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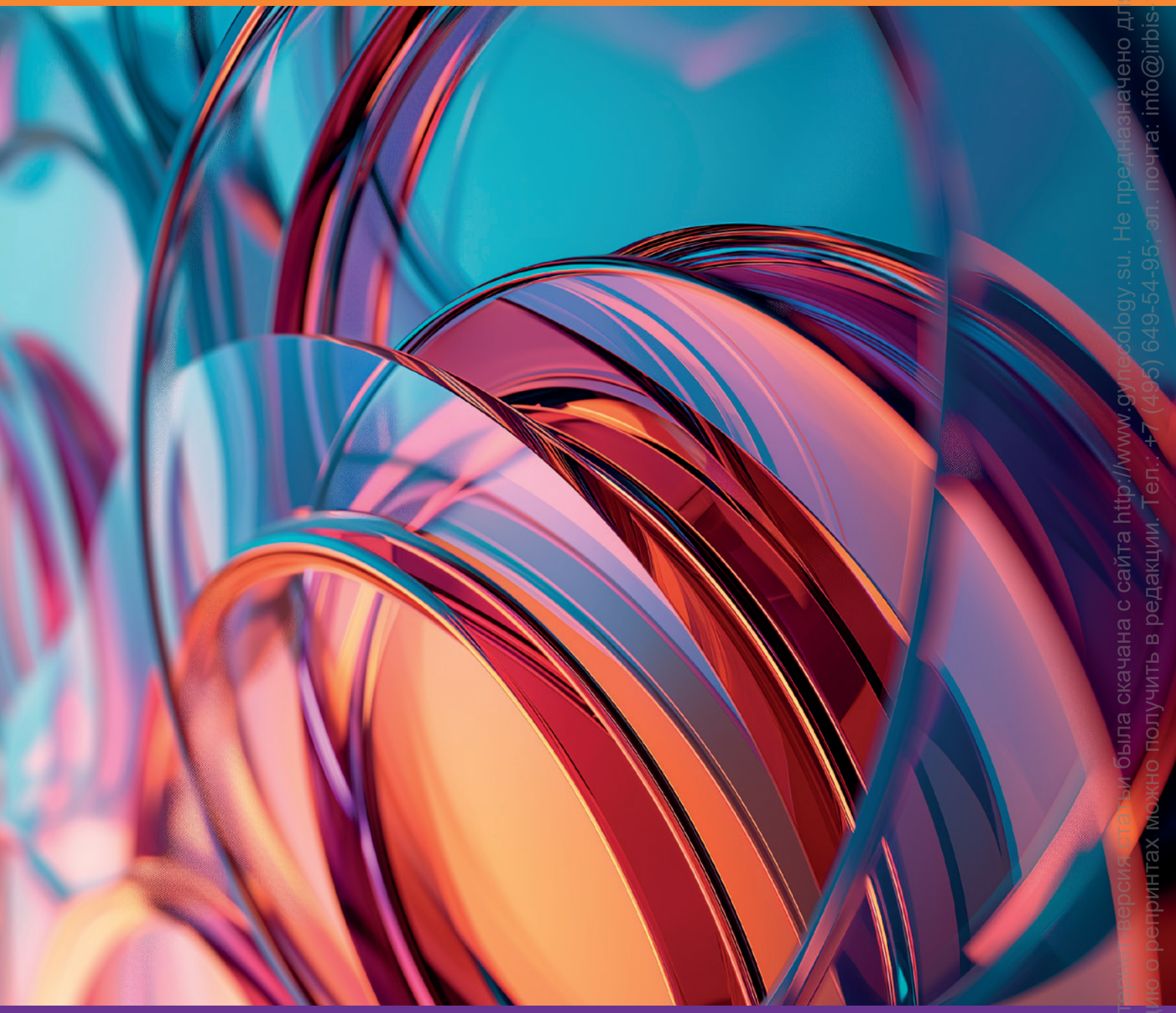

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Antenatal magnesium sulfate ($MgSO_4$) regimens for neuroprotection in preterm neonates

Yasmine Elmasry, Ashraf Mohammed, Amal Elsokary, Shereef Lofty Elshwaikh

Tanta University; Al-Geish Str., Tanta 31527, Egypt

Corresponding author: *Shereef Lofty Elshwaikh, e-mail: frommetou35@gmail.com*

Abstract

Aim: to assess the comparative effectiveness and adverse effects of different magnesium sulfate ($MgSO_4$) regimens for fetus neuroprotection in women who are considered at risk of preterm birth.

Materials and Methods. This randomized controlled clinical single-center study was taken place at the Obstetrics and Gynecology Department of Tanta University Hospital, a tertiary care referral center and neonatology department. The research was carried on pregnant female with gestational age 24–34 weeks with established preterm labor. The patients were sorted into four groups at random. Number of cases in each group was 20 cases, and they were assigned to one of the four groups using a computer-based program. All groups of women had received care in accordance with accepted clinical standards. Throughout the infusion, the protocol required that the mother's heart rate, blood pressure, breathing rate, tendon reflexes, and any negative effects be recorded. Throughout labor, the fetal heart rate had been checked. Mothers and their newborns were monitored until they were released from the hospital.

Results. There are different regimens for its use, and there was no difference between all the regimens in its effect for neuroprotection either clinically or radiologically or in its safety, so we recommend the use of the least dose (loading dose 4 g over 30 minutes) to decrease the risk of side effects.

Conclusion. It is recommended to use $MgSO_4$ for neuroprotection as it is a safe feasible effective and efficient method as well as it can prevent the trans cranial ultrasound positive findings for encephalopathy. $MgSO_4$ prevents cerebral palsy by age 2, but its effect on cognition and behavior at school age remains uncertain and warrants further study.

Keywords: magnesium sulfate, $MgSO_4$, neuroprotection, preterm birth

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Схемы применения сульфата магния ($MgSO_4$) в антенатальный период для нейропротекции у недоношенных новорожденных

Я. Эльмасри, А. Мохаммед, А. Эльсокари, Ш.Л. Эльшвайх

Университет Танта; Египет, 31527 Танта, улица Аль-Гейш

Для контактов: *Шериф Лофти Эльшвайх, e-mail: frommetou35@gmail.com*

Резюме

Цель: оценить сравнительную эффективность и побочные эффекты различных схем приема сульфата магния ($MgSO_4$) для нейропротекции плода у женщин, подверженных риску преждевременных родов.

Материалы и методы. Настоящее рандомизированное контролируемое клиническое одноцентровое исследование длительностью около 9 месяцев проводилось в отделении акушерства и гинекологии больницы университета Танта, специализированном центре третичной медицинской помощи и отделении неонатологии. В исследование вошли беременные со сроком гестации 24–34 недели с начавшимися преждевременными родами, случайным образом

разделенные на 4 группы по 20 женщин, получавших медицинскую помощь в соответствии с принятыми клиническими стандартами. Во время инфузии сульфата магния ($MgSO_4$) по протоколу оценивали частоту сердечных сокращений матери, кровяное давление, частоту дыхания, сухожильные рефлексы и любые негативные эффекты. Сердечный ритм плода измеряли во время родов. Матери и их новорожденные находились под наблюдением до выписки из больницы.

Результаты. Существуют различные режимы применения препарата сульфата магния ($MgSO_4$), для которых в ходе исследования не выявлено различий по нейропротективному эффекту в клинических проявлениях, рентгенологических признаках, а также в профиле безопасности. На основании этого для снижения риска побочных эффектов рекомендуется использовать минимальную дозу (нагрузочная доза 4 г в течение 30 минут).

Заключение. Рекомендуется использовать сульфат магния ($MgSO_4$) для нейропротекции, поскольку это безопасный, эффективный и доступный метод, способный предотвратить появление признаков энцефалопатии при транскраниальном ультразвуковом исследовании. Сульфат магния ($MgSO_4$) предотвращает церебральный паралич к двухлетнему возрасту пациентов, но его влияние на когнитивные и поведенческие показатели в школьном возрасте остается неопределенным и требует дальнейшего изучения.

Ключевые слова: сульфат магния, $MgSO_4$, нейропротекция, преждевременные роды

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Highlights

What is already known about this subject?

- Preterm delivery is associated with high incidence of neonatal cerebral morbidity especially cerebral palsy and encephalopathy.
- Antenatal magnesium sulfate ($MgSO_4$) infusion had been used for neuroprotection for preterm baby, with significant effectiveness.
- There are different protocols for $MgSO_4$ infusion during pregnancy with different dosages, with non-global agreement for the dose or the duration.

What are the new findings?

- There was no difference between all regimen in the effect of neuroprotection.
- The least dose and least duration had the same effect as the larger dose and larger duration.
- Use the least dose and duration (loading dose 4 g over 30 minutes) can protect the female form the side effect of the drug with the same neurprotcetive effect for the baby.

How might it impact on clinical practice in the foreseeable future?

- The use of the smallest dose with shorter duration of $MgSO_4$ (loading dose 4 g over 30 minutes) for neuroprotection is proved and could be generalized, and it could significantly decrease the morbidity and mortality of preterm neonates.

Основные моменты

Что уже известно об этой теме?

- Преждевременные роды связаны с высокой частотой неонатальной церебральной заболеваемости, особенно детского церебрального паралича и энцефалопатии.
- Введение сульфата магния ($MgSO_4$) во время беременности применялось для нейропротекции недоношенных детей и показало значительную эффективность.
- Существуют различные протоколы введения $MgSO_4$ во время беременности с разными дозировками, при этом отсутствует единое мнение относительно дозы и продолжительности.

Что нового дает статья?

- Различий в эффекте нейропротекции между изученными протоколами лечения не наблюдалось.
- Применение сульфата магния в минимальной или большей дозе, кратковременно или более длительно оказывало сходные эффекты.
- Использование наименьшей дозы и продолжительности (нагрузочная доза 4 г в течение 30 минут) может предупредить побочные эффекты у женщин, обеспечивая сходный нейропротективный эффект для ребенка.

Как это может повлиять на клиническую практику в обозримом будущем?

- Доказана нейропротективная эффективность применения минимальной $MgSO_4$ с более коротким периодом действия (нагрузочная доза 4 г в течение 30 минут), что позволяет широко применять такой метод и существенно снизить заболеваемость и смертность недоношенных новорожденных.

Introduction / Введение

Cerebral palsy (CP) is considered one of the most hazardous neurodevelopmental disorders affects approximately 2/1,000 live births. Prematurity is one of the most important causes of CP (about 30 % of CP cases). The need of neuroprotection for premature baby was a necessary step for decreasing the neonatal morbidity and mortality especially with the high incidence of preterm birth (7.5 % of live birth), and it was suggested the use of for that purpose upon the observation of its use as a tocolytic drug and for eclampsia prevention [1].

The mechanism of $MgSO_4$ action is still obscured, it is believed that it protects the preterm brain against cytokine and excitatory amino acid damage, decrease vascular instability, and avoid hypoxic damage. The safety of use of

2026 • Vol. 20 • № 2
Obstetrics, Gynecology and Reproduction

magnesium poisoning, $MgSO_4$ is guarded by the use of intravenous calcium gluconate as antidote [2].

$MgSO_4$ as a tocolytic drug, used in a regimen of 4–6 g loading dose over 15–30 minutes is followed by a continuous infusion of 2 g per hour, and this infusion may be raised up to 4–5 g per hour as needed in the absence of clinical side effects or oliguria [3].

Despite $MgSO_4$ has been used in obstetrics for decades, without any reports or concerns regarding fetal or neonatal problems, Food and Drug Administration (FDA) has revised the medication categorization of $MgSO_4$ from Category A to D as there is a concern for fetal and neonatal bone demineralization and fractures related (9.6 weeks exposure, with an average total dose of 3,700 g). But it is worthy to inform that the dose used and the time of exposure is less than the dangerous total doses [4].

$MgSO_4$ use for the purpose of neuroprotection has its debate as regard the proper dose of its use. But it is approved that the total adult daily dose should not exceed 30 to 40 g of $MgSO_4$. No more than 8 g of $MgSO_4$ should be supplied over 1 hour. It should continue for up to 24 hours or until birth, whichever comes first [5].

$MgSO_4$ should be administered when preterm birth is planned or expected within 24 hours. $MgSO_4$ should be started as close as possible to 4 hours in case of planned preterm birth. Even if delivery is planned or expected to occur in time less than 4 hours $MgSO_4$ should be administered [6].

The controversy of $MgSO_4$ dose in studies include the loading doses which varies between 4 g and 6 g, or even not supplied. $MgSO_4$ toxicity is uncommon, so routine serum magnesium monitoring is not advised [7], but many adverse maternal effects were noted including flushing, sweating, a sense of warmth due to its peripheral vasodilation effects when given intravenous, vomiting, nausea, headaches, palpitations, and, in rare cases, pulmonary edema. There is no evidence of any unintended adverse outcomes in the neonate [8].

The use of $MgSO_4$ injection to prevent preterm labor should not exceed 5–7 days. FDA stated that if it is given for longer period the baby or fetus may experience low calcium levels, bone abnormalities, including osteopenia and fractures, and low calcium levels [4].

Table 1 is showing the different $MgSO_4$ regimens as neuroprotection against cerebral palsy [9–12].

Table 2 show the rest of different $MgSO_4$ regimens as neuroprotector [13–15].

Aim: to assess the comparative effectiveness and adverse effects of different magnesium sulfate ($MgSO_4$) regimens for fetus neuroprotection in women who are considered at risk of preterm birth.

Materials and Methods / Материалы и методы

Study design / Дизайн исследования

This randomized controlled clinical single-center study was taken place from august 2023 at the Obstetrics and Gynecology Department of Tanta University Hospital, a tertiary care referral center and neonatology department. The duration of the study was about 9 months.

Inclusion and exclusion criteria / Критерии включения и исключения

Inclusion criteria: pregnant female with gestational age 24–34 weeks with established preterm labor.

Exclusion criteria: patients with insufficient medical records who have severe congenital anomalies or intrauterine fetal deaths. If the cervix is more than 8 cm dilated, an urgent delivery may be necessary for reasons related to the mother or the fetus, such as electrolyte disorders, renal failure, and maternal cardiac arrhythmia during this pregnancy, myasthenia, or ingestion of calcium channel blockers in the previous two hours.

All patients who participated in the trial gave written consent after being informed of its objectives, benefits, and risks. All their files were kept in confidential way with no discrimination as regard the races or the social standard.

Sample size calculation / Расчет размера выборки

The sample size was calculated using Epi-Info 7 specific program (Center for Disease Control and Prevention, USA). H0 was postulated as the prevalence of preterm labor was about 13.6 % in Egypt. The power was adjusted to be 80 %.

Randomization, grouping, and intervention / Рандомизация, стратификация по группам, вмешательство

All patients had their histories thoroughly recorded. The patients were sorted into four groups at random, and they were assigned to one of the four groups using a computer-based program. Number of cases in each group was 20 cases.

Group I: the patients had received $MgSO_4$ infusion by the following protocol:

1. loading dose 6 g over 20–30 min;
2. maintenance dose 2 g per hour till birth or for 12 hours;
3. treatment was repeated if more than 6 hours since last dose had passed, so additional loading dose was given followed by maintenance.

Group 2: the patients had received $MgSO_4$ infusion by the following protocol:

1. loading dose 4 g over 20 min;
2. maintenance dose 1 g per hour till birth or for 24 hours;
3. no repeated treatment.

Group 3: the patients had received $MgSO_4$ infusion by the following protocol.

1. loading dose 4 g over 30 min,
2. no maintenance dose;
3. no repeated treatment.

Group 4 (control group): the patients had not received $MgSO_4$ infusion at all.

Table 1. Different magnesium sulfate ($MgSO_4$) regimens as neuroprotection against cerebral palsy.

Таблица 1. Различные схемы применения сульфата магния ($MgSO_4$) в качестве нейропротекции для предотвращения детского церебрального паралича.

Study [reference] Исследование [ссылка]	Loading dose Нагрузочная доза	Maintenance dose Поддерживающая доза	Repeat dosing Повторное введение	Timing Сроки
Crowther C.A. et al., 2003 [9]	4 g over 20 minutes 4 г в течение 20 минут	1 g per hour until birth or for up to 24 hours 1 г в час до рождения или в течение до 24 часов	No Нет	When birth was planned or definitely expected with 24 hours median time: 3.7 hours (interquartile range (IQR) 1.4 to 13.8 hours) Роды планируются или определенно ожидаются при медианном времени до родов в 24 часа: 3,7 часа (межквартильный размах (IQR) от 1,4 до 13,8 часов)
Magpie L. et al., 2007 [10]	4 g over 10 to 15 minutes 4 г в течение 10–15 минут	1 g per hour for 24 hours 1 г в час в течение 24 часов	No Нет	Timing before birth not specified (women were given magnesium sulphate for pre-eclampsia) Сроки до родов не указаны (женщинам назначали сульфат магния при преэклампсии)
Marret S. et al., 2007 [11]	4 g over 30 minutes 4 г в течение 30 минут	No Нет	No Нет	When birth was planned or defiantly expected within 24 hours median time: 1.6 hours (IQR 0.08 to 25.08 hours) Роды планируются или определенно ожидаются при медианном времени до родов в 24 часа: 1,6 часа (IQR от 0,08 до 25,08 часов)
Rouse D.J. et al., 2008 [12]	6 g over 20 to 30 minutes 6 г в течение 30 минут	2 g per hour until birth or for up to 12 hours 2 г в час до рождения или в течение до 12 часов	If less than 6 hours had elapsed since cessation maintenance was restarted, if at least 6 hours had elapsed as additional loading dose was given before maintenance was restarted Если с момента возобновления поддерживающей терапии прошло менее 6 часов, или если до возобновления поддерживающей терапии прошло не менее 6 часов с момента введения дополнительной нагрузочной дозы	87 % of women were given magnesium sulphate for preterm prelabor rupture of membrane with a 25 hours median time to birth (IQR 11 to 63 hours) При преждевременном разрыве плодных оболочек сульфат магния получали 87 % женщин, медианное время до родов составляло 25 часов (IQR от 11 до 63 часов).

Table 2. The rest of different magnesium sulfate ($MgSO_4$) regimens as neuroprotection.

Таблица 2. Прочие схемы применения сульфата магния ($MgSO_4$) для нейропротекции.

Recommended regiments [reference] Рекомендуемые протоколы [ссылка]	Loading dose Нагрузочная доза	Maintenance dose Поддерживающая доза	Repeat treatment Повторное введение
NCPG, 2010 [13] Magee L. et al., 2011 [14]	4 g over 20 to 30 minutes 4 г в течение 20–30 минут	1 g per hour continued until birth or for 24 hours 1 г в час, продолжается до рождения или в течение 24 часов	No immediate repeat doses Не требуется немедленного повторного введения препарата
Reeves S.A. et al., 2011 [15]	6 g over 20 minutes to 30 minutes 6 г в течение 20–30 минут	2 g per hour continued until birth or for12 hours 2 г в час, продолжается до рождения или в течение 12 часов	If less than 6 hours have elapsed since cessation, restart maintenance. If at least 6 hours have elapsed give an additional loading dose before restarting maintenance Если с момента прекращения приема прошло менее 6 часов, возобновите поддерживающую терапию. Если прошло не менее 6 часов, введите дополнительную нагрузочную дозу перед возобновлением поддерживающей терапии

2026 • Vol. 20 • № 2
Obstetrics, Gynecology and Reproduction

All groups of women had received care in accordance with accepted clinical standards. Throughout the infusion, the protocol required that the mother's heart rate, blood pressure, breathing rate, tendon reflexes, and any negative effects be recorded. Throughout labor, the fetal heart rate had been checked. If any of the following symptoms were present, treatment had to be stopped: respiration rate 10/min, hypotension, areflexia, disturbances of consciousness, or oliguria/anuria. Mothers and their newborns were monitored until they were released from the hospital.

The following results were found after an examination of neonatal medical records:

1. 1-minute and 5-minute Apgar score < 7;
2. the need for incubator or neonatal intensive care unit;
3. the occurrence of any neonatal complications like intracerebral hemorrhage, necrotizing enterocolitis or hypoxic encephalopathy.

The outcomes / Исходы

Primary outcomes: the effect of $MgSO_4$ in neuroprotection which could be assessed clinically by assessing the neonatal condition for the presence of the signs of encephalopathy including seizure, conscious level, intact reflexes, muscle tone, or could be assessed by trans cranial ultrasound for assessing the signs of encephalopathy even the neonates were clinically normal.

Secondary outcomes included other measures of effectiveness and safety.

For the infant / Исходы для младенца

Apgar score (less than 7 at 5 minutes): use of respiratory support (mechanical ventilation or continuous positive airways pressure, or both) or the occurrence of intrapartum fetal complications including non-reassuring cardiotocography (CTG), meconium-stained amniotic fluid.

For the woman / Исходы для матери

The occurrence of maternal complications related to $MgSO_4$ use including oliguria, hypotension, respiratory problems, are flexia and disturbed conscious level – delivery related complications including postpartum hemorrhage and prolonged labor – or discontinuation of the $MgSO_4$ infusion regimen.

Use of health services / Использование медицинских услуг

- Admission to intensive care unit for the mother.
- Length of postnatal hospitalization for the women.
- Admission to neonatal intensive care for the infant.
- Length of stay in neonatal intensive care unit for the infant.
- Length of neonatal hospitalization for the infant.

Methods of statistical analysis / Методы статистического анализа

Statistical analysis was performed with computerized SPSS (SPSS Inc., USA) version 16 for Windows. Qualitative data were expressed as numbers (N) and percentages, while quantitative data were expressed as mean (M) ± standard deviation (SD). Quantitative variables were analyzed for linearity using the One-Sample Kolmogorov–Smirnov Test and all variables were normally distributed. Student t-test was used to compare between means body mass index (BMI), P-test to measure the strength of evidence against a null hypothesis, ANOVA test to analyze the ratio of variance between groups to variance within groups and other quantitative variables between four groups according to $MgSO_4$ dose. Further, the paired sample t-test was used for analysis of quantitative variables before and after treatment.

Results / Результаты

Table 3 shows distribution of cases according demographic data, and the value of the APGAR score after 1 and 5 minutes.

In our study, 80 cases were enrolled, and they were divided into 4 groups at random. As shown in **Table 3**, there were no significant differences between the four groups in terms of age, gravidity, parity, gestational age at delivery, or length of labor.

Four cases in group 1 (20 %) had developed maternal complications in the form of hypotension , and only one case had hypotension accompanied with oliguria , while 3 cases in group 2 had developed hypotension (15 %) and only one case in group 3 (5 %) had developed hypotension, and no cases developed maternal complications related to $MgSO_4$ in group 4 (control group), but there was no significant difference between all the groups as regard the maternal complications with P value 0.364 (**Table 4**).

Seven cases in group 1 (35 %) had developed fetal complications (5 cases non reassurance CTG and 2 cases developed meconium-stained amniotic fluid), while 8 cases in group 2 (40 %) had developed fetal complications (6 cases non reassurance CTG and 2 cases developed meconium-stained amniotic fluid), and 5 cases in group 3 (25 %) had developed fetal complications (5 cases non reassurance CTG and 1 case developed meconium-stained amniotic fluid) and 2 cases (10 %) developed fetal complications in group 4 (2 cases non reassurance CTG), but there was no significant difference between all the groups as regard the fetal complications with P value 0.153 (**Table 4**).

Seven cases in group 1 (35 %) had developed delivery related complications (6 cases prolonged labor and 3 cases developed postpartum hemorrhage), and 8 cases in group 2 (40 %) had developed delivery related complications (7 cases prolonged labor and 2 cases developed postpartum hemorrhage), and 3 cases in group 3 (15 %) had developed delivery related complications (3 cases prolonged labor), and 3 cases (15 %) developed delivery related complications in group 4 (3 cases prolonged labor and 1 case developed postpartum hemorrhage), but there was no significant difference between all the

Table 3. The difference between the groups according demographic data, and the value of the APGAR score after 1 and 5 minutes.

Таблица 3. Различия между группами по демографическим данным и оценка по шкале Апгар на 1-й и 5-й минутах.

Parameter Показатель		Group 1 Группа 1	Group 2 Группа 2	Group 3 Группа 3	Group 4 Группа 4	F ratio ANOVA test F-критерий ANOVA	P
Age, years Возраст, лет	range / диапазон	23–35	21–40	18–40	20–41	0.842	0.475
	mean / среднее	27.00	28.75	28.10	29.35		
	SD	3.209	4.732	5.726	5.082		
Gravidity Число беременностей	range / диапазон	1–5	1–7	1–5	1–8	0.700	0.554
	mean / среднее	2.3	2.8	2.85	2.9		
	SD	1.187	1.6	1.276	1.67		
Parity Число родов	range / диапазон	0–3	0–3	0–4	0–4	1.04	0.38
	mean / среднее	0.75	1.15	1.3	1.3		
	SD	0.942	1.062	1.187	1.229		
Gestational age, weeks Гестационный возраст, недель	range / диапазон	26–34	27–34	26–34	26–34	0.096	0.962
	mean / среднее	31.6	31.25	31.25	31.35		
	SD	2.31	2.256	2.364	2.351		
Time of delivery, minutes Длительность родов, минут	range / диапазон	250–960	280–880	280–880	270–870	0.199	0.896
	mean / среднее	569.0	558.5	551.5	521.5		
	SD	230.887	189.0	197.59	173.961		
Apgar 1 min, score Баллы по шкале Апгар на 1-й минуте	n range / диапазон	18 4–9	19 4–9	19 4–8	20 4–8	0.289	0.833
	mean / среднее	6.389	6.316	6.212	6.0		
	SD	1.458	1.416	1.239	1.265		
Apgar 5 min, score Баллы по шкале Апгар на 5-й минуте	n range / диапазон	18 4–10	19 5–10	19 4–10	20 5–10	0.429	0.733
	mean / среднее	7.722	7.737	7.895	7.4		
	SD	1.483	1.291	1.372	1.319		

groups as regard the fetal complications with P value 0.147 (**Table 4**).

There was no significant difference between the 3 study groups as regard the completion of the $MgSO_4$ infusion (15, 17, 19 cases in group 1, 2, 3 respectively) with P value 0.208 (**Table 4**).

There was also no significant difference between all the groups as regard the Apgar score evaluation of the neonate after 1 minutes and 5 minutes with P value 0.833 and 0.733 respectively. While by evaluation of the neonatal condition as regard the presence of clinical signs like seizure, loss of consciousness, abnormal tone, abnormal reflexes and the need of ventilator there was non-significant difference between all the groups, despite the number of cases which had abnormal clinical signs were lower in the study groups as compared by the control group (**Table 5**).

Also, there was non-significant differences between four groups as regard the number of neonates diagnosed with intraventricular hemorrhage (P = 0.701), and non-significant difference as regard the number of cases with early neonatal mortality (P = 0.774) (**Table 5**).

While there was a significant difference between the groups as regard the ultrasound findings suggesting encephalopathy with P value 0.009, as the number of cases which had abnormal ultrasound findings in group 1, 2 ,3 and 4 were 6, 7, 5 and 15 cases respectively (**Table 3**).

Discussion / Обсуждение

Many animal studies have investigated the neuroprotective role of $MgSO_4$. In 1984, F.X. Vacanti and A. Ames demonstrated neuroprotective effects of $MgSO_4$ in an adult rabbit spinal cord ischemia model [16]. In 1987, $MgSO_4$ administration to rat hippocampal slices reduced the effect of hypoxia [17]. T.K. McIntosh et al. demonstrated in 1989 that post-traumatic $MgSO_4$ injection decreased neurological disorders in a dose-dependent manner [18].

Many countries have developed national clinical guidelines that support the use of prenatal $MgSO_4$ at impending preterm delivery, but the majority of European nations haven't. As there is no global agreement, due to the lack of the agreement on the ideal gestational age for $MgSO_4$ therapy that provides neuroprotection. For example, the national guidelines of both England and Canada advised the use of prenatal $MgSO_4$ for neuroprotection prior to 34 weeks of gestation, but not by those of Belgium, France, Ireland,

Table 4. The difference between the groups as regard the complications (maternal, fetal and delivery complications).

Таблица 4. Различия между группами в отношении осложнений (осложнения у матери, плода и при родах).

Group Группа	Maternal complications Осложнения у матери		Fetal complications Осложнения у плода		Delivery complications Осложнения при родах		Completed Осложнения закончились	
	No / Нет	Yes / Да	No / Нет	Yes / Да	No / Нет	Yes / Да	No / Нет	Yes / Да
Group 1 Группа 1	16 (80 %)	4 (20 %) Hypotension – 4 (20 %) Oliguria – 1 (5 %) Гипотензия – 4 (20 %) Олигурия – 1 (5 %)	13 (65 %)	7 (35 %) Non reassurance – 5 (25 %) Meconium – 2 (10 %) Плохой прогноз – 5 (25 %) Меконий – 2 (10 %)	13 (65 %)	7 (35 %) Prolonged – 6 (30 %) PPH – 3 (15 %) Длительно – 6 (30 %) ПРК – 3 (15 %)	5 (25 %)	15 (75 %)
Group 2 Группа 2	17 (85 %)	3 (15 %) Hypotension – 3 (15 %) Гипотензия – 3 (15 %)	12 (60 %)	8 (40 %) Non reassurance – 6 (30 %) Meconium – 2 (10 %) Плохой прогноз – 6 (30 %) Меконий – 2 (10 %)	12 (60 %)	8 (40 %) Prolonged – 7 (35%) PPH – 2 (10%) Длительно – 7 (35 %) ПРК – 2 (10 %)	3 (15 %)	17 (85 %)
Group 3 Группа 3	19 (95 %)	1 (5 %) Hypotension – 1 (5 %) Гипотензия – 1 (5 %)	15 (75 %)	5 (25 %) Non reassurance – 5 (25 %) Meconium – 1 (5 %) Плохой прогноз – 5 (25 %) Меконий – 1 (5 %)	17 (85 %)	3 (15 %) Prolonged – 3 (15 %) Длительно – 3 (15 %)	1 (5 %)	19 (85 %)
Group 4 Группа 4	20(100,0 %)	0 (0 %)	18 (90 %)	2 (10 %) Non reassurance – 2 (10 %) Плохой прогноз – 2 (10 %)	17 (85 %)	3 (15 %) Prolonged – 3 (15 %) PPH – 1 (5 %) Длительно – 3 (15 %) ПРК – 1 (5 %)	NA НД	NA НД
χ^2	2.019		5.267		5.359		3.137	
P	0.364		0.153		0.147		0.208	

Note: *PPH – postpartum hemorrhage; NA – no data available.*

Примечание: *ПРК – послеродовое кровотечение; НД – нет данных.*

Table 5. Neonatal neurological and ultrasound findings across groups.

Таблица 5. Неврологические и ультразвуковые данные новорожденных в разных группах

Group Группа	Seizure Судороги		Consciousness Сознание		Absent reflexes Отсутствие рефлексов		Abnormal tone Нарушение тонуса		Need MLV Требуется ИВЛ		Ultrasound suggest encephalopathy УЗИ-признаки энцефалопатии		Cases with IVH Случаи ВЖК	Mortality Смертность
	No / Нет n (%)	Yes / Да n (%)	No / Нет n (%)	Yes / Да n (%)	No / Нет n (%)	Yes / Да n (%)	No / Нет n (%)	Yes / Да n (%)	No / Нет n (%)	Yes / Да n (%)	No / Нет n (%)	Yes / Да n (%)	No / Нет n (%)	Yes / Да n (%)
Group 1 Группа 1	16 (89.0)	2 (11.0)	16 (89.0)	2 (11.0)	17 (94.0)	1 (6.0)	16 (89.0)	2 (11.0)	15 (83.0)	3 (17.0)	12 (67.0)	6 (33.0)	4	2
Group 2 Группа 2	15 (79.0)	4 (21.0)	15 (79.0)	4 (21.0)	15 (79.0)	4 (21.0)	11 (58.0)	8 (42.0)	14 (74.0)	5 (26.0)	12 (63.0)	7 (37.0)	3	1
Group 3 Группа 3	17 (89.0)	2 (11.0)	18 (95.0)	1 (5.0)	15 (79.0)	4 (21.0)	12 (63.0)	7 (37.0)	15 (79.0)	4 (21.0)	14 (74.0)	5 (26.0)	4	1
Group 4 Группа 4	14 (70.0)	6 (30.0)	15 (75.0)	5 (25.0)	12 (60.0)	8 (40.0)	9 (45.0)	11 (55.0)	16 (80.0)	4 (20.0)	5 (25.0)	15 (75.0)	6	3
χ^2	3.3		3.552		6.548		8.181		0.538		11.462		1.419	1.111
P	0.348		0.314		0.878		0.042		0.91		**0.009**		0.701	0.774

Note: *IVH – intraventricular hemorrhage; MLV – mechanichal lung ventilation; significant differences are highlighted in bold.*

Примечание: *IVH – внутрижелудочковое кровоизлияние; ИВЛ – искусственная вентиляция легких; выделены значимые различия.*

or the WHO administration. In Australia, $MgSO_4$ is recommended before 30 weeks of gestation [19].

The dosage of $MgSO_4$ varied between studies, with loading dosages range between 4 g and 6 g and inconsistent administration of a maintenance dose. The positive effects of $MgSO_4$ maintained even in studies with lower overall dosages, according to a meta-analysis, although there insufficient data to establish a minimal effective dose or the best course of treatment [1].

E. Shepherd et al., studied $MgSO_4$ adverse effect including flushing, sweating, sensation of warmth and, in rare cases, pulmonary edema which is linked to dosage, infusion rate and mode of administration (intravenous). This side effect is due to the peripheral vasodilator effect. But they found no evidence of neonatal adverse effect. Our findings corroborated their findings about the absence of fetal side effects, but also we found no maternal side effects with various $MgSO_4$ dosages which may attributed to the single dose of infusion with long infusion time [19].

As regard the dose-related perinatal adverse outcomes, no clear differences between different dose regimens of $MgSO_4$ were seen for the outcome of perinatal death (relative risk (RR) = 1.01; 95 % confidence interval (CI) = 0.75–1.36; 6 trials, 543 babies; analysis 2.1), nor for stillbirth or neonatal death [19].

As there are several different dosing regimens were used in the randomized controlled trial (RCTs). The data of a meta-analysis concluded that $MgSO_4$ should be administered at the smallest effective dose (4 g with or without 1 g per hour maintenance dose until birth) [20]. Our results corroborated this recommendation. Another meta-analysis (2017), studied the effect of neuroprotection of $MgSO_4$, which comprised 5 RCTs, and it was found that it was decreased in the subgroup of children exposed to antenatal $MgSO_4$ at 28 weeks of gestation. This finding is consistent with our own. Children exposed between 28 and 31 weeks of pregnancy showed a comparable reduced risk [21].

Our study agreed with The BEAM trial who studied by randomized controlled trial 2241 women in preterm labor before 32 gestational weeks at 20 centers with regard to the fetal outcome, the effect of $MgSO_4$ with a dose of a 6-g bolus followed by a 12-hour 2 g per hour maintenance dosage (1,096 women and 1,188 fetuses) versus as a placebo (1,145 women and 1,256 fetuses). They found that although major outcomes – stillbirth, death at one year, or cerebral palsy at two years – in both groups were identical, the $MgSO_4$ group saw a markedly lower rate of moderate or severe cerebral palsy (1.9 % versus 3.5 %; RR = 0.55; 95 % CI = 0.32–0.95) [12].

The MAGPIE was a multinational trial had studied the effectiveness of antenatal $MgSO_4$ treatment in the prevention of eclampsia over 10,141 women, as they gave them $MgSO_4$ (4 g bolus followed by 1 g per hour maintenance dosage for 24 hours) or a placebo was given to the women, one of the secondary outcomes of the study was the neonatal outcome, they found that 1,593 fetuses were born

2026 • Vol. 20 • № 2
Obstetrics, Gynecology and Reproduction

before 37 weeks of gestation. A pediatric follow-up study with 4,483 children (2,254 in the $MgSO_4$ group and 2,229 in the placebo group, respectively) found no differences in mortality or neurological outcomes at 18 months (as measured by the Ages and Stages questionnaire). There result was different from ours and this may be attributed to that their study was focusing in the prevention of preeclampsia, and neglect the effect of preeclampsia of the neonates, also the dose of $MgSO_4$ was different as the goal was not neuroprotection [22].

Our study agreed with 4 meta-analyses that have been conducted on data from 5 RCTs that studied prenatal $MgSO_4$ administered to mothers at risk of preterm delivery and linking to the risk of cerebral palsy in children; all produced consistent findings and conclusions. With an RR ranging from 0.61 to 0.70 and no effect on mortality, minor side effects for the mother (such as flushing, nausea or vomiting, sweating, and soreness at the injection site) were more common in the $MgSO_4$ groups. But these studies did not evaluate the dose and the regimen. They concluded the positive effect of $MgSO_4$ whatever the dose is [6, 23].

The MAGNET trial had studied the effect of the highest neuroprotective dose of $MgSO_4$ and they found that the high dose of $MgSO_4$ may lead to the vasculopathy and high mortality due to cerebral hypoperfusion, whereas the lowest dose did not. These data agreed with our study, as $MgSO_4$ treatment had no effect on neonatal morbidity or pediatric mortality in any RCTs or meta-analyses performed to date. Similarly, there were no significant adverse effects on the mother from $MgSO_4$ therapy. The benefit remained constant whatever the gestational age, the reason for prematurity, the dose, or if the maintenance dose was administered after the loading dose. These findings support the use of low doses $MgSO_4$ [24].

In agreement with the meta-analysis done by X. Zeng et al. (2016), they have shown that antenatal $MgSO_4$ exposure does not improve 5-minute Apgar scores that are < 7 [23]. Also, in second analysis of the BEAM cohort did not show any difference in rates of intubation, chest compressions, hypotension, or mechanical ventilation between the $MgSO_4$ and placebo groups [25]. These findings support the safety of antenatal $MgSO_4$ exposure on short-term neonatal outcomes.

The authors did not observe any significant difference in the Apgar score according to the use or not of $MgSO_4$ when it was greater than or equal to 7. They also did not find significant differences in the resuscitation of neonates at birth. Indeed, newborns were resuscitated in 21.8 % of the exposed and 21.2 % of the unexposed [25]. Our results corroborated that issue.

Our results are in line with the meta-analysis of 4 neuroprotection trials which stated that maternal exposure to $MgSO_4$ did not affect neonatal resuscitation in the short term with no significant effect on Apgar score, need for assisted ventilation at birth [26].

Conclusion / Заключение

In conclusion there are different regimens for use of $MgSO_4$ for neuroprotection for preterm baby, and there was no difference between all the regimens in its effect for neuroprotection either clinically or radiologically or in its safety, so we recommend the use of the least dose (loading dose 4 g over 30 minutes) to decrease the risk of side effects. It is recommended to use $MgSO_4$ for neuroprotection as it is a safe feasible effective and efficient method as well as it can prevent the trans cranial ultrasound positive findings for encephalopathy.

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References / Литература:

1. Conde-Agudelo A., Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks 'gestation: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2009;200(6):595–609. https://doi.org/10.1016/j.ajog.2009.04.005.
2. Rouse D. Magnesium sulfate for the prevention of cerebral palsy. *Am J Obstet Gynecol*. 2009;200(6):610–2. https://doi.org/ 10.1016/j.ajog.2009.04.004.
3. Hutchison H.T., Nichols M.M., Kuhn C.R., Vaisaka A. Effects of magnesium sulfate on uterine contractility, intrauterine fetus, and infant. *Am J Obstet Gynecol*. 1964;88:747–58. https://doi.org/10.1016/0002-9378(64)90608-8.
4. FDA recommends against prolonged use of magnesium sulfate to stop pre-term labor due to bone changes in exposed babies. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-recommends-against-prolonged-use-magnesium-sulfate-stop-pre-term. [Accessed: 15.05.2025].
5. Magnesium sulfate use in obstetrics. Committee Opinion No. 652. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2016;127:e52–3. https://doi.org/10.1097/AOG.0000000000001267.
6. Crowther C.A., Middleton P.F., Voysey M. et al. Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: an individual participant data meta-analysis. *PLoS Med*. 2017;14(10):e1002398. https://doi.org/10.1371/journal.pmed.1002398.
7. American College of Obstetricians and Gynecologists Committee on Obstetric Practice Society for Maternal-Fetal Medicine. Committee Opinion No. 573: Magnesium sulfate use in obstetrics. *Obstet Gynecol*. 2013;122(3):727–8. https://doi.org/10.1097/01.AOG.0000433994.46087.85.
8. Shennan A., Suff N., Jacobsson B; on behalf of the FIGO Working Group for Preterm Birth. FIGO good practice recommendations on magnesium sulfate administration for preterm fetal neuroprotection. *Int J Gynecol Obstet*. 2021;155(1):31–3. https://doi.org/10.1002/ijgo.13856.
9. Crowther C.A., Hiller J.E., Doyle L.W., Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth. *JAMA*. 2003;290(20):2669–76. https://doi.org/10.1001/jama.290.20.2669.
10. Magpie Trial Follow-Up Study Collaborative Group. The Magpie Trial: a randomized trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for children at 18 months. *BJOG*. 2007;114(3):289–99. https://doi.org/10.1111/j.1471-0528.2006.01165.x.
11. Marret S., Marpeau L., Zupan-Simunek V. et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomized controlled PREMAG trial. *BJOG*. 2007;114(3):310–8. https://doi.org/10.1111/j.1471-0528.2006.01162.x.
12. Rouse D.J., Hertz D.G., Thom E. et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. *N Engl J Med*. 2008;359(9):895–905. https://doi.org/10.1056/NEJMoa0801187.
13. The Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel. Antenatal Magnesium Sulphate Prior to Preterm Birth for Neuroprotection of the Fetus, Infant and Child: National Clinical Practice Guidelines. *Adelaide: The University of Adelaide*, 2010. 140 p.
14. Magee L., Sawchuck D., Synnes A., von Dadelszen P. Magnesium sulphate for Fetal Neuroprotection Consensus Committee. Maternal Fetal Medicine Committee. SOGC Clinical Practice Guideline. Magnesium sulphate for fetal neuroprotection. *J Obstet Gynecol Can*. 2011;33(5):516–29. https://doi.org/10.1016/S1701-2163(16)34886-1.
15. Reeves S.A., Gibbs R.S., Clark S.L. Magnesium for fetal neuroprotection. *Am J Obstet Gynecol*. 2011;204(3):202.e1–4. https://doi.org/10.1016/j.ajog.2011.01.014.
16. Vacanti F.X., Ames A. Mild hypothermia and Mg++ protect against irreversible damage during CNS ischemia. *Stroke*. 1984;15(4):695–8. https://doi.org/10.1161/01.str.15.4.695.
17. Clark G.D., Rothman S.M. Blockade of excitatory amino acid receptors protects anoxic hippocampal slices. *Neuroscience*. 1987;21(3):665–71. https://doi.org/10.1016/0306-4522(87)90027-3.
18. McIntosh T.K., Vink R., Yamakami I., Faden A.I. Magnesium protects against neurological deficit after brain injury. *Brain Res*. 1989;482(2):252–60. https://doi.org/10.1016/0006-8993(89)91188-8.
19. Shepherd E., Salam R.A., Manhas D. et al. Antenatal magnesium sulphate and adverse neonatal outcomes: a systematic review and meta-analysis. *PLoS Med*. 2019;16(12):e1002988. https://doi.org/10.1371/journal.pmed.1002988.
20. Vilchez G., Dai J., Lagos M., Sokol R.J. Maternal side effects & fetal neuroprotection according to body mass index after magnesium sulfate in a multicenter randomized controlled trial. *J Matern Fetal Neonatal Med*. 2018;31(2):178–83. https://doi.org/10.1080/14767058.2017.1279143/.
21. Jayaram P.M., Mohan M.K., Farid I., Lindow S. Antenatal magnesium sulfate for fetal neuroprotection: a critical appraisal and systematic review of clinical practice guidelines. *J Perinat Med*. 2019;47(3):262–9. https://doi.org/10.1515/jpm-2018-0174.
22. Mittendorf R., Covert R., Boman J. et al. Is tocolytic magnesium sulphate associated with increased total pediatric mortality? *Lancet*. 1997;350(9090):1517–8. https://doi.org/10.1016/s0140-6736(97)24047-x.
23. Zeng X., Xue Y., Tian Q. et al. Effects and safety of magnesium sulfate on neuroprotection: a meta-analysis based on PRISMA guidelines. *Medicine (Baltimore)*. 2016;95(1):e2451. https://doi.org/10.1097/MD.0000000000002451.
24. Lecuyer M., Rubio M., Chollat C. et al. Experimental and clinical evidence of differential effects of magnesium sulfate on neuroprotection and angiogenesis in the fetal brain. *Pharmacol Res Perspect*. 2017;5(4):e00315. https://doi.org/10.1002/prp2.315.
25. Millogo-Traoré T.F.D., Sawadogo O., Zongo-Kondé S.W. Evaluation of the fetal neuroprotection protocol with magnesium sulfate in a University Hospital in Burkina Faso. *Open J Obstet Gynecol*. 2022;12(10):1042–55. https://doi.org/10.4236/ojog.2022.1210087.
26. Maged M.C., Weiner S.J.; Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal–Fetal Medicine Units Network (MFMU). Effects of antenatal exposure to magnesium sulfate on neuroprotection and mortality in preterm infants: a meta-analysis. *Obstet Gynecol*. 2009;114(2 Pt 1):354–64. https://doi.org/10.1097/AOG.0b013e3181ae98c2.

About the authors / Сведения об авторах:

Yasmin Elmasry / Эльмасри Ясмин, MD.

Ashraf Mohamed / Мохамед Ашраф, MD.

Amal Elsokary / Эльсокари Амаль, MD. ORCID: https://orcid.org/0000-0003-4389-2347.

Shereef Lofty Elshwaikh / Эльшвайх Шериф Лофти, MD. E-mail: frommetou35@gmail.com. ORCID: https://orcid.org/0000-0002-8910-3465.