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How Reliable are Meta-Analyses? An Appraisal Using the Example of Magnesium Tocolysis

Original title: Wie verlässlich sind Metaanalysen? Eine Überprüfung am Beispiel der Magnesiumtokolyse

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Introduction: Crowther et al. analysed the effectivity of magnesium tocolysis in preventing preterm birth. They conclude that there is no evidence for protection. In its latest guidelines, based on this Cochrane-Analysis, the DGGG does not recommend any more the use of magnesium for tocolysis. Magnesium tocolysis is said neither to delay nor to prevent preterm birth. Therefore, in their most recent guidelines, the German Society of Gynecologists and Obstetricians (DGGG) did not recommend the use of magnesium anymore. Moreover, magnesium could be responsible for increased mortality in infants. These conclusions are mostly based on the research of Mittendorf et al.

Method: Having successfully applied magnesium tocolysis for many years, these surprising conclusions lead us to review the soundness of the publications mentioned above. Combining the practical experience of many years with the outcomes of a comprehensive literature retrieval, this knowledge was related to the findings of the above-mentioned publications that caused the DGGG to withdraw the recommendation in favour of magnesium.

Result and short discussion: The statements of meta-analyses very much depend on the careful selection of studies that are included in the review, their relevance and unbiased selection. If these preconditions are not met, the results and conclusions of the review will not be reliable. It is very unlikely that the cases of death in infants, as stated by Mittendorf et al., are caused by magnesium. Moreover, the studies that were included in the Cochrane review of Crowther et al. are very heterogeneous (see table 1) and are not suitable for concluding on poor or even lacking effectiveness of magnesium tocolysis. There is no distinction between intravenous und oral administered tocolysis with magnesium, 30.4% of the patients receive a mix of various tocolytics. In 91.3% of the studies, the primary study objective is the comparison of different tocolytics and not the prevention of preterm births. In doing so, the tocolysis is administered for 24 hrs to 48 hrs, or even suspended after preliminary stop of labour and continued only when labour starts again. Therefore, we can find information on the number of preterm births and on mature births in less than half of the studies (47.8%), only. Only in 60.8% of the studies, ruptures of membranes are mentioned, and intrauterine infections were excluded in 30.4%. Tocolyses are symptomatic therapies. Their effectiveness cannot be evaluated without taking into account additional circumstances. Neonatal diseases are mentioned in 30.4% of the respective studies, infantile mortality in 26%, only. However, all authors, except one, find that magnesium is a good or even a very good tocolytic. In a second most recent study Crowthers et al. again encountered contradictory findings. The criteria for selecting studies that have to be included and the approach applied haven't changed. However, this does not improve convincibility. The pros and cons of tocolysis with magnesium are discussed here as well as the reliability of meta-anyalyses. The DGGG withdraw the guidelines for tocolysis with magnesium in the meantime. The guidelines will be revised.

Conclusion: The critical view of magnesium should be reconsidered. To prevent any misjudgement a thorough knowledge of the studies that are included in Cochrane meta-analyses seems essential. In the sense of evidence-based medicine (EbM), longstanding, scientifically proven therapeutic successes should be incorporated into meta-analyses, also. Furthermore, efforts should be made to facilitate the access to Cochrane reviews following the first year after publication. Up to now, the service is not free of charge – there is a compulsory fee for licensing agreements.

Table 1 Confirmation of applied measures and data from 23 studies (in %) included in the Cochrane review by Crowther et al.

Comparison of different tocolytics with Magnesium	91,3%
Therapy applying different tocolytics on the same patient	30,4%
Rupture of membranes excluded before starting therapy	60,8%
Intraunterine infections taken into account	30,4%
Information on preterm birth and on maturity of infant given	47,8%
Information on neonatal infections given	30,4%
Information on infant mortality given	26,0%
Information on infant malformation given	8,7%

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