

# INPLASY PROTOCOL

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None declared

## Magnesium sulphate prophylaxis in severe preeclampsia-lessons learnt from recent trials conducted in low-middle-income-countries – a systematic review

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**Review question / Objective:** The main objective of this research is to find answers to whether an adjusted low dose or an abbreviated regimen or even a single loading dose of magnesium sulphate prophylaxis is capable of preventing eclampsia in severe preeclampsia instead of applying full traditional dosing and if so, which regimen among them can be suggested safely and finally, even if chosen, can any of this modified regimen be applicable for all severely preeclamptic women indiscriminately?

With the above context, we have done a systematic review of available studies that compared the effectiveness of different magnesium sulphate regimens applied to severely preeclamptic women of LMIC aiming to prevent eclampsia. Implementation of this study result might be helpful to re-evaluate or strengthen the present guidelines and recommendations of prophylactic magnesium sulphate application in severely preeclamptic women of LMIC who are often under-cared and thus, susceptible to developing toxicity of magnesium sulphate.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 April 2023 and was last updated on 11 April 2023 (registration number INPLASY202340031).

### INTRODUCTION

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eclampsia in severe preeclampsia instead of applying full traditional dosing and if so, which regimen among them can be suggested safely and finally, even if chosen, can any of this modified regimen be applicable for all severely preeclamptic women indiscriminately?

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Implementation of this study result might be helpful to re-evaluate or strengthen the present guidelines and recommendations of prophylactic magnesium sulphate application in severely preeclamptic women of LMIC who are often under-cared and thus, susceptible to developing toxicity of magnesium sulphate.

**Condition being studied:** Hypertensive disorders of pregnancy are among the three top causes of maternal morbidity and mortality throughout World . As per the recent data from WHO, 3-10 % of pregnant women suffer from hypertensive disorders during pregnancy and it is a 14 % contributor to worldwide maternal mortality. Preeclampsia, a spectrum of hypertensive disorders of pregnancy, is characterized by the development of hypertension[139/90] with proteinuria, which usually develops after twenty weeks of gestation[3]. In World Bank classified low-middle-income countries, preeclampsia can be complicated in 10% of cases as severe preeclampsia. This is defined when the blood pressure of preeclamptic women rises more than 170/110 along with the development of different features of severe upper quadrant epigastric pain, thrombocytopenia, impaired liver function, progressive renal insufficiency, pulmonary oedema, unexplained new-onset headache or visual disturbances<sup>4</sup>. Five percent of all cases of PET can progress to life-threatening eclampsia which is characterized by the onset of generalized convulsions and/or coma. Low middle-income countries [LMIC] have a higher rate of eclampsia amounting to 16-69 cases per 10,000 births in contrast to Europe where the rate is 2 to 3 per 10,000 births.

## METHODS

**Search strategy:** Bibliographic databases of PubMed, Scopus and Cochrane library.

The following search items were used using combinations of MeSH and free text terms.

The search terms were: 'eclampsia', 'pre-eclampsia', 'eclampsia hypertension', 'eclampsia pre-eclampsia', 'eclampsia gestational hypertension', 'eclampsia pre-eclampsia magnesium sulfate', 'magnesium sulfate', 'eclampsia pre-eclampsia severity symptoms-headache, visual disturbance, epigastric pain, vomiting', 'type of eclampsia-antepartum, intrapartum, post-partum, late post-partum' and 'pregnancy induced hypertension'. The selected search terms

were combined alternatively with the Boolean logic (AND, OR and NOT).

Searches were limited to English [both American and UK English spelling]. Records retrieved were reviewed and duplicates were removed. Additional studies were identified manually from the reference lists of eligible studies and similar review articles.

**Participant or population:** Severely preeclamptic women of low middle income countries.

**Intervention:** Application of abbreviated regimen and low dose or loading dose of magnesium sulphate as prophylaxis in severe preeclampsia.

**Comparator:** Standard prophylaxis of magnesium sulphate regimens.

**Study designs to be included:** systematic review.

**Eligibility criteria:** Studies were included if all five of the following criteria met 1] Randomized controlled trials or quasi-experimental studies where the study and control group enrolled only severely preeclamptic women.2] Comparing magnesium sulphate regimens of low dose or abbreviated durations or loading dose or placebo with any of the standard

magnesium sulphate regimens. 3] Primary or any secondary outcome of the trials was "incidences of eclampsia" or " occurrence of fit".4] Conducted in LMIC and published on or after 2000. 5] Full-text articles with an entire manuscript in English

**Information sources:** Bibliographic-databases of PubMed, Scopus and Cochrane library.

**Main outcome(s):** 1. Incidents of eclampsia in the study and control group. 2. Number of women who needed dose extension or restart.

**Quality assessment / Risk of bias analysis:** The risk of bias in studies was assessed, according to the Cochrane handbook. Selection, performance, detection, attrition, reporting and other biases of each study were considered individually.

**Strategy of data synthesis:** After the data extraction was carried out by two reviewers independently [SKB and DNS], any discrepancy was sorted out by discussion. A third reviewer [RB] and fourth reviewer[PM] were consulted if required, to conclude. Qualitative data were described by using textual narrative synthesis.

**Subgroup analysis:** Studies were subgrouped as per the regimen of magnesium sulphate they had chosen and analysis of secondary outcomes was assessed accordingly.

Eight studies have been found to compare different abbreviated regimens of magnesium sulphate with standard prophylaxis [Conventional vs short maintenance]. Two studies compared a lower maintenance dose of magnesium sulphate with standard maintenance[Conventional vs low dose]. Four studies found evaluated the efficacy of only loading dose of magnesium sulphate as prophylaxis [Conventional vs loading dose]. One study evaluated placebo in the postpartum period in contrast to the standard regimen [Conventional vs Placebo].

**Sensitivity analysis:** 1. This systematic review contains a mixture of randomised and non-randomised clinical trials and multi-centre and single-centre studies.

2. Studies perceived to be of a lower quality are removed as one trial at a time and the analysis is then repeated to determine whether any one study was particularly influential .

3. Publication bias was tested with an Egger test and funnel plot using metabias and metafunnel programme respectively in Stata.

**Language restriction:** Only literatures in English language selected.

**Country(ies) involved:** India.

**Keywords:** Preeclampsia; Prophylaxis; Magnesium Sulphate; Severe; Eclampsia

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