paediatric training courses primarily based on models developed in high-income countries.

Although this review did not evaluate the effectiveness of training programmes for maternity care per se, as obstetricians, midwives, anaesthetists and neonatologists we should heed the authors' recommendations. The authors propose that the success of in-service training of health-care professionals depends on a number of factors, but two are especially important: appropriately skilled instructors in sufficient numbers and suitable, locally adapted training materials.

Many courses have been developed that include simulations of obstetric emergencies to train staff in low-resource settings. Examples include the Pacific Emergency Obstetric Course (www.psrh.org.nz), the Life Saving Skills Course (www.rcog.org.uk/international) and the Practical Obstetric Multi-Professional Training (PROMPT) course (www.prompt-course.org). Challenges, in addition to those outlined above, include the wide variation in local settings, practices and staffing, as well as under-resourced health services that are often overwhelmed. Care must be taken to ensure that areas with the highest maternal and neonatal mortality and, perhaps, with the most need for training are given appropriate support to develop and evaluate sustainable, clinically effective training programmes.

Conclusions. Significant progress has been made over

the last 10 years in the availability, and evidence supporting the use, of practical simulation training for maternity care. New training courses have been planned, implemented and evaluated, and new training equipment has been developed. There is an increasing global effort to ensure that training reaches all those in need, not just those with sufficient financial resource. We must ensure that training, in whatever setting, is both clinically and cost-effective, and sustainable. Simply exporting maternity training courses that have been effective in one setting might not achieve the same improvements in morbidity and mortality in others. There is a need for continued research to measure the effect of training on clinical outcomes in a wide variety of clinical settings to establish what works, where and why. Future work must also study the implementation and sustainability of training programmes, evaluating the costs of, and human resources needed for, the conduct of training for maternity care in both low- and high-income settings.

Perspectives. Recent research has highlighted the potential of practical simulation for maternity care to improve outcomes for mothers and their babies. We must ensure that there is continued development, evaluation and dissemination of clinically effective training equipment and courses to ensure that maternity staff, in all clinical settings, have the necessary skills required to prevent unnecessary maternal and neonatal morbidity and mortality.

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СОВРЕМЕННЫЕ КЛИНИЧЕСКИЕ АСПЕКТЫ ПОДГОТОВКИ АКУШЕР-ГИНЕКОЛОГОВ

Резюме. *В настоящем обзоре обобщены последние достижения по оценке эффективности имитационного обучения относительно охраны материнства и представляет собой видение обеспечения практической подготовки моделирования для охраны материнства, что может стать эффективным инструментом для сокращения материнской, перинатальной заболеваемости и смертности.*

Ключевые слова: *беременность, моделирование обучения по охране материнства, дистоция плечиков, эклампсия, послеродовое кровотечение, реанимация новорожденных.*

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СУЧАСНІ КЛІНІЧНІ АСПЕКТИ ПІДГОТОВКИ АКУШЕР-ГІНЕКОЛОГІВ

Резюме. *У даному огляді узагальнені останні досягнення по оцінці ефективності імітаційного навчання відносно особливостей охорони материнства і являє собою бачення забезпечення практичної підготовки моделювання для охорони материнства, що може стати ефективним інструментом для скорочення материнської, перинатальної захворюваності і смертності.*

Ключові слова: *вагітність, моделювання навчання з охорони материнства, дистоція плечиків, еклампсія, післяпологова кровотеча, реанімація новонароджених.*

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ЕКСПЕРИМЕНТАЛЬНІ МІОМИ МАТКИ

Резюме. *Для експериментального створення фіброми необхідне безперервне і тривале введення гормональних препаратів естрогенної дії, дози яких значно перевищують патологічний рівень ендогенних гормонів, який можливий у хворих міомою матки. Морфогенез експериментальних фібром відрізняється від міом матки переважно сполучнотканинною структурою. Експериментальні роботи дозволили простежити розвиток у матці фібром, а не міом.*

Ключові слова: *міома матки, експеримент, гормони.*

Вступ

Незважаючи на велику кількість досліджень, які здавалося б розкрили багато питань патогенезу, діагностики, лікування міоми матки, кількість публікацій, дисертацій, присвячених цій патології, в останні роки не зменшується [Вихляєва, Палладі, 1982; Савицкий и др., 1986;; Яковлева, Кукуте, 1997; Тихомиров, Лубнін, 2006; Brosens, 2006; Стрижаков та ін., 2008]. Великий інтерес до цієї проблеми пов'язаний насамперед з високою частотою міоми матки та різними патогенетичними варіантами її розвитку.

Експериментальні роботи лягли в основу обґрунтування естрогенної теорії міоми, але виявили багато суперечливих результатів. Ми вважаємо за необхідне проаналізувати ці роботи з метою підтвердження інших варіантів розвитку міоми матки.

Фіброму матки вдалося відтворити в експерименті не у всіх тварин. Високу чутливість до естрогенів виявляє морська свинка [Lipschutz et al., 1938; Кленицький, 1950; Гилязутдинова, 1967; Мейпалу, 1968].

Спроба одержати міому у ближчих до людини тварин - мавп, завершилася лише поодиноким дифузним потовщенням у деяких ділянках матки. A. Lipschutz [1942] повідомив, що йому із співробітниками не вдалося одержати абдомінальні фіброми в пацюків навіть при введенні значно більшої кількості естрадіолу, ніж це потрібно було для морських свинок.

Суперечливість у своїх міркуваннях щодо патогенезу міоми матки допустив Я.С. Кленицький [1966], який у своїй монографії, присвяченій міомі, писав, що фіброїди, одержувані експериментальним шляхом, своєю будовою відрізняються від міоми матки і це є одним із контраргументів щодо естрогенної теорії міоми. Надалі ж він вказує, що остаточно переконливим фактом, який підтверджує роль гіперестрогенії в патогенезі міом матки є "одержання істинних міом матки в результаті тривалого введення тваринам великих доз естрогенних гормонів". E. Novak [1955], висловлюючись з приводу експериментальних робіт A. Lipschutz [1942] і його