"Comparative study of the obstetric outcome in eclamptic and imminent eclamptic patients treated with low dose magnesium sulphate regimen versus Zuspan's regimen"

By

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In partial fulfilment of the requirements for the degree of

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IN
OBSTETRICS & GYNECOLOGY

Under the Guidance of

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I hereby declare that this dissertation entitled **"Comparative study of the obstetric outcome in eclamptic and imminent eclamptic patients treated with low dose magnesium sulphate regimen versus Zuspan's regimen"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. GOMATHY E**, Professor, Department of Obstetrics & Gynecology, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**M.S. DEGREE IN OBSTETRICS AND GYNECOLOGY**", the examination to be held in April, 2017 by SDUAHER. This has not been submitted by me previously for the award of any degree or diploma from the university or any other university.

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Dr. ADITI C. RAMACHANDRA

LIST OF ABBREVIATIONS

APE – Antepartum eclampsia

B.P- Blood Pressure

Da- Daltons

NMDA- N-Methyl D-Aspartate

LSCS- Lower Segment Caesarean Section

d- day

IUD- Intrauterine death

USG- Ultrasound

LFT-Liver function test

RFT- Renal function test

IE- Imminent eclampsia

Hr- Hour

ICU- Intensive care unit

NICU- Neonatal Intensive care unit

Mg- Magnesium

MgSO4- Magnesium sulphate

I.V- Intravenous

I.M- Intramuscular

GCS- Glasgow Coma Scale

SBP- Systolic blood pressure

DBP- Diastolic blood pressure

CDI- convulsion to delivery interval

BMI- Body mass index

Hb- hemoglobin

Plt- Platelets

ABSTRACT

Background: Preeclampsia is a pregnancy specific syndrome which can affect virtually every organ.

Pre eclampsia when complicated with tonic clonic seizures is eclampsia. This causes an increased risk to the wellbeing of the both mother and fetus.

Imminent eclampsia is also called impending eclampsia where signs and symptoms in pre-eclamptic patients would suggest eclampsia is impending. These signs and symptoms are persistent headache, visual disturbances, epigastric pain, nausea , vomiting , and restlessness.

Aims and Objectives: To compare low dose magnesium sulphate regimen with Zuspan's regimen for patients presenting with imminent eclampsia and eclampsia and to find out the maternal and fetal outcome

Methodology: An analysis of 60 cases of imminent eclampsia and eclampsia patients admitted at R.L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar-563101 during August 2015– July 2016. Clinical history was collected from 30 cases of eclampsia and 30 cases of imminent eclampsia who were admitted in the labour room in the the department of Obstetrics and Gynecology at R.L Jalappa hospital and research centre in the period of August 2015–July 2016.

Written informed consent was obtained from the patient or patients attender. A standard proforma was used to collect the data. The above selected patients were randomized to receive either low dose magnesium sulphate or Zuspans regimen. Investigations such as Complete blood count, Blood grouping and Rh typing, HIV, HbSAg, VDRL ,Coagulation profile, Renal function test, Liver Function Test, Urine routine, serum magnesium was done, Fetal monitoring using Obstetric ultrasound with biophysical profile, and Cardiotocograph monitoring was done.

Results: The dose given to the mother was significantly lower in the low dose magnesium sulphate group compared to Zuspan regimen. There was no signs of magnesium toxicity in the low dose group but the Zuspan regimen was associated with signs of magnesium toxicity. With the most common sign of magnesium toxicity being tachypnea. When serum levels were estimated in these patients all the patients in the Zuspan group showed signs of toxicity and increased serum magnesium levels.

There was no significant difference between the recurrence of convulsions between both the groups.

The mean convulsion to delivery interval measured was lower in the low dose magnesium sulphate group that was 13.8 hours compared to the Zuspan group which was 15.2 hours.

There was no maternal mortality . But two cases of abruption placenta and one case admitted to the ICU in view of status eclampticus.

The total dose of drug administered was significantly lower in the low dose group compared to the Zuspan regimen With respect to the fetal outcome there were lesser admissions to

NICU in the low dose magnesium sulphate group than Zuspan group with the most common reason for NICU admission being preterm care followed by low birth weight.

Perinatal mortality was 22.2% in the low dose group . The number of days spent in NICU was similar in both the groups.

Conclusion: This comparative study shows the efficacy of intravenous low dose magnesium sulphate regimen compared to the Zuspan regimen in respect to recurrence rate of convulsion, chance of toxicity and maternal and perinatal outcome. There was also a significantly lower dose administered in the low dose group compared to the Zuspan group. The present study suggests that low dose magnesium sulphate is as effective as Zuspan regimen

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Introduction

INTRODUCTION

Preeclampsia and eclampsia are pregnancy specific syndromes and can virtually effect any organ in the body. It is the most important and preventable cause of maternal mortality and morbidity. Preclampsia when complicated with tonic clonic seizures is called eclampsia. Imminent eclampsia is also called impending eclampsia where the signs and symptoms of preeclamptic patients would suggest eclampsia is pending. These signs and symptoms are persistent headache, epigastric pain, visual disturbances, nausea , vomiting and generalized restlessness with irritability.

Eclampsia was initially recognized centuries ago in ancient Egypt as seizures occurring in pregnancy and resolving with delivery. Preeclampsia and eclampsia account for about 9% of maternal deaths in Asia, With the incidence in India being around 1 in 100-1700 deliveries from rural to urban populations respectively. An estimated 50,000 women die from eclampsia every year.[1]

According to the Census of sample registration system Of India 2013 Maternal Mortality Rate in the state of Karnataka is 133/ 100,000 live births and eclampsia remains the most important cause of maternal morbidity and mortality.[2]

Depending on the timing of occurrence of convulsions with respect to the onset of labour it can be subcategorized as antepartum, intrapartum and postpartum eclampsia. The major complications include – placental abruption, neurological deficits, aspiration pneumonia, pulmonary edema, cardiopulmonary arrest and acute renal failure.

Eclampsia is most common in the last trimester and becomes increasingly frequent as term approaches. A good obstetric care aims at reduction of maternal morbidity and

mortality and perinatal morbidity and mortality. As the morbidity and mortality are most related to the number of convulsions and it is thereby important for us to control convulsions. The treatment of eclampsia is symptomatic and definitive treatment is to deliver the fetus.

Magnesium sulphate has become the mainstay in the treatment of eclampsia worldwide. It is the drug of choice in the control of convulsions in eclampsia. It is a neuroprotector and not only as the first line of treatment of eclampsia but also as a prophylactic agent in the management of eclampsia. It is administered either intravenously as continuous infusion or can be given intermittently as intramuscular injections.

Magnesium sulphate was first introduced by Horn in Germany in 1906 for managing eclampsia. It was injected intrathecally. In 1925 Lazard and in 1926 Dorsett recommended the intravenous and intramuscular routes of magnesium sulphate regimen. Pritchard popularized the magnesium sulphate regimen by his treatment of patients at Parkland Hospital for eclampsia and now this is popularly known as Pritchards regimen.[3]

Magnesium sulphate was first introduced in 1925 to control convulsions but it was only after the Multicentre Collaborative Eclampsia Trial Group[4] (Magpie trial) published in 1995, magnesium sulphate was proven to be the most effective anticonvulsant drug with a maternal death rate of 4%. Women in this trial treated with Magnesium sulphate had a 52% and 67% lower recurrence of convulsions than those treated with diazepam and phenytoin respectively. The effect of Magnesium sulphate has also been studied on the perinatal outcome demonstrating significantly improved outcomes in newborns compared to phenytoin.[5]

There are many regimens for the administration of magnesium sulphate for eclampsia and imminent eclamspia . Two of the more popular ones include Zuspans [6] regimen and Pritchard Regimen.

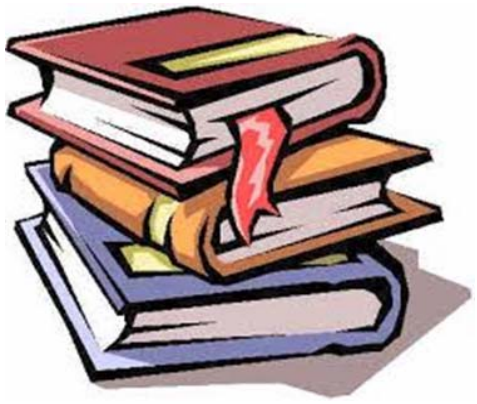
The dosages for Zuspans regimen and Pritchard regimen was formulated for women of western countries having a higher body mass than their Indian counterparts. Many obstetricians in India have used lower dosages for the control of eclamptic convulsions as well as prevention of the same. These lower dose modifications of magnesium sulphate regimen have reduced drug toxicity.

This study aims to compare and study whether the low dose magnesium sulphate regimen is as effective in controlling eclamptic seizures in the Kolar district as compared to the standard Zuspans regimen which was already being used in our tertiary hospital.

Objectives

AIMS AND OBJECTIVES

To compare low dose magnesium sulphate regimen with Zuspan's regimen for patients presenting with imminent eclampsia and eclampsia and to find out the maternal and fetal outcome.



Review of Literature

REVIEW OF LITERATURE

Obstetrical hypertensive emergencies are life-threatening conditions involving significant risk to both the mother and foetus. Aggressive treatment of the maternal hypertensive state requires an initial consideration of the effect of treatment on the foetus, which can occur via changes to the uteroplacental circulation with treatment[7]

Eclampsia as defined earlier is rare in developed countries due to early diagnosis and treatment of preeclampsia. The incidence of eclampsia in our country varies from 0.5%-1.8%. More than half the cases are ante partum, and approximately 20% of the cases occurred post partum. Maternal Mortality is 4 -6 % and the perinatal loss is 45% .The developed world has a much lower rate of this complication - incidence in UK – 4.9/10,000 with case fatality rate of 1.4%[8]

The aim of antenatal care is to detect pre-eclampsia early to prevent any onset of serious complications which include eclampsia

Because we are unclear on the exact pathogenesis of eclampsia , strategies at preventing it are very limited.

A study done by Katz et al done aimed to characterize aspects of the natural history of eclampsia. A retrospective analysis was performed on the record of patients with eclampsia to patients who were delivered in two tertiary care hospitals. It resulted in 53 pregnancies complicated by eclampsia being identified. There were 37 nulliparous women and the mean age was 22 years (range, 15-38 years). Mean gestational age at the

time of seizures was 34.2 weeks' gestation (range, 22-43 weeks' gestation). Antepartum seizures were seen in 28 of the patients (53%); 23 of the 28 had seizures at home. Intrapartum seizures were seen in 19 (36%) of the patients. Eight of these women had seizures while receiving magnesium sulfate, and 7 had therapeutic magnesium levels. Six women had postpartum seizures (11%), 4 >24 hours after delivery. Among the imminent signs seen headache was the most common and preceded seizures in 34 cases. Visual disturbance preceded seizures in 16 cases. There were no maternal deaths or permanent morbidities. There were 4 perinatal deaths. Two patients had intrauterine fetal deaths at 28 and 36 weeks' gestation. These mothers had seizures at home. Of the 53 cases of eclampsia, only 9 were potentially preventable. Only 7 women could be considered to have severe preeclampsia before seizure (13%), and 4 of these 7 women were receiving magnesium sulfate. They hence concluded that eclampsia was not found to be a progression from severe preeclampsia. In 32 of 53 cases (60%) seizures were the first signs of preeclampsia. In this series eclampsia appeared to be more of a subset of preeclampsia. Only 9 cases of eclampsia were potentially preventable with current standards of practice. They concluded that the paradigm for this disease, as well as the approach to seizure prophylaxis, should be reevaluated.[9]

Prevention can either be primary or secondary. Primary prevention is by preventing the development of preeclampsia with preventing avoidable risk factors. Secondary prevention is by using pharmacologic agents that prevent convulsions in women with established preeclampsia.

Current management schemes designed to prevent eclampsia are based on early detection of preeclampsia and subsequent use of preventive therapy such as; use of antihypertensive to maintain blood pressure at an acceptable level, timely delivery, and

prophylactic use of magnesium sulphate during labor and immediate postpartum period in those with severe preeclampsia and to prevent eclampsia.

PATHOGENESIS OF PREECLAMPSIA[10]

Two stages of preeclampsia

Stage -1

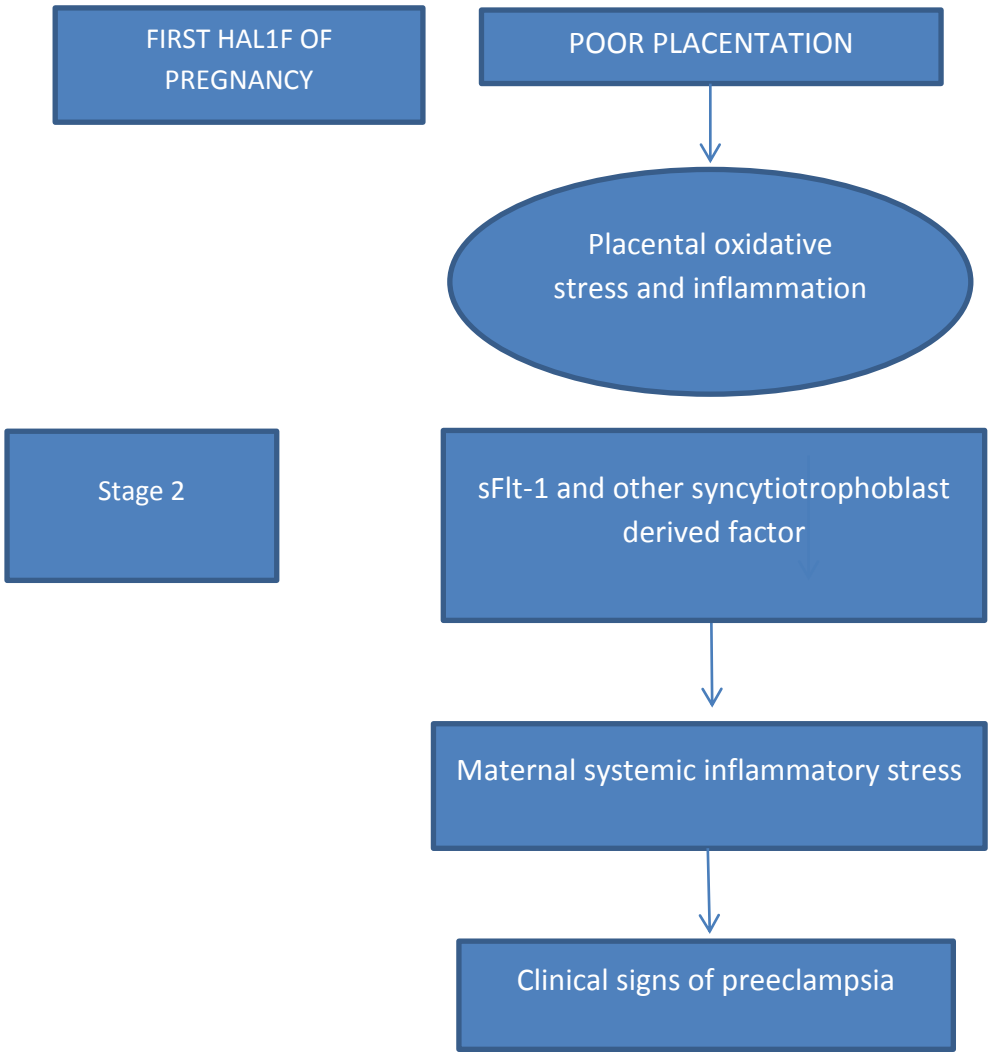


Figure 1: Pathogenesis of Pre Eclampsia

Inhibition of uterovascular development[10]

These changes are due to the interaction between fetal and maternal allografts and result in systemic and vascular changes. It has bee nshown that in patients with eclampsia development of uteropalcental arteries is hindered

Endothelial dysfunction[10]

Factors associated with endothelial dysfunction has been shown to be increased in the systermic circulation of women suffering from eclampsia. These include:

- Cellular fibronectin
- Von Willibrand factor
- Cell adhesion molecules
- Intercellular adhesion molecule -1
- Cytokines
- Tumor necrosis factor alpha

Leakage of the proteins from the circulation and generalized edema are sequelae of endothelial dysfunction and thus a defining factor associated with preeclampsia and eclampsia

Oxidative stress[10]

Leptin molecules increase in the circulation of women with eclampsia, including oxidative stress,. The leptin increase also results in platelet aggregation most likely contributing to the coagulopathy associated with eclampsia.

Oxidative stress has been stimulate the production and secretion of antiangiogenic factor activin A from placental and endothelial cells.

PATHOGENESIS OF CONVULSIONS IN ECLAMPSIA

This includes cerebral vasoconstriction or vasospasm, hypertensive encephalopathy , cerebral edema or infarction , cerebral hemorrhage and metabolic encephalopathy. It is not so clear however, if these findings are the causes or are the effect of the convulsions. The diagnosis of eclampsia is secure in the presence of generalized edema , hypertension , proteinuria and convulsions.[10]

But not all women have straight out of a textbook signs and they can develop a wide spectrum of signs , ranging from severe hypertension , severe proteinuria and generalized edema to absent or minimal hypertension , no proteinuria and no edema.

CEREBRAL PATHOLOGY OF ECLAMPSIA

Cerebral pathology in cortical and subcortical white matter in the form of edema, infarction, and hemorrhage (microhemorrhage and intracerebral parenchymal hemorrhage) is a common autopsy finding in patients who die from eclampsia**.** [11-13]

Although eclamptic patients may initially manifest a variety of neurologic abnormalities, including cortical blindness, focal motor deficits, and coma, most of them have no permanent neurologic deficits.[14,15]

These neurologic abnormalities are probably due to a transient insult, such as hypoxia, ischemia, or edema.[14]

EEG is acutely abnormal in the majority of eclamptic patients, but these abnormalities are not pathognomic of eclampsia. In addition, the abnormal EEG findings are not affected by the use of magnesium sulfate.[16]

The results of CT and MRI reveal the presence of edema and infarction within the subcortical white matter and adjacent gray matter, mostly in the parieto-occipital lobes in approximately 50% of cases.[14, 16-18] Cerebral angiography and Doppler velocimetry suggest the presence of vasospasm.[16, 19]

On the basis of cerebral imaging findings, attention has been directed to hypertensive encephalopathy as a model for the central nervous system abnormalities in eclampsia. The 2 conditions share many clinical, radiologic, and pathologic features.[14,17,19] There is failure of normal cerebral blood flow autoregulation in patients with hypertensive encephalopathy and in some patients with eclampsia. [14, 16-21] Two theories have been proposed to explain these cerebral abnormalities: forced dilation and vasospasm. [14] The forced dilation theory suggests that the lesions in eclampsia are caused by loss of cerebrovascular autoregulation. At increased arterial pressures, normal cerebral vasoconstriction initially occurs.

However, when the upper limit of autoregulation is reached, cerebral vasodilation starts to occur, allowing local hyperperfusion with subsequent interstitial or vasogenic edema.[14] According to the vasospasm theory, cerebral overregulation occurs in response to acute severe hypertension with resultant ischemia, cytotoxic edema, and infarction.[14,16-19] In summary, most women with eclampsia will have evidence of vasogenic edema on brain imaging. This suggests that hypertensive encephalopathy plays a central role in the pathogenesis of eclamptic convulsions.

Recently, various forms of brain imaging were used to characterize the relative frequency of vasogenic and cytotoxic edema in 2 small series of eclamptic women. [20,21]

Cerebral edema (mostly vasogenic) was present in up to 93–100% of these women.[20,21] However, concurrent foci of infarction were present in 6 of 27 eclamptic women studied

by Zeeman et al[20] and in 3 of 17 eclamptic and preeclamptic women studied by Loureiro et al.[21] In addition, 5 of these 6 women reported by Zeeman et al had persistent abnormalities on repeat MRI testing 6–8 weeks later, suggesting that these lesions might not be reversible. Moreover, 4 of the 17 women reported by Loureiro et al had persistent MRI abnormalities at a follow-up at 8 weeks (median).[21]

In summary, cerebral imaging findings in eclampsia are similar to those found in patients with hypertensive encephalopathy. Cerebral imaging is not necessary for the diagnosis and management of most women with eclampsia. Cerebral imaging is indicated for patients with focal neurologic deficits or prolonged coma. In these patients, hemorrhage and other serious abnormalities requiring specific pharmacologic therapy or surgery must be excluded. Cerebral imaging may also be helpful in patients who have atypical presentation for eclampsia (onset before 20 weeks of gestation or more than 48 hours after delivery, and eclampsia refractory to adequate magnesium sulfate therapy).[16] It is hoped that advances in MRI and MR angiography as well as in cerebral vascular Doppler velocimetry will aid our understanding of the pathogenesis of this condition and thus improve long-term outcome.

EDENS CRITERIA[22]

Assessing the severity of eclampsia. These are also indications for CT scan. If the following are present, eclampsia is considered severe.[14]

- Coma of >6hours
- Temperature of >39C
- Pulse rate of 120/min

- Systolic blood pressure of 200mmHg
- Respiratory rate >40/min
- More than 10 convulsions

STAGES OF ECLAMPSIA[12]

- *Premonitory stage*- Eyes rolled up. There is twitching on face and limbs. Duration is around half a minute.
- *Tonic stage*- Generalized tonic contractions of the entire body. There is opisthotonus and cessation of respiration. Lasts for half a minute.
- *Clonic stage*- There are alternative contraction and relaxation of muscles. Tongue maybe bitten. Breathing becomes stertorous. Lasts for a minute.
- *Coma or post convulsion stage*-Lasts for a few minutes

TYPES OF ECLAMPSIA

There are three types of eclampsia[13]

Antepartum eclampsia

Intrapartum eclampsia

Postpartum eclampsia

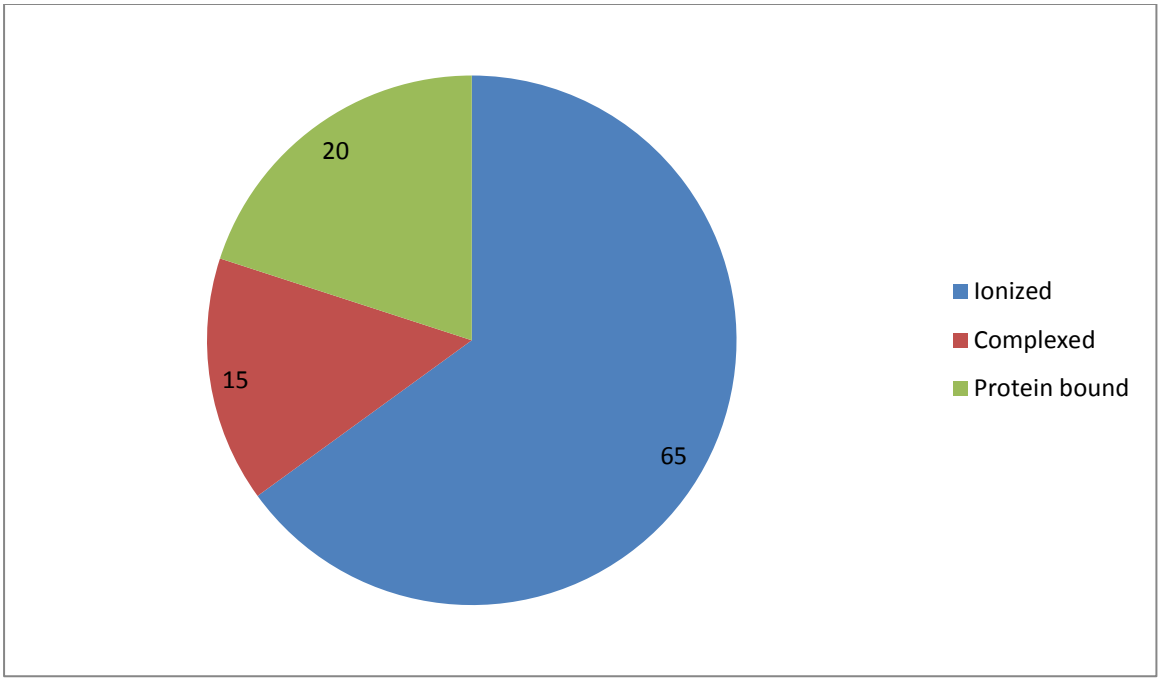
Several Authors consider two subtypes of eclampsia as well Early cases and Intercurrent eclampsia

MAGNESIUM

Magnesium is a Group 2 (alkaline earth) element within the periodic table and has a relative atomic mass of 24.305Da. Magnesium salts dissolve easily in water and are relatively more soluble than their calcium salts. Traditionally, magnesium salts are used as antacids or laxatives in the form of Magnesium hydroxide, magnesium citrate or magnesium sulphate. The total magnesium content of the body is reported to be 20mmol/kg of fat free tissue. About 90% of total body magnesium is located in the bones, muscles and non muscular soft tissues. Extracellular magnesium accounts for 1% of the total body. [23]

Serum magnesium is categorized into three fractions. It is either free/ ionized, bound to protein or complexed with anions such as phosphate, bicarbonate , citrate and sulphate. However of the three fractions in plasma ionized magnesium has the greatest biological activity. Magnesium is found primarily within the cells where it acts as a counter ion for the energy rich ATP and nuclear acids. Magnesium is a cofactor in more than 300 enzymatic reactions. Magnesium critically stabilizes the enzymes , including many ATP generating reactions. Magnesium contributes to the regulation of vascular tone, heart rhythm, platelet activated thrombosis and bone formation. [23]

Graph 1: Distribution of magnesium present in three different states



Distribution and plasma levels

Maternal plasma levels of magnesium after parenteral administration depend on the volume of distribution and renal excretion of the magnesium ions. In the presence of severe oliguria or advanced renal failure , the volume of distribution alone determines the serum concentration. Infused magnesium is distributed rapidly throughout the entire extracellular fluid space and some is taken up by the bone, none by the red blood cells. With intravenous loading dose of 4-6g it results in an immediate but transient increase in plasma levels to 4.2-7.6 mEq/l which falls to 2.6-3.4mEq/l within 60 minutes , within 90 minutes about 50% of the infused magnesium moves into bones and other cells.[24]

The rapid distribution in a large pool is a buffering action that prevents accumulation and attainment of toxic concentrations in plasma the therapeutic level is considered to be between 4- 7 mEq/L. However this is based on clinical experience and not direct suppression of eclamptic convulsions.[24]

Many studies have been done regarding the pharmacokinetic basis of the action of magnesium in magnesium sulphate dosing regimens in imminent eclampsia and eclampsia.

In 2015 two authors extracted data from 28 studies done investigating the pharmacokinetic properties of 17 magnesium sulphate regimens. Baseline magnesium concentrations where consistently <1 mmol/l across studies. Intravenous loading dose between 4 and 6 g was associated with a doubling of this baseline concentration half an hour after injection. Maintenance infusion of 1 g/hour consistently produced concentrations well below 2 mmol/l, whereas maintenance infusion at 2 g/hour and the Pritchard intramuscular regimen had higher but inconsistent probability of producing concentrations between 2 and 3 mmol/l. Volume of distribution of magnesium varied (13.65–49.00 l) but the plasma clearance was fairly similar (4.28–5.00 l/hour) across populations. They concluded that the profiles of Zuspan and Pritchard regimens indicate that the minimum effective serum magnesium concentration for eclampsia prophylaxis is lower than the generally accepted level. Exposure–response studies to identify effective alternative dosing regimens should target concentrations achievable by these standard regimens.[25]

Mechanism of Action :

Magnesium sulphate acts by blockade of NMDA (N Methyl D Aspartate) subtype of glutamate channel receptor in voltage dependent manner.[26]

The peripheral action is at the neuromuscular junction causing blockage of calcium entering the cell and blocking of calcium at intracellular sites, reducing the presynaptic

acetyl choline release at the end plate, reducing motor and end plate sensitivity to the acetyl choline.[27]

The central action is by preferential uptake by the hippocampus and cerebral cortex rich in NMDA receptors. Also inhibits platelet activation. Decreases systemic vascular resistance and dilates the orbital vessels, increases the cardiac output, renal blood flow and uteroplacental flow.[26]

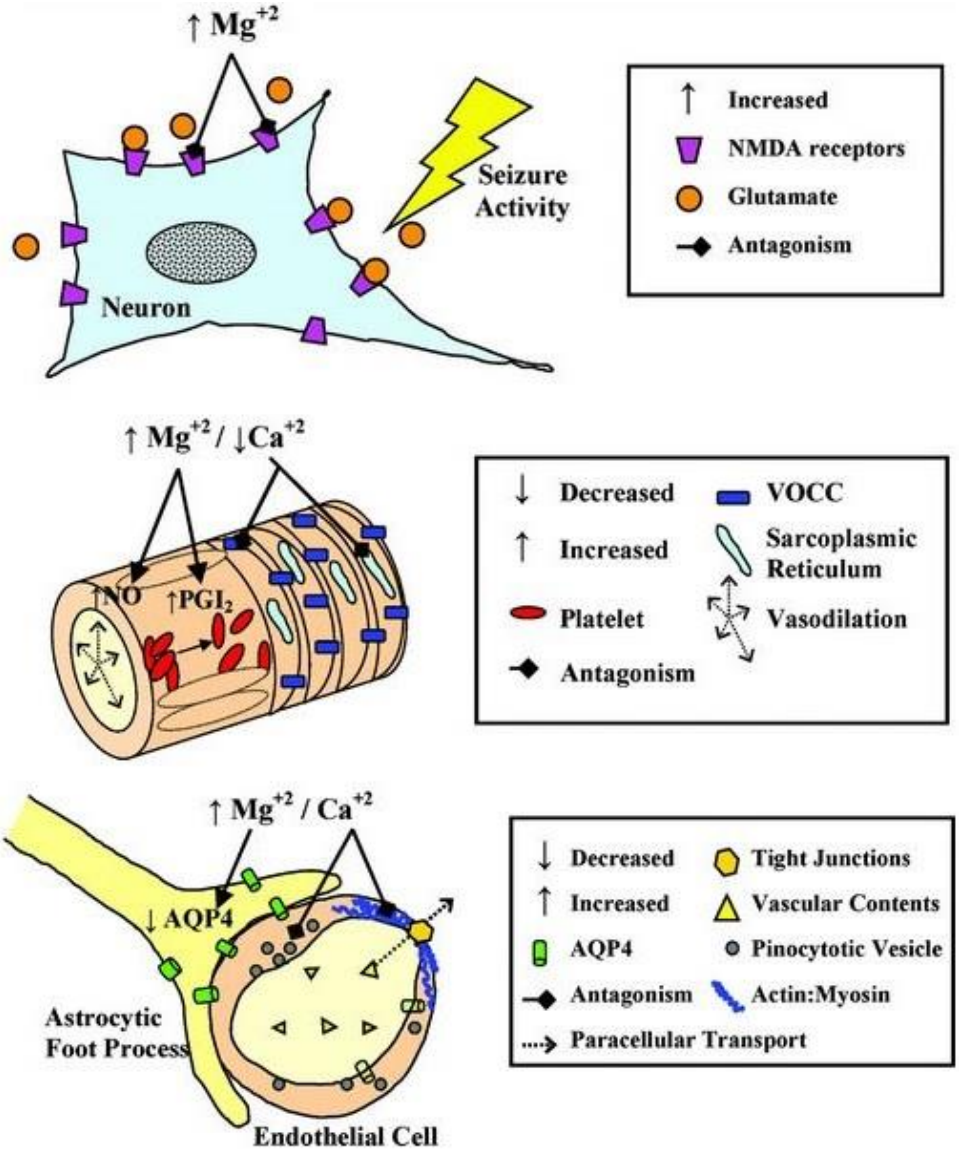


Figure 2: Mechanism of action of Magnesium sulphate

Although the mode of treatment of magnesium sulphate is not completely understood, experiments in rats have shown that it is mediated through the N- Methyl D-Aspartate (NMDA) antagonist. Magnesium is a calcium channel antagonist, and smooth muscle relaxant. It therefore affects the cerebral endothelium which forms the blood brain barrier by lowering intracellular calcium by limiting paracellular transport of vascular contents such as ions and proteins effectively decreasing factors which promote cerebral oedema and seizure activity.[26]

Pharmacokinetics:

Only 0.3% of total body magnesium is found in serum of which 33% is protein bound 5% are complexed to anions like citrate and phosphate and 62% are in ionized form. The normal serum values vary from 1.6-2.1mEq/L[27]

Excretion

Mangnesium is excreted almost solely by the kidneys and after four hours about 50% of the infused dose is excreted in the urine. The renal clearance of magnesium increases linearly and steeply with an increase in the plasma level in the presence of oliguria or significant renal failure, the maintenance dose should be either reduced or discontinued and maternal plasma levels should be monitored frequently. [27]

Rapid urinary excretion of magnesium has been reported by various authors. Cruikshank et al[28] demonstrated that urinary magnesium excretion increased twentyfold during magnesium sulphate infusion , of which75% of the infused dose was excreted during the infusion , by 24 hours after the infusion 90% had been eliminated. Chelsey and Tepper , noted excretion of 44% of 10g intramuscular dose within four hours and Chelsey found

that 38% to 53% of a 13g dose (10g intramuscularly and 3g intravenously) was excreted within four hours.[29]

Magnesium sulphate toxicity and side effects:

There are several effects of magnesium sulphate on both the mother and fetus and regimens with higher doses have a tendency to produce this effect.

The main fear of toxicity was laid to rest with the Magpie trial[4]. Toxicity of drug was monitored with clinical parameters

The therapeutic levels of magnesium sulphate are 4-7mEq/L[30]

Maternal side effects include the disappearance of patellar reflex (8-10mEq/l) and is considered as the first signs of magnesium sulphate toxicity.[30]

This is followed by dry mouth , flushing , drowsiness ,blurred ,vision , slurred speech, nausea, vomiting (9-12mEq/l) followed by respiratory depression at 12mEq/l and cardiotoxicity-prolonged PR,QT,QRS(10-15mEq/l) and cardiac arrest at 30mEq/l. These clinical parameters were compared to serum levels of magnesium suphate.[30]

After administration, about 40% of plasma magnesium is protein bound. The unbound magnesium ion diffuses into the extravascular-extracellular space, into bone, and across the placenta and fetal membranes and into the fetus and amniotic fluid. In pregnant women, apparent volumes of distribution reach constant values between the third and fourth hours after administration, and range from 0.250 to 0.442 L/kg. Magnesium is almost exclusively excreted in the urine, with 90% of the dose excreted during the first 24 hours after an intravenous infusion of MgSO4. The pharmacokinetic profile of MgSO4 after intravenous administration can be described by a 2-compartment model with a rapid distribution (α) phase, followed by a relative slow β phase of elimination. The clinical

effect and toxicity of MgSO4 can be linked to its concentration in plasma. A concentration of 1.8 to 3.0 mmol/L has been suggested for treatment of eclamptic convulsions. The actual magnesium dose and concentration needed for prophylaxis had never been estimated. Maternal toxicity is rare when magnesium sulphate is carefully administered and monitored.[30]

Treatment of magnesium toxicity includes ; those with depressed patellar reflex, avoid and withhold further administration of magnesium sulphate. Fluid and nutritional support is sufficient as serum magnesium will fall with excretion in urine . Those with respiratory depression , muscular paralysis and cardio respiratory arrest , the patient must be intubated immediately and managed with assisted ventilation till resumption of spontaneous respiration.[31]

It is important to keep an ampoule containing 1g (10ml of a 10% solution) calcium gluconate at the bedside to be used for intravenous administration as an antidote in cases of magnesium toxicity. This medication should be administered slowly to avoid hypotension or bradycardia. There are no absolute contraindications to magnesium toxicity other than myasthenia gravis and heart muscle damage.[31]

An integrative review of the side effects related to the use of magnesium sulphate for preeclampsia and eclampsia management done in 2013 compared a total of 24 studies. Magnesium sulfate regimen against other drug regimens was compared to examine the side effects. Prospective clinical studies were included if magnesium sulfate was used to manage pre eclampsia or eclampsia in low or middle income countries were included . The study included the recording of the incidence of any adverse side effect resulting from magnesium sulphate use. Around 34 subject groups were included. The overall rate of absent patellar reflex among all 9556 aggregated women was 1.6% , the overall rate of

respiratory depression was 1.3%. Delay in the repeat administration of magnesium sulphate occurred in 3.6% of cases. They concluded that adverse effects occurred very infrequently, and when they occurred a delay in the repeat administration was generally sufficient to mitigate the effect.[32]

Maternal adverse effects of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes were reviewed. A total of 143 publications were included in the review which had 21 randomized trials, 15 non randomized comparative studies, 32 case series and 75 reports of individual cases. Compared with the placebo or no treatment , magnesium sulphate was not associated with an increased risk of maternal death, cardiac arrest or respiratory arrest. Few subgroup differences were however noted. In one trial, a lower dose regimen 2g every 3rd hourly compared to higher dose regimen (5g/4th hourly) significantly reduced treatment cessation. Adverse effect estimates from studies of other designs largely supported data from randomized trials. Case reports supported an association between iatrogenic overdose of magnesium sulphate and life threatening consequences. It concluded that appropriate antenatal magnesium sulphate administration was not shown to be associated with serious maternal adverse effects. Larger trials may be needed to determine optimal regimens.[33]

Effect on the fetus

The effect of magnesium sulphate on the fetal heart rate variability has been controversial. Atkinson et al[34] using computerized fetal heart rate analysis, concluded that although magnesium sulphate was associated with an objectively measured statistically significant decrease in short term variability , the decrease was not clinically

significant, furthermore it was not associated with a decrease in long term variability or in the number of accelerations measured.

A study by IMordechai Hallak et al [35] concluded that prolonged administration of magnesium sulphate was associated with decreased fetal heart rate baseline values and variability, but the clinical significance of these findings was questionable.

Interaction with drugs

Nifedepine and Magnesium sulphate are both calcium channel blockers. A depressive effect on blood pressure (Increased hypotensive effect) has been observed when these agents are combined. A theoretical risk of interaction between the two does exist but in practice maybe relatively uncommon. [36]

At the neuromuscular junction magnesium decreases the presynaptic release of acetylcholine. Reduced sensitivity of the post junctional membrane (motor end plate) decreased excitability of the muscle fibres have also been reported. Such neuromuscular blocking effects of magnesium would be expected to potentiate the non depolarizing blocking agents and to antagonize the depolarizing block of succinyl choline. Magnesium has however been shown to potentiate the activity of both the depolarizing and non depolarizing neuromuscular blocking agent.[36]

Excretion in breast milk

Many pre –eclamptic or eclamptic patients who are treated with magnesium sulphate are too ill or babies too premature for consideration of feeding immediate postpartum.

Cruikshank et al [37] demonstrated that intrapartum magnesium sulphate treatment increases breast milk – colostrum magnesium levels significantly for , only 24 hours after discontinuation of the infusion. After 24 hours milk magnesium levels are the same as those women acting as controls. The breastfed infant of a treated mother would receive only 1.5mg of magnesium more than the infant of a non treated mother. The serum magnesium levels of bottle fed infants whose mothers received magnesium sulphate return to control values by 48 hours after birth.

THE COLLABORATIVE ECLAMPSIA TRIAL[38]

This was large multicentre trial done in the year 1995 in 25 developing countries found magnesium sulphate to be a better drug for controlling and preventing convulsion. Indian women are smaller in built. Indian women from lower socioeconomic groups weigh much less than their counterparts in western world. Hence low dose magnesium sulphate may be equally effective in with significant reduction in toxicity of the drug as well. Clinical monitoring appears to be sufficient which can reassure health professionals at primary and secondary level hospital about the safety of this drug.

VARIOUS MAGNESIUM SULPHATE REGIMENS FOR ECLAMPSIA

Magnesium sulphate is also called Epsom salt. It is MgSO4.7H2O.USP. Its molecular weight is 120.366 g/mol salt which contains 98mg of elemental magnesium. Magnesium sulphate can be administered IV , IM or SC as 15% SC, 20-25% IV and 50% IM solution.

Table 1: Regimens of Magnesium Sulphate

Sl. No	Regimen name	Loading dose	Maintainence dose
1.	Prichard[3]	4g IV(25%) over 5-10 mins	5g MgSo4(50%) IM into each buttock followed by 5g 50% MgSo4 IM 4TH Hourly into each buttock for 24 hours following delivery on last convulsion
2.	Zuspan[6]	4g IV (20%)	1g/hr for 24 hours after delivery or seizure whichever comes later.
3.	Sibai[39]	6g MgSo4 IV over 20 mins	2g/hr MgSo4 infusion
4.	Dhaka[40]	4g (20%) IV over 15mins and 3g(50%) given IM in each buttock	2.5g every 4th hourly IM alternate buttock
5.	Phadhar[41]	10g [2g (20%) IV and 4g (50%) IM in each buttock]	4g (50%) IM every 4h for 24h after delivery or after last convulsion whichever was later

6.	Sardesai[42]	4g MgSo4 given IV OR IM	2g IV/IM every 3rd hourly
7.	Charles Flowers[44]	4g IV in 250ml of 5% D	5g every 6th hourly as IM
8.	Sokoto[45]	4g IV followed by 10g IM (5g in each buttock)	nil

Studies Comparing Low Dose Magnesium Sulphate Regimens To Higher dose magnesium sulphate regimens

Eclampsia is a serious complication in pregnancy, being a life threatening emergency causing serious maternal and perinatal morbidity and mortality.

Standard regimens followed the world over include the Prichard's regimen[3] and the Zuspan's regimen[6]. Flower et al. [43] in 1962 first started adjusting doses of magnesium sulphate according to body weight, plasma levels and urinary excretion of magnesium sulphate.

Ekele B et al. [45] in Sokoto Nigeria did a prospective, cohort study of eclamptic patients admitted between July 2007 and June 2008 who were given 4 grams magnesium sulphate intravenously and 10 grams intramuscularly (5 grams in each buttock) as the sole anticonvulsant agent. Main outcome measure was the absence of a repeat fit. Other aspects of eclampsia management were as in standard practice. One hundred and twenty

one (121) patients were managed with this regimen. There were 29 ante partum, 76 intrapartum and 16 post partum cases of eclampsia. Most of the patients were primigravidae (100; 83%) with an average age of 18.7 years. There were nine cases (7.4%) of recurrent fits that occurred within four hours of the loading dose. One recurrent fit occurred in the ante partum group, seven in the intra partum and one in the post partum group. There were 12 maternal deaths giving a case fatality rate of 9.9%. They concluded that the limiting the dosage of magnesium sulphate to 14 grams loading dose (4 grams intravenous and 10 grams intramuscular) was effective in controlling fits in 92.6% of cases in the study group.[45]

In 1993 a study conducted by Phuapradit et al. in Thailand studied serum magnesium levels in severe preeclampsia patients who were given magnesium sulphate infusions. Forty four patients diagnosed with severe preeclampsia between 30-41 weeks were given 5g bolus magnesium sulphate followed by 1g/hour continuous infusion and was continued 24 hours postpartum. The pre treatment values and post delivery levels were measured immediate delivery, at 12 hours and at 24 hours and it was found that serum levels varied with maternal weight and that the dosing regime in this study was suitable for Asian women weighing less than 70kgs.[46]

Identifying barriers in availability and required resources to monitor magnesium sulphate in remote areas many studies were thus conducted to come up with more suitable regimens to combat these problems as well as to address issues requiring effect of magnesium sulphate dosing based on body weight to avoid potential toxicity complications from the same.

Thus in 2003 Suman Sardesai[42] et al. studied a magnesium sulphate regimen which was more convenient and suitable to the Indian women based on body weight. They found

that low dose magnesium sulphate regimen was more suitable, required less monitoring and manpower and did not cause any potential toxicity to the patients for whom it was administered.

Thus after this several other studies were done with low dose magnesium sulphate regimens. In 2009, a prospective study was done in Padhar Hospital in Phadhar.[41] They studied 95 eclamptic women in two different magnesium sulphate groups , Group A that directly came to the hospital and Group B who has already received diazepam or Phenargan at the referral hospital.Group A received 10g and Group B received 6g loading dose of magnesium sulphate. Both groups received 4g maintenance dose every 4 hours. Out of the 95 eclamptic women only one woman in group B had recurrent convulsion. All women maintained normal respiratory rates. 39 (41%) women has absent knee jerks on atleast one occasion and for them the maintenance dose was omitted. Urine output was more than 30m/hr in 92 (96.8%) of women. In 5 women maintenance dose had to be augmented to 5g as reflexes were exaggerated. [41]

They thus concluded that low dose regime appears to control and prevent convulsions effectively in Indian women and clinical monitoring appears to be sufficient.[41]

Bangal V [47] et al. in 2009 compared a low dose magnesium sulphate regime in Government Rural Hospital in Loni where a loading dose of 4g of magnesium sulphate (20% solution) was given intravenously over 5 minutes followed by a maintenance dose of 2g (50% solution) deep intramuscularly in alternate buttocks every four hours till 24 hours after delivery or after the last convulsion whichever was later. They compared this to the standard Prichard regimen which was 5g given deep intramuscularly every four hours.

Fifty cases of eclampsia were randomized and analysed .Maternal and perinatal outcomes of magnesium toxicity were analyzed. It was observed that 86% of cases responded to initial intravenous dose of 4g of 20% magnesium sulphate. Eight percent cases had recurrence of convulsions and were controlled by additional 2g of 20% magnesium sulphate. Six percent of cases required shifting to standard Prichard regimen as they did not respond to low dose magnesium sulphate regimen. The average total dose of magnesium sulphate required to control convulsions was 20g i.e 54.4% less than that compared to standard Prichard regimen. The perinatal and maternal mortality were comparable to those of standard Prichard regimen. They did not find a single case of magnesium related toxicity to low dose magnesium sulphate regimen and hence they concluded low dose magnesium sulphate was safe and effective in eclampsia.[47]

A randomized comparative study between low dose intravenous magnesium sulphate and standard intramuscular regime for treatment for eclampsia was done by Bhattacharjee et al. A total of 144 women were divided into a study and control group of 72 women. The study group received 0.75g/hr of magnesium sulphate regimen intravenously after a loading dose of 4g and the control group was given the standard intramuscular regimen by Prichard. The primary outcome was to measure the recurrence rate of the seizures and secondary outcomes if any was development of magnesium toxicity if any, and maternal and perinatal outcomes.[48]

In this study the incidence of fit recurrence was statistically insignificant for both the groups compared (7.46% vs 8.57% with a p= 0.939). The total dose of magnesium sulphate was significantly lower in the intravenous group (p= 0.0001) in which no patient developed magnesium toxicity. They thus concluded that low dose magnesium sulphate was found as effective as the standard intramuscular regimen, while maintaining a high safety margin.[48]

A randomized control trial was carried out in the Obstetric unit of Koirala Institute of Health Sciences in Nepal to study the suitability of different dosage schedule for patients over a span of a year and a half. A total of 80 eclamptic patient were randomized to receive either standard Prichard Regimen (loading and maintenance) or loading dose of magnesium sulphate. Both groups were evaluated for recurrence of seizures and outcomes. There were no recurrent seizures in the standard regimen group but there were 2 patients with recurrent seizures in the loading dose group (p= 0.184). They thus concluded that loading dose magnesium sulphate was a good alternative for standard Prichard regimen.[49]

Another similar study[50] was conducted in 2013 where they determined the efficacy and safety of a single dose magnesium sulphate regimen in treating eclamptic seizures and its effect on maternal and fetal outcomes. This was a prospective study conducted in VIMs Bellary from 2003 to 2007 where 513 eclamptic women received single doses of 4g diluted 50% magnesium sulphate intravenously with simultaneous 4g 50% magnesium sulphate intramuscularly. The recurrent seizures, maternal mortality and perinatal mortality were measured. Around 9.16% of recurrence and 3.3% maternal mortality with 24.8% perinatal mortality was observed. They concluded that a single dose magnesium sulphate regimen was effective and safe in controlling eclamptic convulsions. This VIMs regimen can be first used at referral units before shifting to tertiary care centres. This approach was aimed at reducing the morbidities at the primary health care level where standard obstetric care is not available.[50]

Gaddi and Somegowda, who were from the same institution, reported the data on 791 cases (from 1998–2004). They treated patients having severe pre eclampsia and

eclampsia with low dose magnesium sulphate regime consisting of 4g loading dose infused intravenously followed by 2g intramuscularly every 3 hours as maintenance dose. Among these, 621 received the low dose MgSo4 regimen, 90 women received the single dose as has been described earlier and 72 cases were treated with the standard regimen of Pritchard. The recurrence rate of the convulsions was 9.2% in these cases. The maternal mortality is 3.3% in this study.[51]

Studies involving single dose magnesium sulphate were done with the aim to find out the efficacy and safety profile and to prevent any dosing related toxicity of magnesium sulphate in developing countries where resources to monitor magnesium sulphate administration is low.

In Gulbarga, 2013 efficacy of a single dose of magnesium sulphate was done to reduce adverse effects of magnesium sulphate and also improve the maternal and fetal outcome. It was a prospective study of 100 cases with a clinical diagnosis of eclampsia were given a single loading dose of magnesium sulphate (4g of 20% IV and 10g of 50% IM) , there was no maintenance dose. The effect of a single loading dose of magnesium sulphate in controlling convulsions, recurrence rates, toxicity and maternal and fetal outcomes were studied. The results showed a favorable outcome with the reduction of the dose and duration of magnesium sulphate therapy. The primary outcomes were comparable with all other regimens in use. The cases that were on single dose regimen had a significantly lower incidence of cesarean section with upto 74% of patients having vaginal deliveries. The maternal mortality was 3% and the perinatal mortality was 29%. They concluded that single loading dose of magnesium sulphate was effective in controlling and preventing recurrence of convulsions in eclampsia. There was a complete absence of magnesium sulphate toxicity. This regimen is easy to administer and painful injections and

monitoring of magnesium suphate toxicity seen with maintenance dose can be avoided with this regimen.[52]

A single dosing regimen given as a prophylactic for women with severe preeclampsia or with imminent signs versus the conventional 24 hours of therapy of modified Prichard regime was also studied in 2013. Patients of severe preeclampsia were randomly allocated to study group (n=50) and control group (n=50). Patients in the study group received only the loading dose of magnesium sulphate and patients in the control group received loading dose of magnesium sulphate followed by maintenance dose every fourth hourly according to Prichard regimen.[53]

There was one case of seizures in both the groups. There were 6 cases of absent knee jerk and 4 cases of oliguria in those receiving the 24 hour magnesium sulphate while none of those complications were seen in those receiving only loading dose (p= 0.012, p=0.022) Neonatal mortality was more in the control group. They thus concluded that loading dose by the Prichard regimen alone maybe effective in preventing seizures in patients with severe preeclampsia with the added advantage of reduced toxicity and better neonatal outcome.[53]

The safety and efficacy of a lower dose of magnesium has been studied very extensively in India. A study done in Maharashtra was based on a lower dose regimen than Prichard which was suitable for Indian women who are smaller built than their western counterparts. The prospective study included 50 eclampsia patients receiving low dose magnesium sulphate which was a loading dose of 9g of magnesium sulphate followed by 2.5g given intramuscularly every 6 hours for 24 hours after administering the loading dose. Patients were monitored every hour to observe for any signs of magnesium toxicity. The total dose of magnesium sulphate required to control convulsions was around 20g ,

less than that required by the Prichard regimen. They found that maternal and perinatal mortality were comparable in both the groups. The study did not find a single case of magnesium related toxicity with low dose magnesium sulphate regime.[54]

The Dhaka regimen was compared to Pritchards regimen for managing eclampsia published in 2015. It was a hospital based prospective study done in Burla from October 2012 to October 2014. They included a total of 300 patients of elcampsia and randomly distributed them into two groups of Dhaka regimen and Prichard regimen. The loading dose for the Dhaka regimen and Pritchard regimen was the same 4g (20% solution) magnesium sulphate intravenously. In the Dhaka regimen 3g magnesium sulphate was given in each buttock followed by a maintenance of 2.5g magnesium sulphate every fourth hourly intramuscularly. The Prichard was followed as stated above. There was no recurrence of convulsions in both the groups. The Dhaka regimen was associated with significantly lower deep tendon reflex loss, significantly lower amount of magnesium sulphate requirement and lower maternal mortality as compared to Pritchard regimen. They thus concluded that the Dhaka regimen was equally effective and safe in the management of eclampsia in a region where most women had low body weight.[55]

The role of magnesium sulphate was studied in eclamptic and imminent eclamptic patients in 2015 by Asani et al[56] It was done on 94 patients of eclampsia and imminent eclampsia. These patients were divided into two groups. A study group in which low dose regimen was administered I.E for eclampsia 4g 20% IV over 15-20 minutes followed by 2g 50% deep IM 3 hourly till 24 hours after delivery or last convulsion and imminent eclampsia 2g 50% IM 3 hourly till premonitory signs and symptoms disappeared. The control group was administered Prichard regimen. They concluded that there was no significant difference in prevention of convulsions between the two groups but signs of impending toxicity were less in the low dose group. With respect to perinatal outcome

there were lesser NICU admissions with better APGAR scores. So low dose magnesium sulphate regimen was as efficacious as standard Prichard regimen to control convulsions, maternal and perinatal outcome was better with less chances of magnesium toxicity in the low dose regimen and hence was highly suitable for Indian women with lesser weight compared to their western counterparts.[56]

T.S Savitha et al[57] conducted a prospective randomized study in a tertiary level hospital from January 2009 to June 2010 which included 60 patients admitted with eclampsia and imminent eclampsia. Patients were divided into two groups of 30 patients each. The study group received low dose magnesium sulphate and the control group received Zuspan regimen. They concluded that both the groups were comparable in terms of type of convulsion, number of convulsions, therapeutic drug level , maternal complications and perinatal outcome. Low dose magnesium sulphate was equally effective as Zuspan regimen.[57]

Another study done using only low dose Magnesium sulphate treatment according the Sardesai[42] regimen where out of 1622 deliveries 9 had eclampsia, 32 had imminent eclampsia and 48 patients had severe pre eclampsia. Their study found that low dose magnesium sulphate was useful to prevent recurrence of convulsions. Clinical monitoring for magnesium toxicity is sufficient. Hence low dose magnesium sulphate regimen is safe, which suits Indian women who have relatively low body mass index as compared to their western counter parts.[58]

A study conducted by Krishsagar et al in Karad studied the effect of low dose magnesium sulphate regimen versus Pritchard regimen for eclampsia and imminent eclampsia. They had a sample size of 60 patients. They estimated the serum magnesium levels in each patient. In 90 % of patients treated with low dose and 91.6% patients with Pritchards

regimen convulsions were controlled. Prophylaxis was 100% in both the groups. Hence they concluded that low dose was equally as efficacious in controlling eclampsia and preventing eclampsia and standard Pritchard regimen.[59]

MANAGEMENT OF ECLAMPSIA

The first priority in the management of eclampsia is to prevent maternal injury and to support respiratory and cardiovascular functions. During or immediately after the acute convulsive episode, supportive care should be given to prevent serious maternal injury and aspiration, assess and establish airway potency, and insure maternal oxygenation.[16]

During this time, the bed's side rails should be elevated and padded, a padded tongue blade is inserted between the teeth (avoid inducing gag reflex), and physical restraints may be needed.[16]

To minimize the risk of aspiration, the patient should lie in lateral decubitus position, and vomitus and oral secretion are suctioned as needed.[16]

During the convulsive episode, hypoventilation and respiratory acidosis often occur. Although the initial seizure lasts only a few minutes, it is important to maintain oxygenation by supplemental oxygen administration via a face mask with or without oxygen reservoir at 8–10 L/min.[16]

After the convulsion has ceased, the patient begins to breathe again and oxygenation is rarely a problem. However, maternal hypoxemia and acidosis may develop in women who have had repetitive convulsions and in those with aspiration pneumonia, pulmonary edema, or a combination of these factors. Arterial blood gas analysis is required if the pulse oximetry results are abnormal (oxygen saturation at or below 92%).

The next step in the management of eclampsia is to prevent recurrent convulsions. Magnesium sulfate is the drug of choice to treat and prevent subsequent convulsions in women with eclampsia.[60]

Depending on the regimens of choice as innumerated above and hospital protocol magnesium sulphate is administered in loading dose and maintenance. If there is any recurrence of seizures, 2g bolus of magnesium sulphate is administered intravenously over 3-5 minutes. [60]

The next step in the management of eclampsia is to reduce the blood pressure to a safe range but at the same time avoid significant hypotension. The objective of treating severe hypertension is to avoid loss of cerebral autoregulation and to prevent congestive heart failure without compromising cerebral perfusion or jeopardizing uteroplacental blood flow that is already reduced in many women with eclampsia. Intravenous route of administration is preferred to the oral administration given the condition and responsiveness of the patient. Diuretics are not used except in the presence of pulmonary edema.

Maternal hypoxemia and hypercarbia cause fetal heart rate and uterine activity changes during and immediately following a convulsion. Fetal heart rate changes can include bradycardia, transient late decelerations, decreased beat-to-beat variability, and compensatory tachycardia. Changes in uterine activity can include increased frequency and tone.[60]

These changes usually resolve spontaneously within 3–10 minutes after the termination of convulsions and the correction of maternal hypoxemia. The patient should not be rushed for an emergency cesarean delivery based on these findings, especially if the maternal condition is not stable. It is considered to be advantageous to the fetus to allow

in utero recovery from hypoxia and hypercarbia due to maternal convulsions. However, if the bradycardia and/or recurrent late decelerations persist beyond 10–15 minutes despite all resuscitative efforts, then a diagnosis of abruptio placentae or nonreassuring fetal status should be considered.

The presence of eclampsia is not an indication for caesarean delivery. The decision to perform cesarean delivery should be based on fetal gestational age, fetal condition, presence of labor pains, and cervical Bishop score.[61]

Patients having labor pains or rupture of membranes are allowed to deliver vaginally in the absence of obstetric complications. When labor is indicated, it is initiated with either oxytocin infusions or prostaglandins in all patients with a gestational age of 30 weeks or more, irrespective of the Bishop score. A similar approach is used for those before 30 weeks of gestation if the cervical Bishop score is at least 5. Maternal pain relief during labor and delivery can be provided by either systemic opioids or epidural anaesthesia as recommended for women with severe preeclampsia.[62]

Either epidural, spinal, or combined techniques of regional anaesthesia can be used for cesarean delivery. Regional anaesthesia is contraindicated in the presence of coagulopathy or severe thrombocytopenia (platelet count less than 50,000/mm^3).[62]

General anaesthesia increases the risk of aspiration and failed intubation due to airway enema and is associated with marked increases in systemic and cerebral pressures during intubation and extubation.[61] Women with airway or laryngeal enema may require awake intubation under fiber optic observation with the availability of immediate tracheostomy. Changes in systemic or cerebral pressures may be attenuated by pre-treatment with labetalol or nitroglycerine injections.[62]

After delivery, patients with eclampsia should receive close monitoring of vital signs, fluid intake and output, and symptoms for at least 48 hours. These women usually receive large amounts of intravenous fluids during labor, delivery, and postpartum. In addition, during the postpartum period there is mobilization of extracellular fluid leading to increased intravascular volume. As a result, women with eclampsia, particularly those with abnormal renal function, those with abruptio placentae, and those with pre-existing chronic hypertension, are at increased risk for pulmonary enema and exacerbation of severe hypertension postpartum.[62,63] These women should receive frequent evaluation of the amount of intravenous fluids, oral intake, blood products, and urine output, as well as monitoring by pulse oximetry and pulmonary auscultation.

Parenteral magnesium sulfate should be continued for at least 24 hours after delivery and/or for at least 24 hours after the last convulsion. If the patient has oliguria (less than 100 mL/4 h), the rate of both fluid administration and the dose of magnesium sulfate should be reduced.[63]

Once delivery has occurred, other oral antihypertensive agents such as labetalol or nifedipine can be used to keep systolic blood pressure below 155 mm Hg and diastolic blood pressure below 105 mm Hg. The recommended dose of oral labetalol is 200 mg every 8 hours (maximum dose of 2,400 mg/d), and the recommended dose of nifedipine is 10 mg orally every 6 hours (maximum dose of 120 mg/d). The drug of choice is oral nifedipine because it offers the benefit of improved diuresis in the postpartum period.[64]

Materials & Methods

MATERIAL AND METHODS

This is a cross sectional study in which patients presenting with imminent eclampsia and eclampsia in R.L. Jalappa Hospital & Research Centre were recruited.

Minimum of 30 cases in each group were included in the study.

Sample size was calculated using the following formula-

$$= \frac{2(Z\alpha/2 + Z\beta)2\ P(1-P)}{(p1 - p2)2}$$

Where ,

Zα/2= Z0.05/2=Z0.025 = 1.96 at type 1 error of 5%

Zβ=Z0.20= 0.842= At 80% power

p1 –p2= Difference in proportion in the two different groups

p= Pooled prevalence =[Prevalence in Low dose Magnesium group (p1) +Prevalence in Zuspans Group (p2)]/2

Clinical history was collected from 30 cases of eclampsia and 30 cases of imminent eclampsia who are admitted in the labour room in the department of Obstetrics and Gynaecology at R.L Jalappa hospital and research centre in the period of August 2015– July 2016.

Written informed consent was obtained from the patient or patient's attender. A standard proforma was used to collect the data. The above selected patients were randomized to receive either low dose magnesium sulphate or Zuspans regimen.Vitals of the patient was checked on admission. Level of consciousness was assessed according to Glasgow Coma Scale (GCS).[65] Investigations such as Complete blood count, Blood grouping and Rh typing, HIV, HbSAg , VDRL ,Coagulation profile, Renal function test, Liver Function Test, Urine microscopy, serum magnesium were done, Fetal monitoring using Obstetric ultrasound with biophysical profile, and Cardiotocograph monitoring was done.

Serum magnesium levels have been estimated if signs of magnesium toxicity are observed. Serum magnesium levels will be estimated using Formazan dye method.

The selected patients who fulfilled the inclusion criteria were randomized to receive either low dose magnesium or Zuspans Regimen

Patients were randomized according to a computer generated randomization table.

30 patients received low dose magnesium sulphate with loading dose of 4g magnesium sulphate IV and maintenance dose of 2g/3hrly IV infusion for 24 hours. Recurrent convulsions were treated with an additional dose of 2g IV and changed over to Zuspans regimen.

30 patients received Zuspans regime with a loading dose of 4g of magnesium sulphate followed by maintenance of 1g/ hr IV infusion. Recurrent convulsions were treated with an additional dose of 2g IV. If any recurrence they were switched over to phenytoin regimen (600mg i.v stat followed by 100mg i.v TID) and CT/MRI brain will be advised.

Patients were monitored with respiratory rate, knee jerk, urine output. Serum magnesium levels were estimated if signs of toxicity as present. and Inj. Calcium Gluconate 1 g slow IV was given in these cases.

Magnesium sulphate was discontinued 24 hours after delivery or last convulsion whichever was later.

Inclusion criteria :

- Patients with imminent eclampsia and eclampsia

Exclusion criteria :

- History of convulsions due to cerebrovascular accident and epilepsy
- Patients with cardiac disease
- Chronic lung disease
- Less than 20 weeks of gestational age
- Postnatal cases
- Myasthenia Gravis

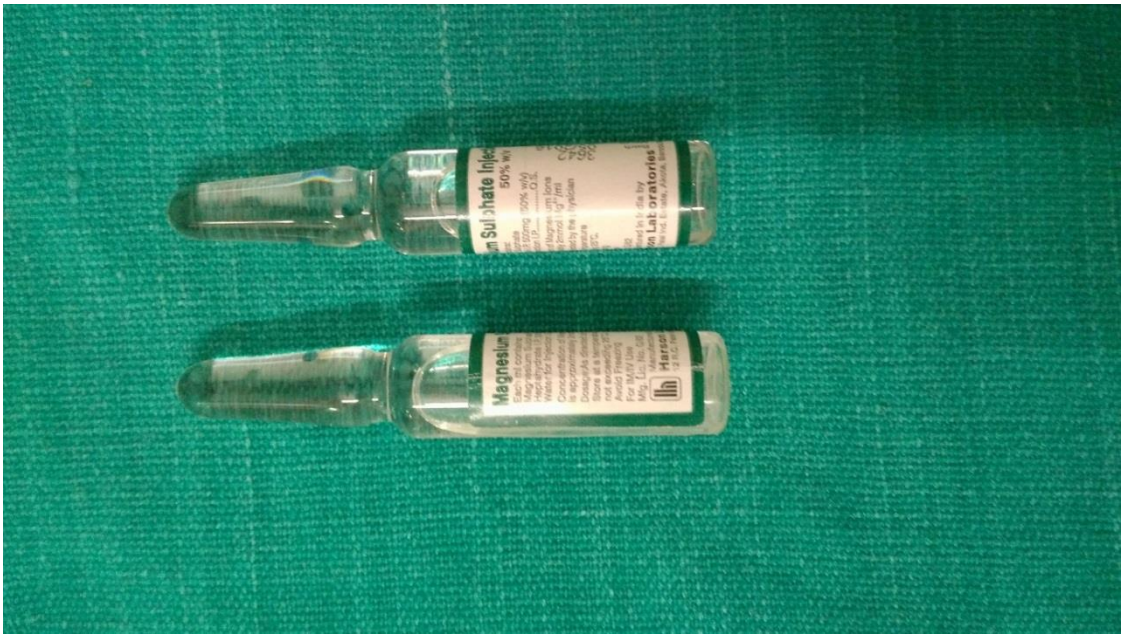


Figure 3: Magnesium Sulphate vials

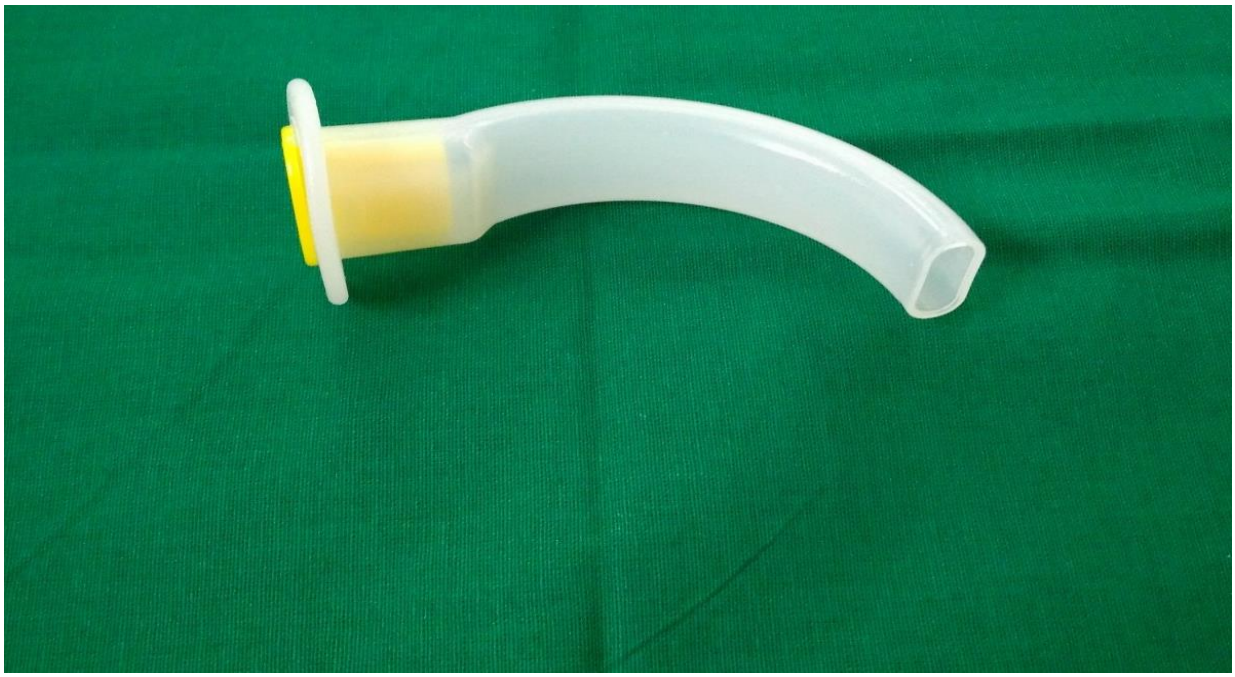


Figure 4: Mouth gag

Figure 5: Eclampsia ward in RLJ Hospital

Figure 6: Eclampsia kit

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test of Fischer's exact test (for 2x2 tables only) was used as test of significance for qualitative data. Yates correction was applied were ever chi-square rules were not fulfilled (for 2x2 tables only).

Continuous data was represented as mean and standard deviation. Independent t test or Mann Whitney U test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram and Scatter plots.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse data. EPI Info (CDC Atlanta), Open Epi, Med calc and Medley's desktop were used to estimate sample size, odds ratio and reference management in the study.

Paired t test or Wilcoxon Signed rank test is the test of significance for paired data such as before and after surgery for quantitative and qualitative data respectively.

Observations & Results

RESULTS

Group A = Zuspan Regime

Group B = Low dose MgSo4

Table 2: Association between age distribution and groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Count	%	Count	%
Age distribution	<20 years	9	30.0%	7	23.3%
	21 to 25 years	13	43.3%	17	56.7%
	>25 years	8	26.7%	6	20.0%

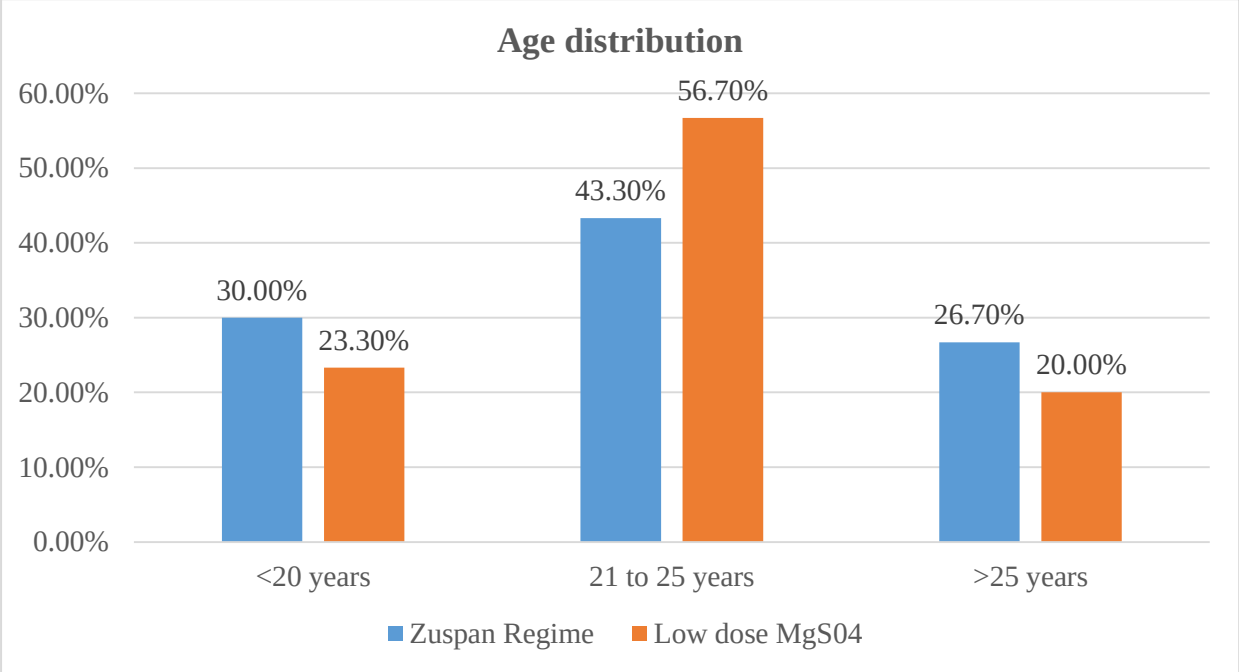
χ 2 = 1.069, df = 2, p = 0.586

In Zuspan group, 30% of them were below 20 years, 43.3% were between 21 to 25 years and 26.7% were >25 years, Similarly in the low dose MgsO4 group, 23.3% were <20 years, 56.7% were between 21 to 25 years and 20% were >25 years. There was no significant association between age and the two groups.

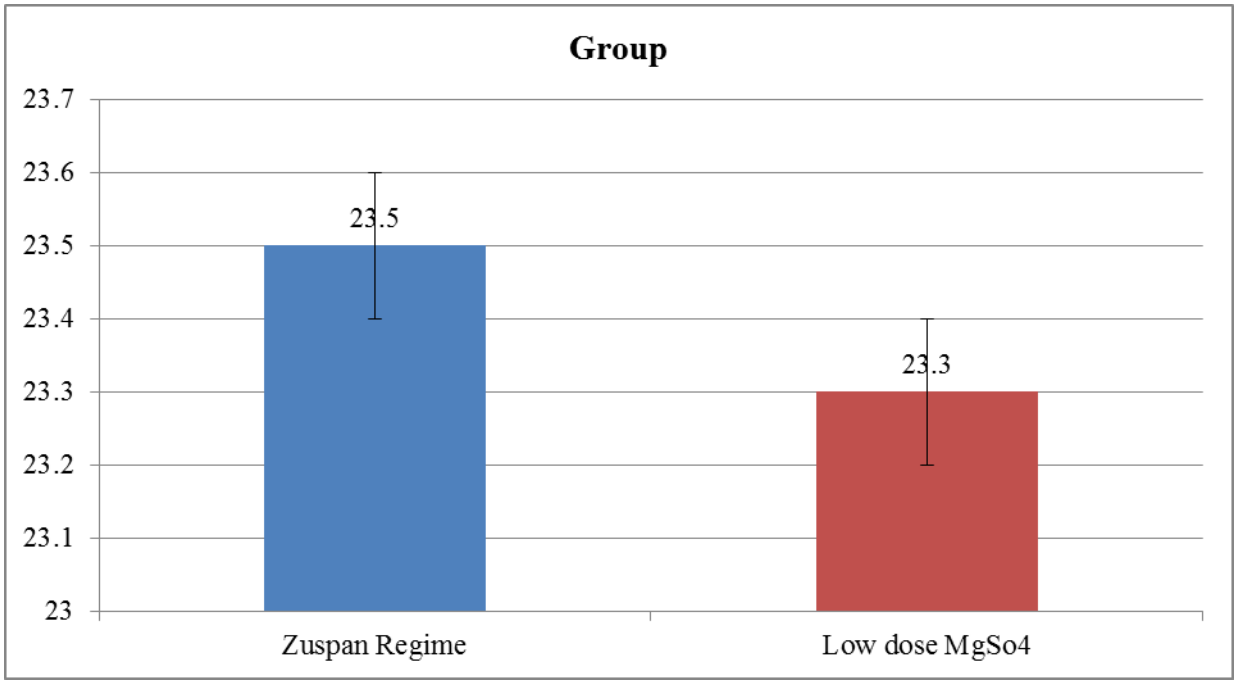
Table 3: **Mean age of subjects in the study**

		Age		P value
		Mean	SD	
Group	Zuspan Regime	23.5	3.8	0.800
	Low dose MgSo4	23.3	3.3	
	Total	23.4	3.5	

Mean age of subjects in group A was 23.5 ± 3.8 years and in group B was 23.3 ± 3.3 years. There was no significant difference in mean age between two groups. Hence age matching has achieved.



Graph 2: Age distribution in both groups

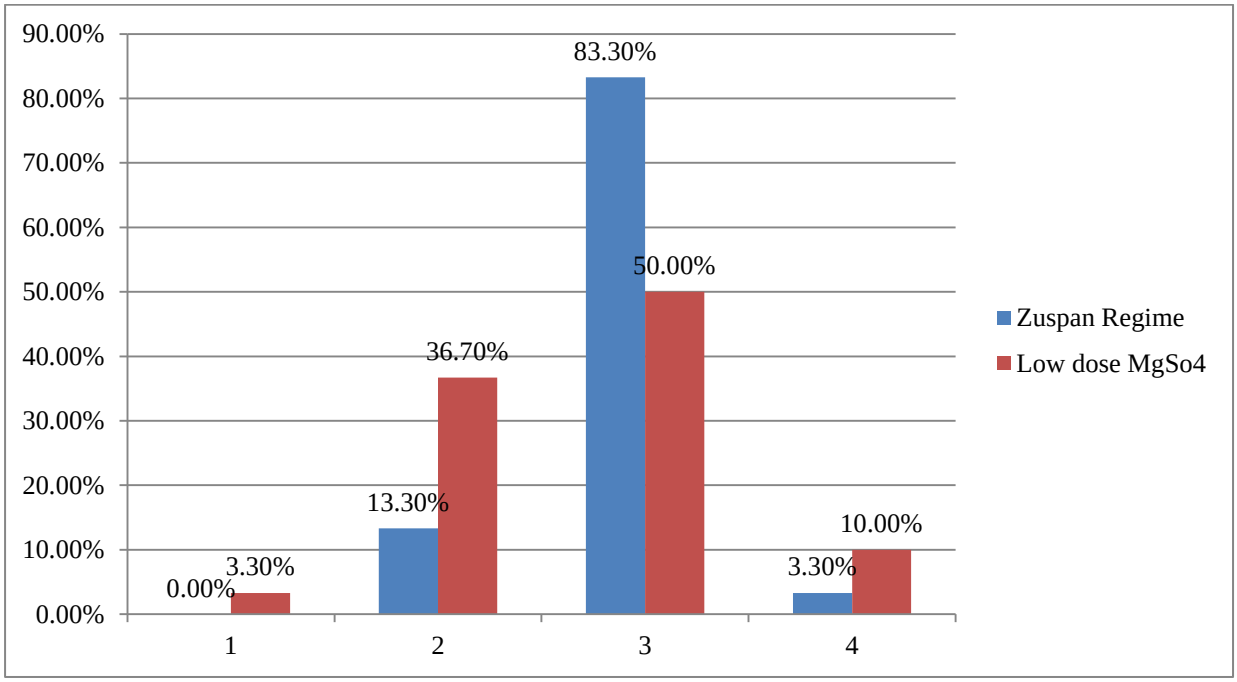


Graph 3: Mean age between the two groups

Table 4: Socioeconomic status of subjects in the study

		Group						P value
		Zuspan Regime		Low dose MgSo4		Total		
		Count	%	Count	%	Count	%	
SES	1	0	0.0%	1	3.3%	1	1.7%	0.051
	2	4	13.3%	11	36.7%	15	25.0%	
	3	25	83.3%	15	50.0%	40	66.7%	
	4	1	3.3%	3	10.0%	4	6.7%	

Majority of subjects in both the groups belonged to Socio economic status of 3. There was no significant difference between two groups.



Graph 4: Socioeconomic status of both the groups

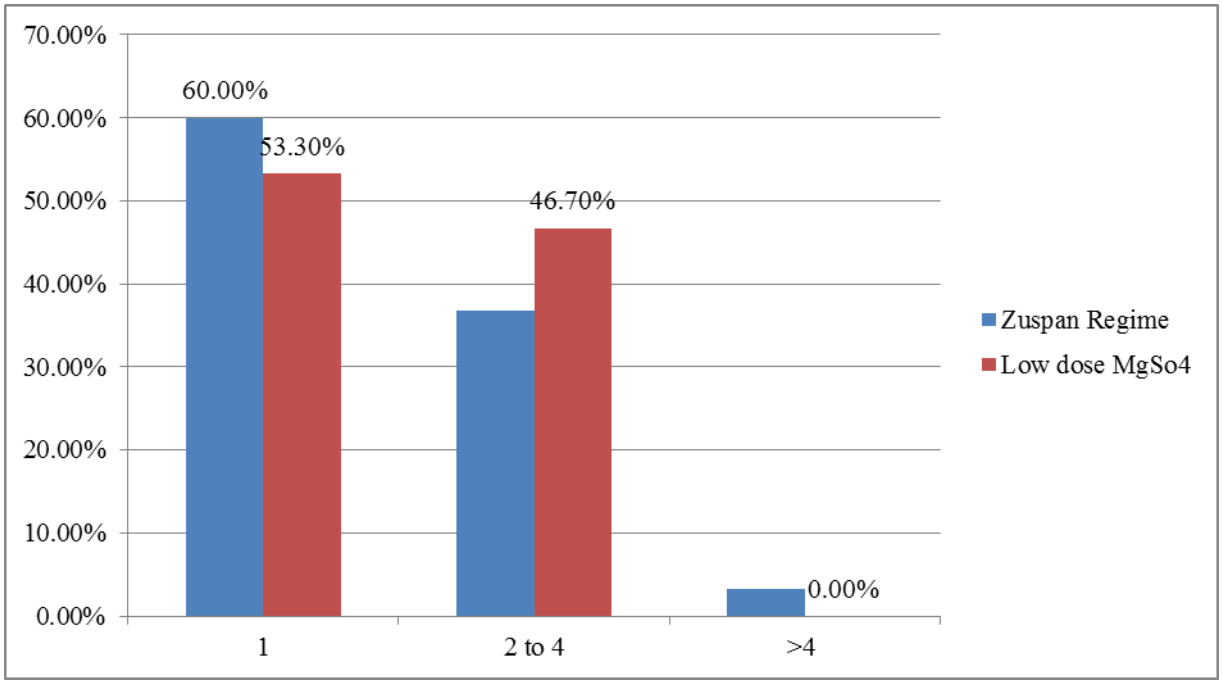
Majority of subjects in both the groups belonged to Socio economic status of 3. There was no significant difference between two groups.

Table 5: Comparison of Parity between two groups

		Group					
		Zuspan Regime		Low dose MgSo4		Total	
		Number	%	Number	%	Number	%
Gravida	1	18	60	16	53.3	34	56.7
	2 to 4	11	36.7	14	46.7	25	41.6
	>4	1	3.3	0	0.0	1	1.7
	Total	30	100	30	100	60	100

$\chi 2 = 5.851$, df = 2, p = 0.211

Majority of subjects in the study were primigravida in both the groups. There was no significant difference in gravida status between two groups.



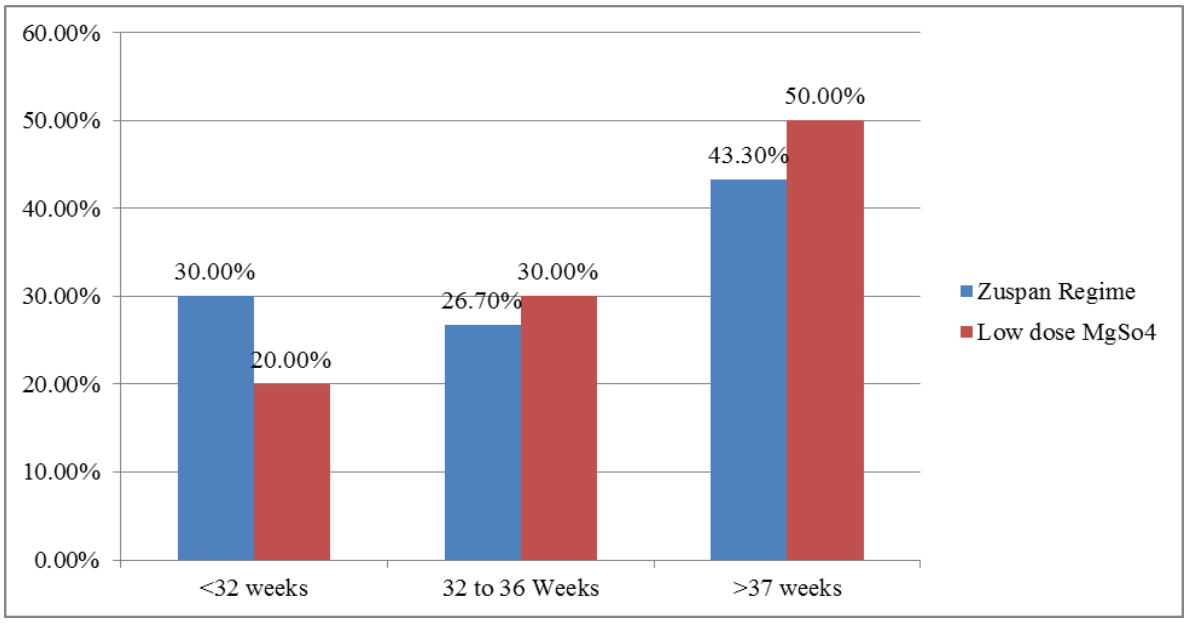
Graph 5: Comparison of Parity between the two groups

Table 6: Comparison of Gestational age between two groups

		Group					
		Zuspan Regime		Low dose MgSo4		Total	
		Count	%	Count	%	Count	%
Gestational age	<32 weeks	9	30.0%	6	20.0%	15	25.0%
	32w+0d to 36w+6d	8	26.7%	9	30.0%	17	28.3%
	>37 weeks	13	43.3%	15	50.0%	28	46.7%
	Total	30	100.0%	30	100.0%	60	100.0%

$\chi 2 = 0.802$, df = 2, p = 0.670

In Group A, 30% were at <32 weeks, 26.7% were at 32 to 36 weeks and 43.3% were at >37 weeks, similarly in Group B, 20% were at <32 weeks, 30% at 32 to 36 weeks and 50% at >37 weeks of gestation. There was no significant difference in gestational age between two groups.

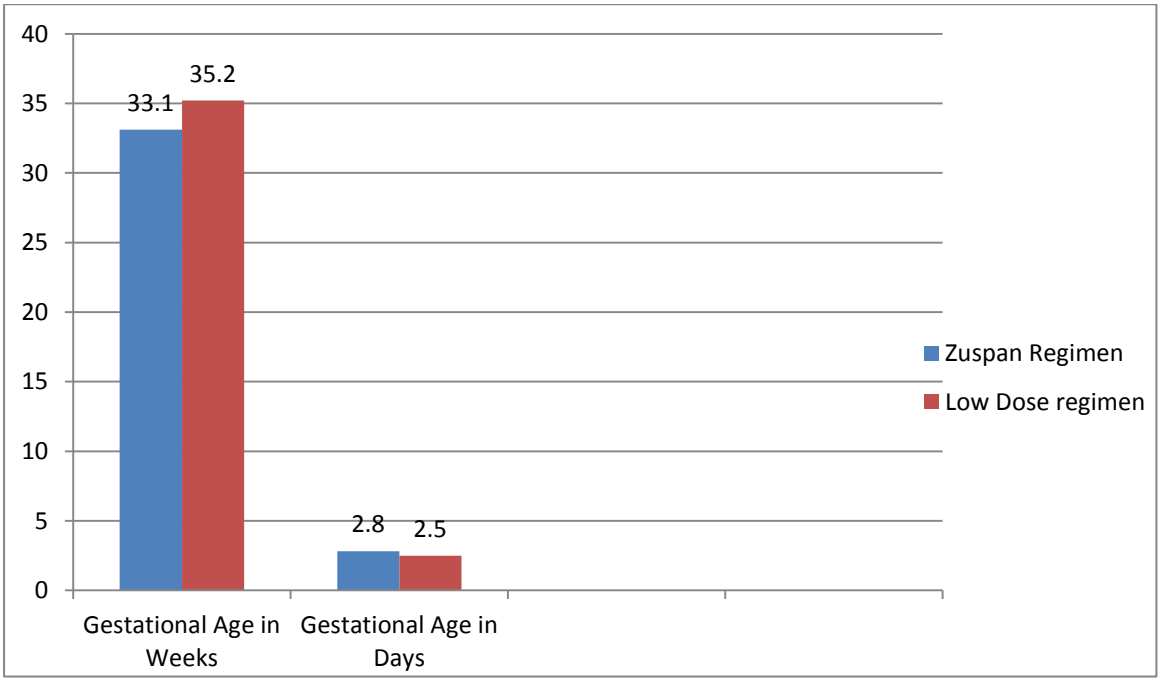


Graph 6: Gestational age in weeks in both the groups

Table 7: Mean Gestational age in both the groups

	Group						P value
	Zuspan Regime		Low dose MgSo4		Total		
	Mean	SD	Mean	SD	Mean	SD	
Gestational age in Weeks	33	5.1	35	5.0	34.1	5.2	0.109
Gestational age in days	2.8	2.2	2.5	1.9	2.6	2.1	0.505

The mean gestational age in both the groups were 33 weeks and 3 days in the Zuspan group whereas 35 weeks and 2 days in the low dose group. This was not statistically significant and hence also comparable.



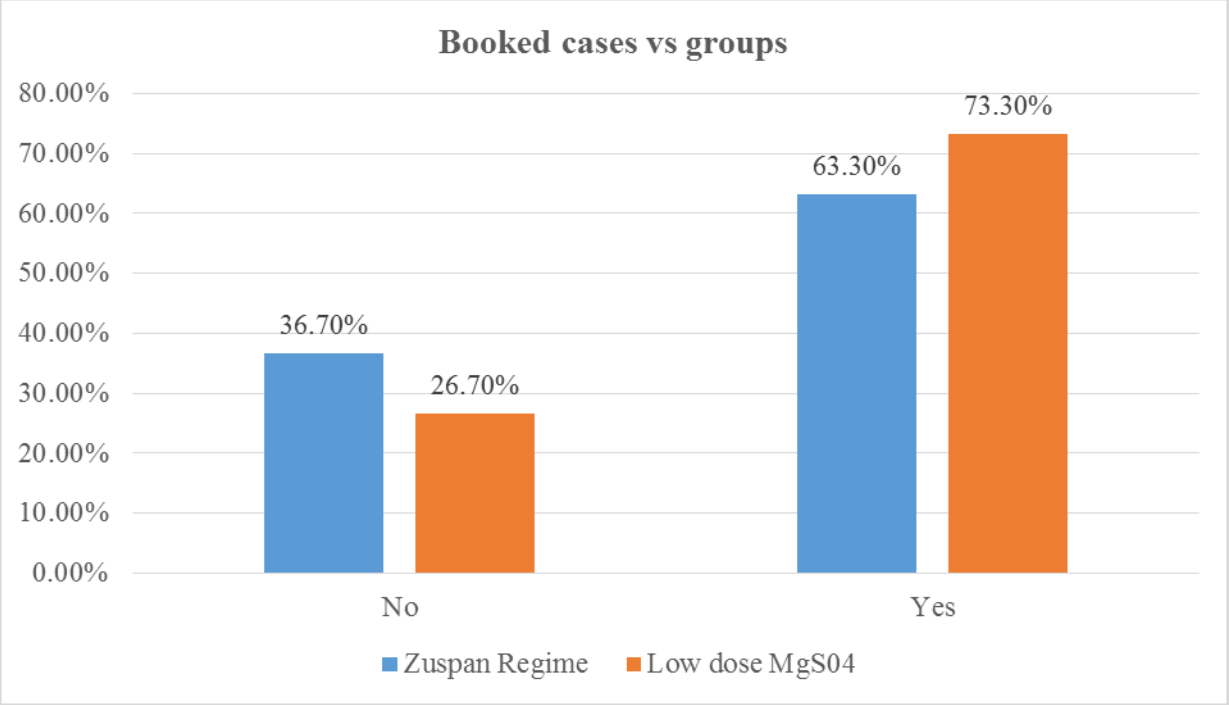
Graph 7: Mean gestational age in both the groups in weeks and days

Table 8: Association between Booked and unbooked cases in both the groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
Booked	No	11	36.7%	8	26.7%
	Yes	19	63.3%	22	73.3%

χ 2 = 0.693, df = 1, p = 0.405

In Group A 63.3% were booked case and in group B 73.3% were booked cases. There was no significant difference in booked cases between two groups.



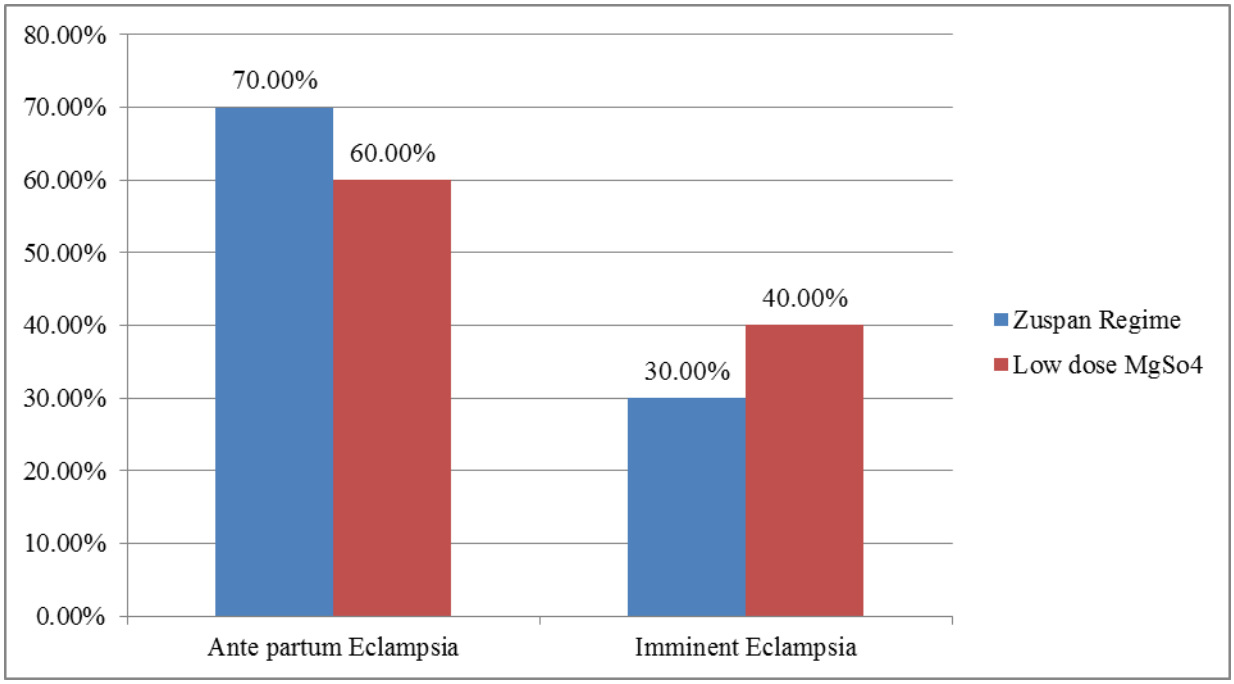
Graph 8: Association between booked and unbooked cases in both the groups

Table 9: Comparison of Type of Eclampsia between two groups

		Group			
		Zuspan Regime		Low dose MgSo4	
		Number	%	Number	%
Eclampsia	Ante partum Eclampsia	21	70.0%	18	60.0%
	Imminent Eclampsia	9	30.0%	12	40.0%
	Total	30	100.0%	30	100.0%

$\chi 2 = 0.659$, df = 1, p = 0.417

In Group A, 70% had antepartum eclampsia and 30% had imminent eclampsia. In group B, 60% had antenatal eclampsia and 40% had imminent eclampsia. There was no significant difference in type of eclampsia between two groups.



Graph 9: Association of type of eclampsia in both the groups

Table 10: Imminent symptoms on presentation comparison between two groups

		Group				P value
		Zuspan Regime		Low dose MgSo4		
		Number	%	Number	%	
H/o increased BP readings	No	15	50.0	10	33.3	0.190
	Yes	15	50.0	20	66.7	
Headache	No	11	36.7	13	43.3	0.598
	Yes	19	63.3	17	56.7	
Blurring of Vision	No	21	70.0	22	73.3	0.774
	Yes	9	30.0	8	26.7	
Epigastric Pain	No	28	93.3	25	83.3	0.228
	Yes	2	6.7	5	16.7	
Vomiting	No	20	66.7	19	63.3	0.787
	Yes	10	33.3	11	36.7	

There was no significant difference in symptoms on presentation between two groups. Most common symptom on presentation was Headache in Group A and raised Blood Pressure in Group B.

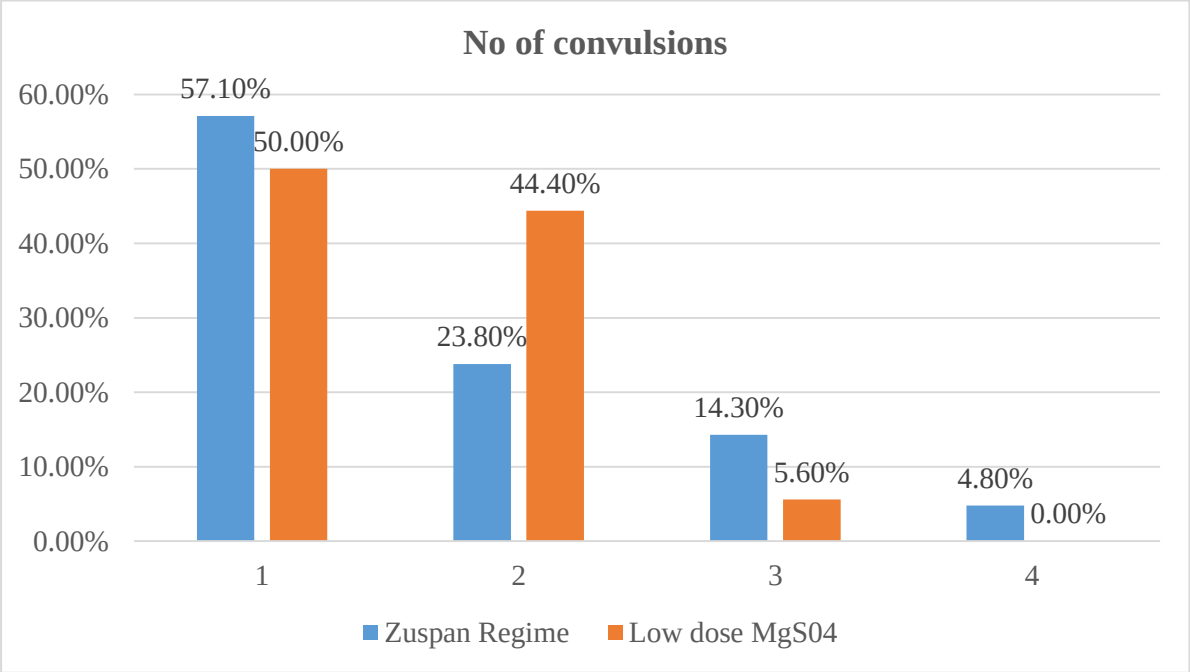
Table 11: Association between Number of convulsions in both groups at admission

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
No of convulsions	1	12	57.1%	9	50.0%
	2	5	23.8%	8	44.4%
	3	3	14.3%	1	5.6%
	4	1	4.8%	0	0.0%

$\chi 2 = 2.907$, df = 3, p = 0.406

There was no significant association between no of convulsions and two groups.

57.1% of them had one convulsions, 23.8% 2 convulsions, 14.3% had 3 episodes of convulsions and 4.8% had 4 episodes of convulsions.

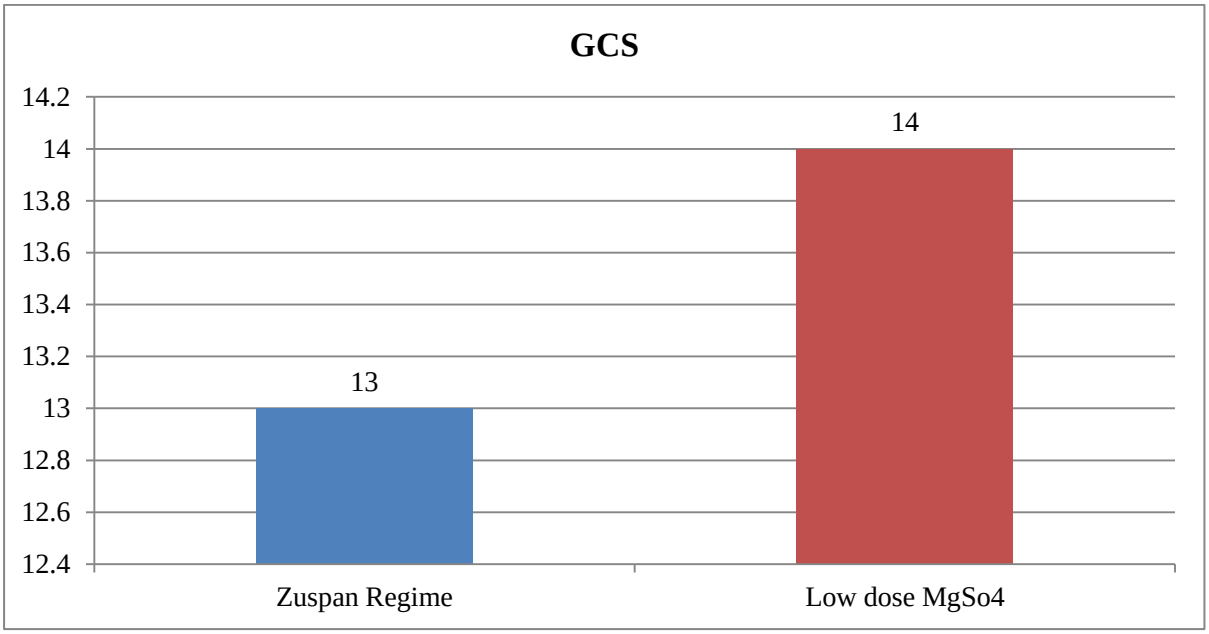


Graph 10: Number of convulsions in both the groups on admission

Table 12: GCS score comparison between two groups

	Group				P value
	Zuspan Regime		Low dose MgSo4		
	Mean	SD	Mean	SD	
GCS	13	3	14	2	0.290

Mean GCS score in Group A was 13 ± 3 and in Group B was 14 ± 2. There was no significant difference between two groups with respect to GCS.

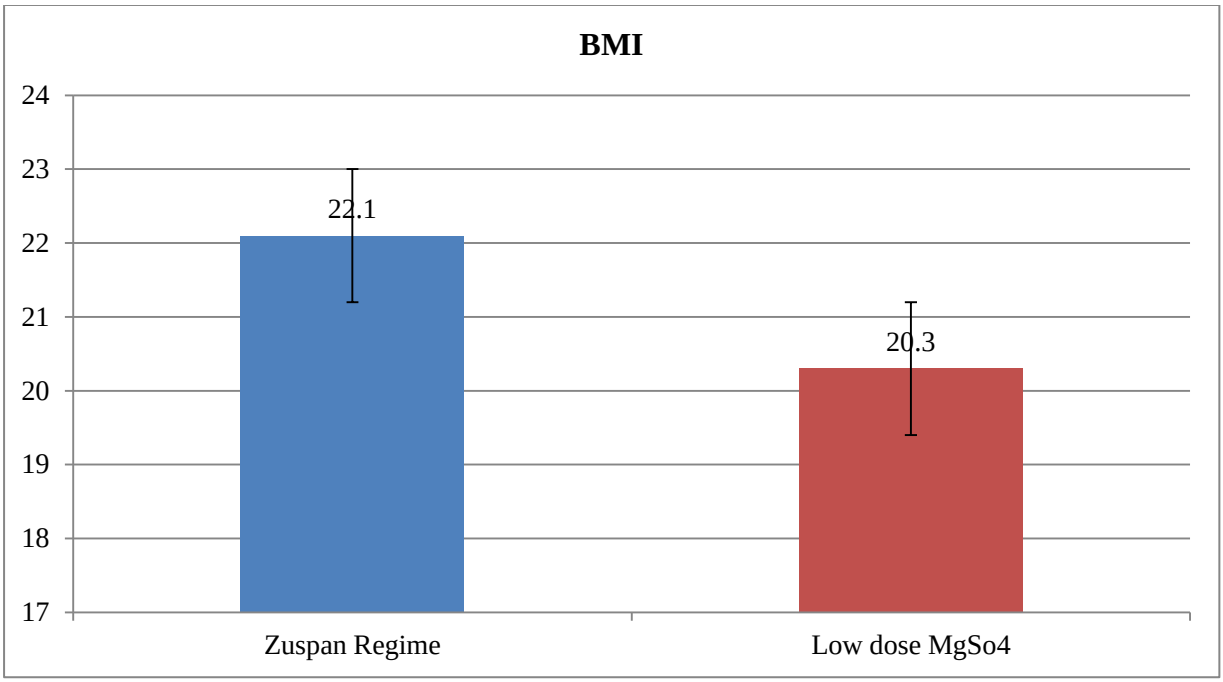


Graph 11: Mean GCS score in both the groups

Table 13: BMI comparison between two groups

	Group				P value
	Zuspan Regime		Low dose MgSo4		
	Mean	SD	Mean	SD	
BMI	22.1	2.5	20.3	1.6	0.002*

Mean BMI of subjects in Group A was 22.1 ± 2.5 and in group B was 20.3 ± 1.6. There was no significant difference in mean BMI between two groups.

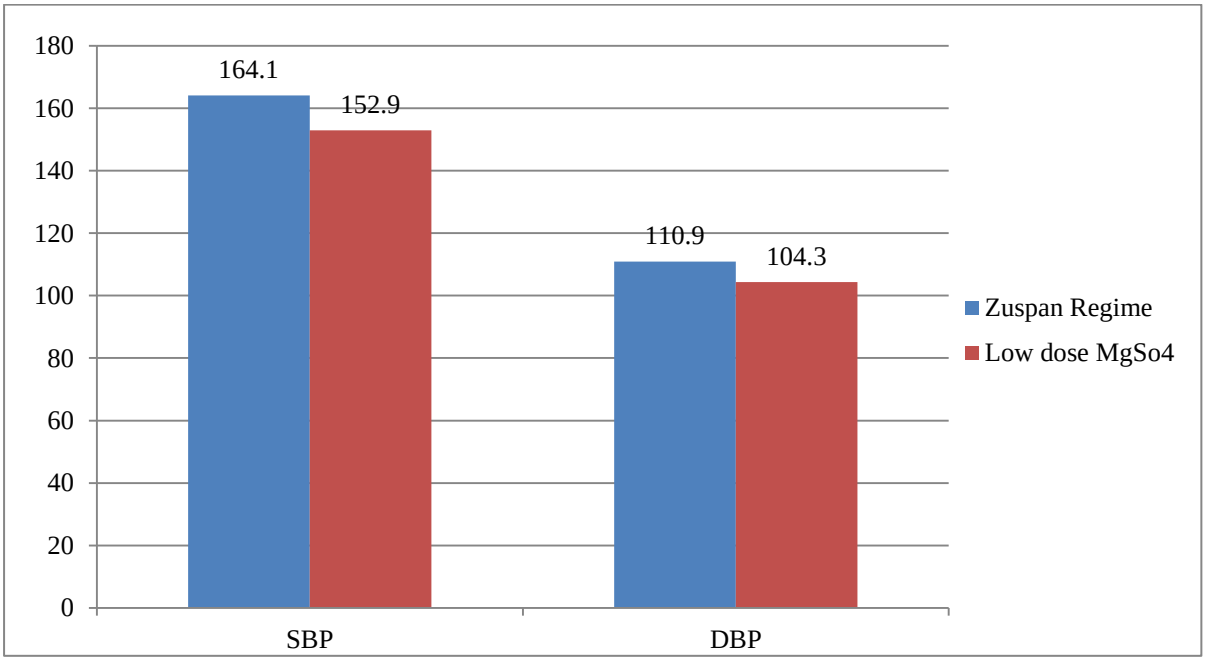


Graph 12: BMI comparison between both the groups

Table 14: Blood pressure comparison at admission between two groups

	Group				P value
	Zuspan Regime		Low dose MgSo4		
	Mean	SD	Mean	SD	
SBP	164.1	18.8	152.9	15.5	0.014*
DBP	110.9	13.7	104.3	15.0	0.081

Mean SBP was significantly higher in Group A compared to Group B. No difference in DBP was observed between two groups.

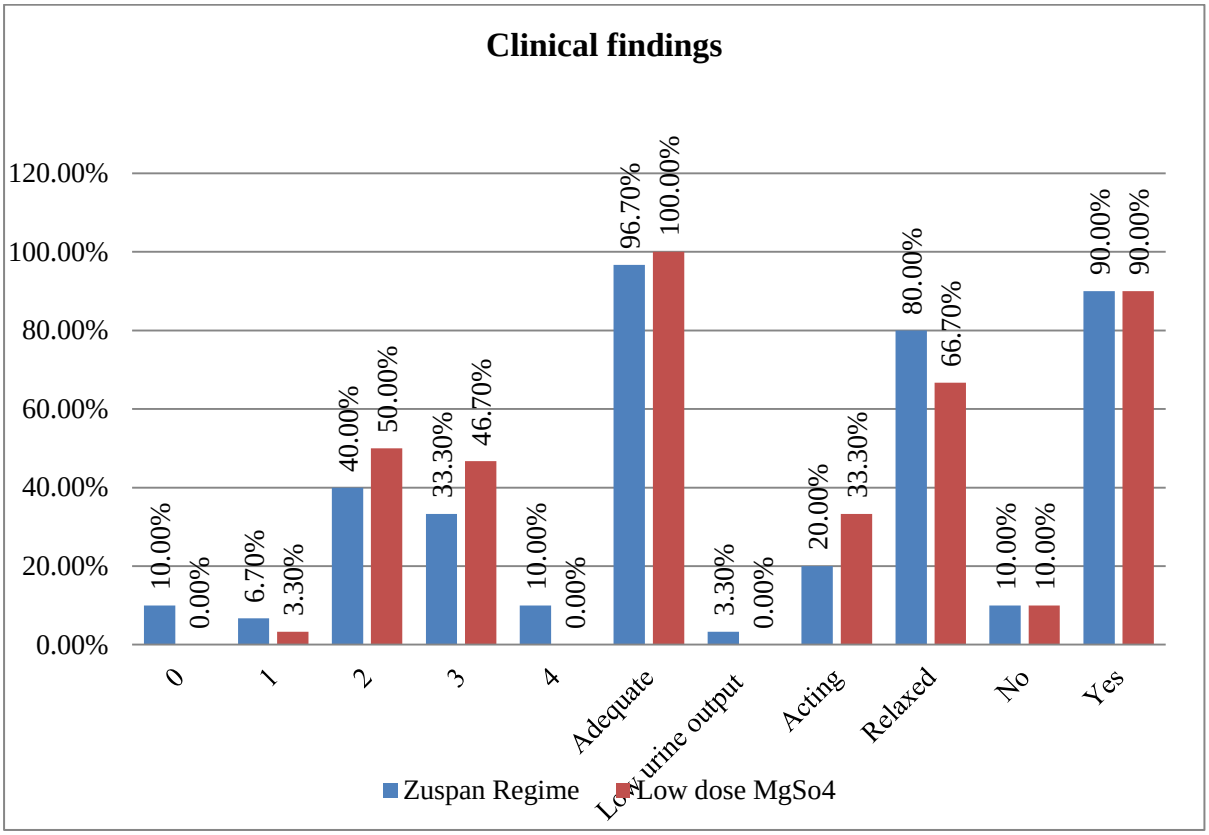


Graph 13: SBP and DBP comparison between both the groups on admission

Table 15: Clinical findings in subjects and comparison between two groups

		Group				P value
		Zuspan Regime		Low dose MgSo4		
		Number	%	Number	%	
Pedal Edema	0	3	10.0%	0	0.0%	0.119
	1	2	6.7%	1	3.3%	
	2	12	40.0%	15	50.0%	
	3	10	33.3%	14	46.7%	
	4	3	10.0%	0	0.0%	
Urine	Adequate	29	96.7%	30	100.0%	0.313
	Low urine output	1	3.3%	0	0.0%	
PA	Acting	6	20.0%	10	33.3%	0.243
	Relaxed	24	80.0%	20	66.7%	
FHR	No	3	10.0%	3	10.0%	1.000
	Yes	27	90.0%	27	90.0%	

All the subjects were afebrile in both the groups. Majority of subjects in both the groups had grade 2 pedal edema; in group A 3.3% of subjects had inadequate urine output. Among 10% of subjects in Group A and group B, FHR was absent

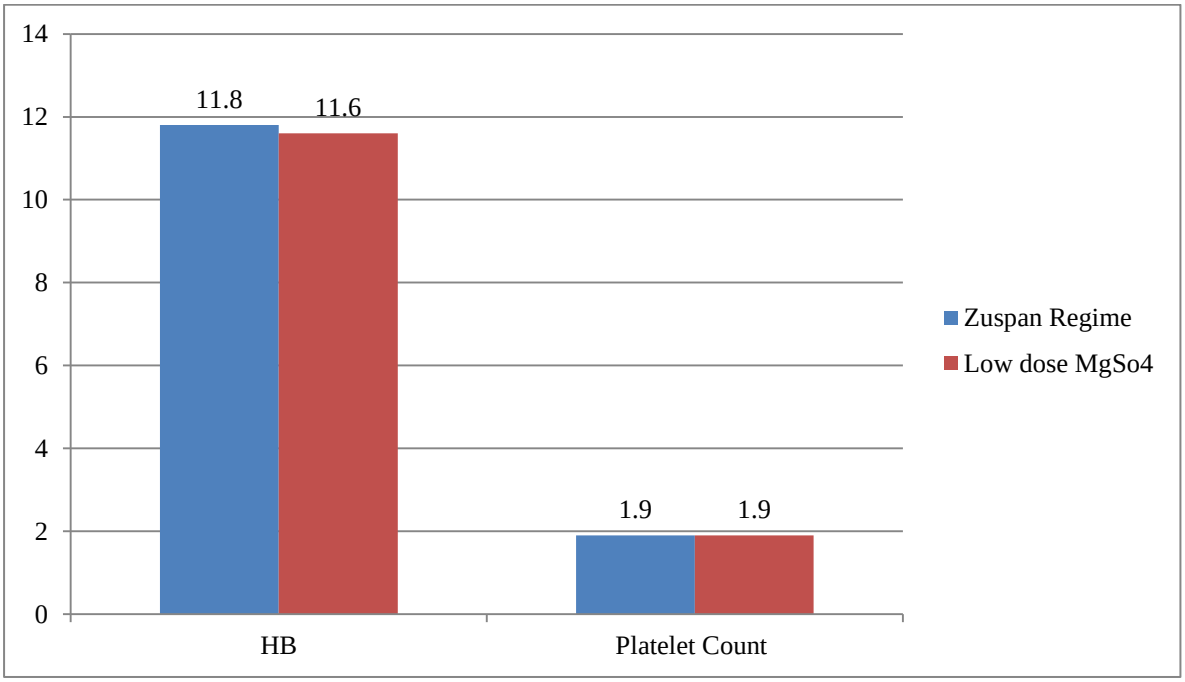


Graph 14: Clinical findings comparison between both the groups

Table 16: Hemoglobin and Platelet count comparison between two groups

	Group				P value
	Zuspan Regime		Low dose MgSo4		
	Mean	SD	Mean	SD	
HB	11.8	2.2	11.6	2.0	0.770
Platelet Count	1.9	0.7	1.9	0.6	0.724

There was no significant difference in hemoglobin and platelet count between two groups.



Graph 14: Hemoglobin and platelet count in both the groups

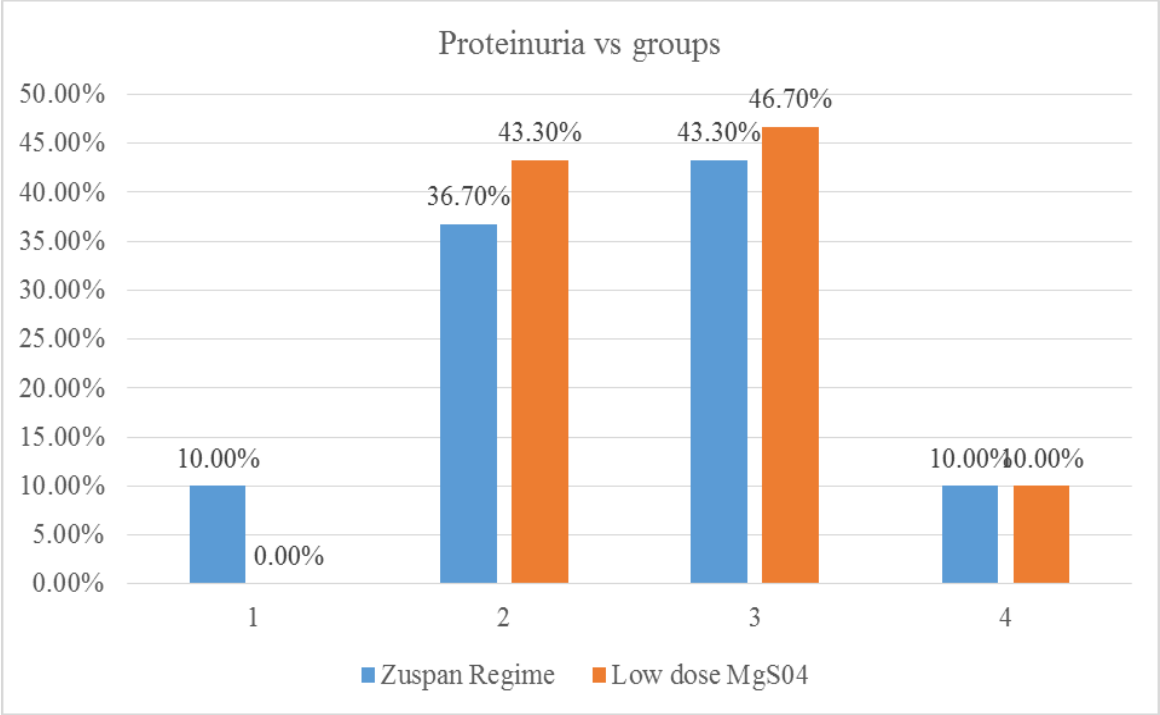
Table 17: Association between Proteinuria and groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
Proteinuria	1	3	10.0%	0	0.0%
	2	11	36.7%	13	43.3%
	3	13	43.3%	14	46.7%
	4	3	10.0%	3	10.0%

$\chi 2 = 3.204$, df = 3, p = 0.361

In Group A and Group B, majority of subjects 43.3% and 46.7% had grade 3 proteinuria.

There was no significant difference in proteinuria between two groups.



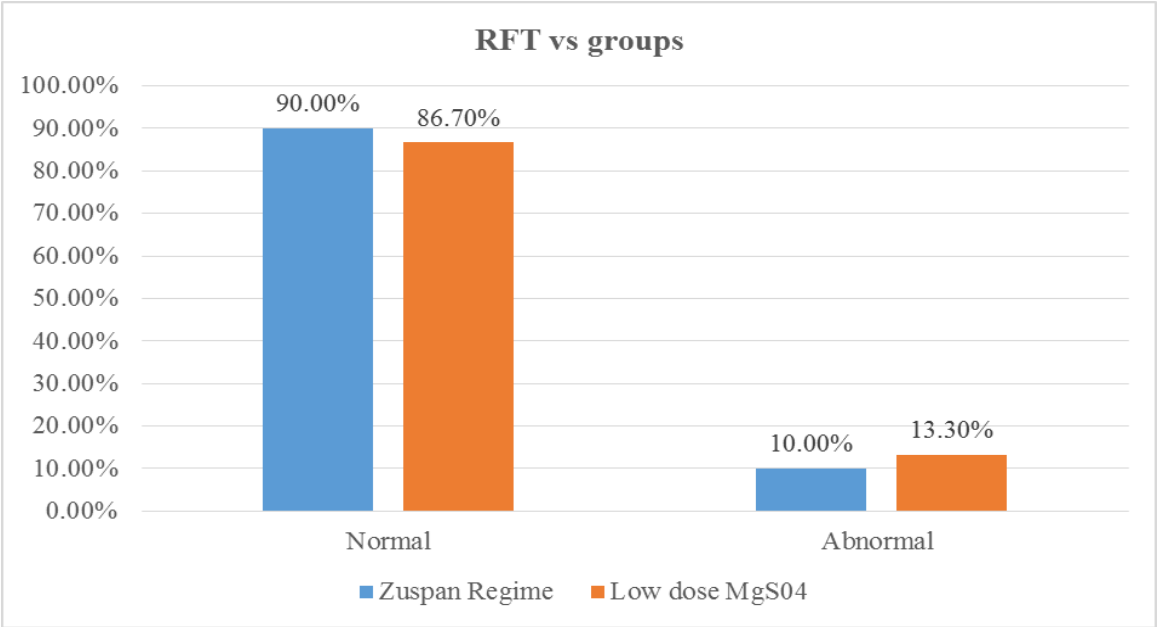
Graph 15: Association of proteinuria in both the groups

Table 18: Association between RFT and groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
RFT	Normal	27	90.0%	26	86.7%
	Abnormal	3	10.0%	4	13.3%

$\chi 2 = 0.162$, df = 1, p = 0.688

In Group A 10% of subjects and in Group B 13.3% had abnormal RFT. There was no significant difference in RFT levels between two groups.



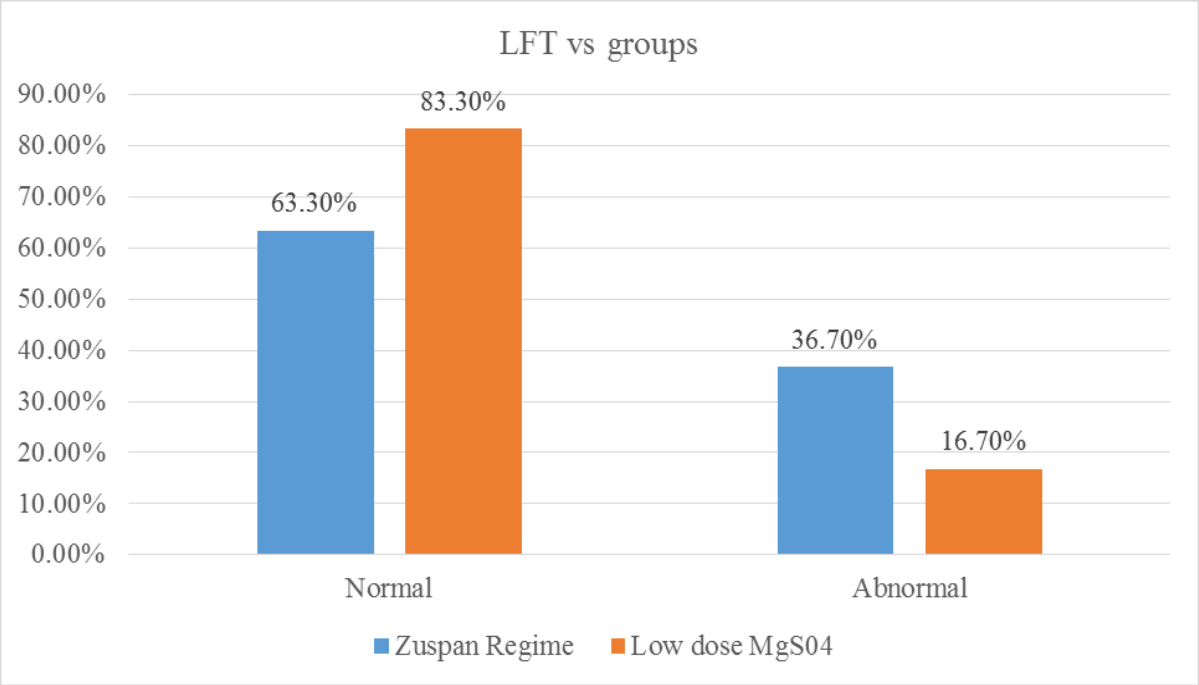
Graph 16: Association between RFT and groups

Table 19: Association between LFT and groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
LFT	Normal	19	63.3%	25	83.3%
	Abnormal	11	36.7%	5	16.7%

$\chi 2 = 3.068$, df = 1, p = 0.080

In Group A 36.7% had abnormal LFT and in Group B 16.7% had abnormal LFT. There was no significant difference in LFT between two groups.



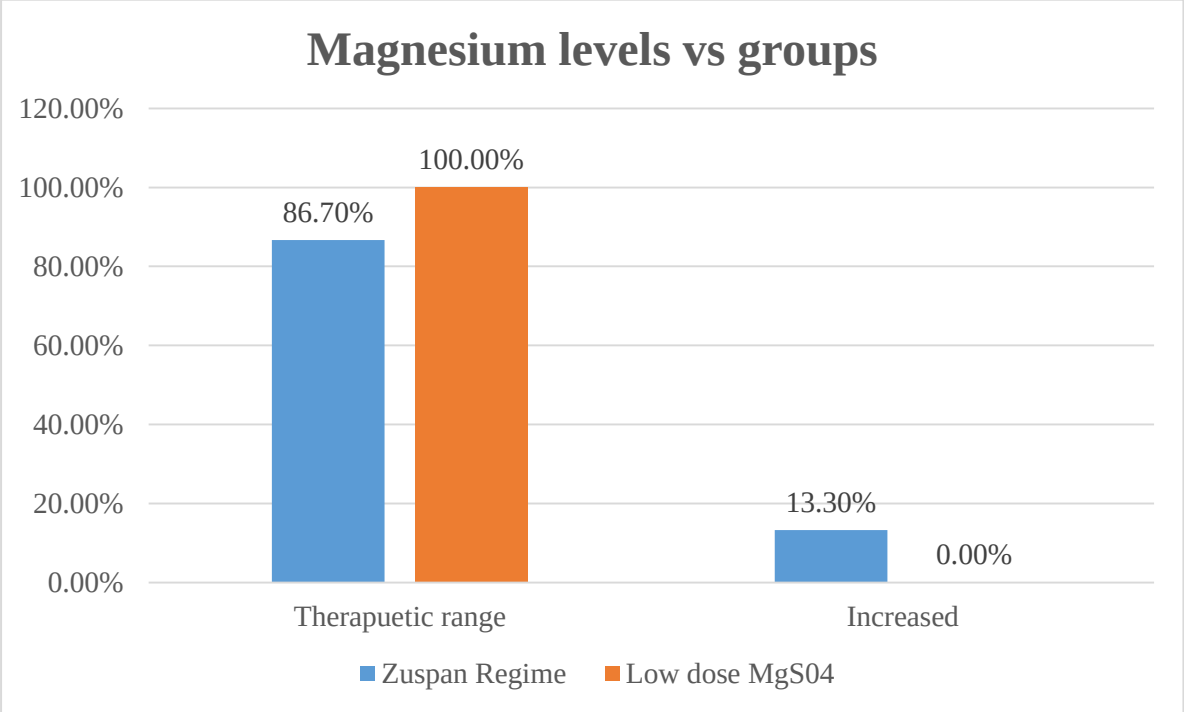
Graph 17: Association between LFT and both the groups

Table 20: Association between Magnesium levels and groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
Mg	Therapeutic range	26	86.7	30	100
	Increased	4	13.3	0	0

$\chi 2 = 4.28$, df = 1, p = 0.038*

In the study in Group A, 13.3% had increased Mg, were as none of them had Mg toxicity in group B. This difference in magnesium toxicity between two groups was statistically significant.



Graph 18: Association between magnesium levels and groups

Table 21: Mode of delivery comparison between two groups

		Group			
		Zuspan Regime		Low dose MgSo4	
		Count	%	Count	%
Mode of delivery	Vaginal delivery	19	63.3%	13	43.3%
	LSCS	11	36.7%	17	56.7%

$\chi 2 = 2.411$, df = 1, p = 0.121

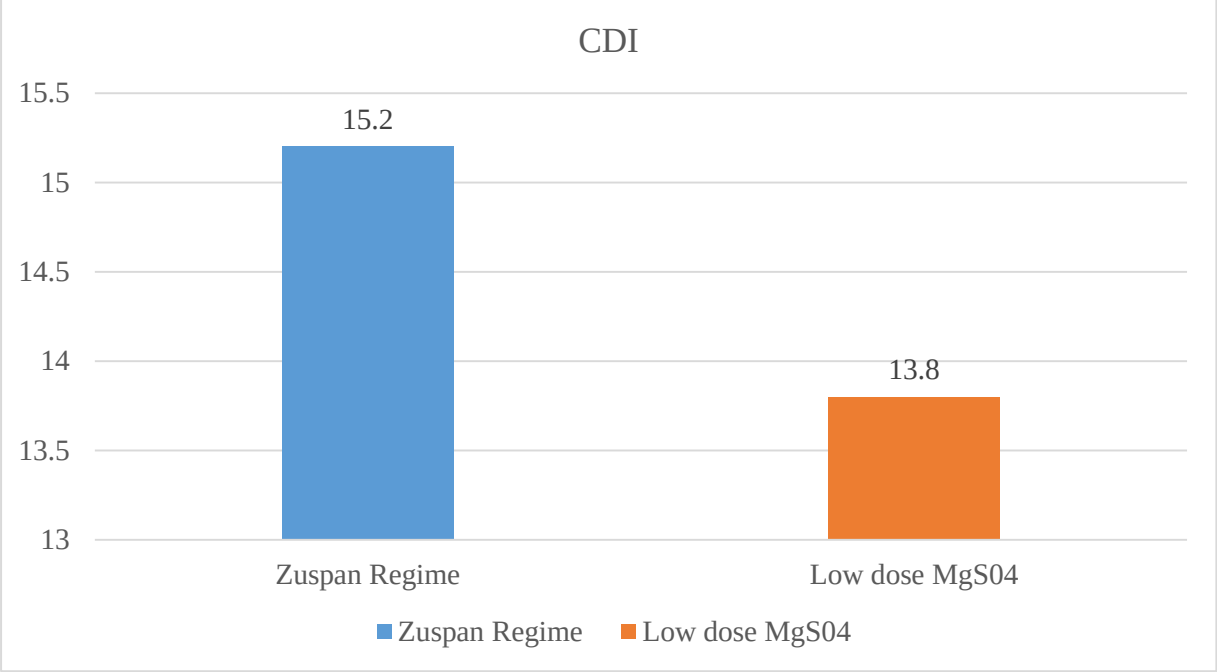
No significant difference was observed between two groups with respect to mode of delivery.

Table 22: Comparison of CDI between two groups

	Group				P value
	Zuspan Regime		Low dose MgS04		
	Mean	SD	Mean	SD	
CDI	15.2	7.7	13.8	9.0	0.615

Mean CDI in Zuspan group was 15.2 ± 7.7 mins and in MgSo4 group was 13.8 ± 9 mins.

This difference in CDI between two groups was not statistically significant.



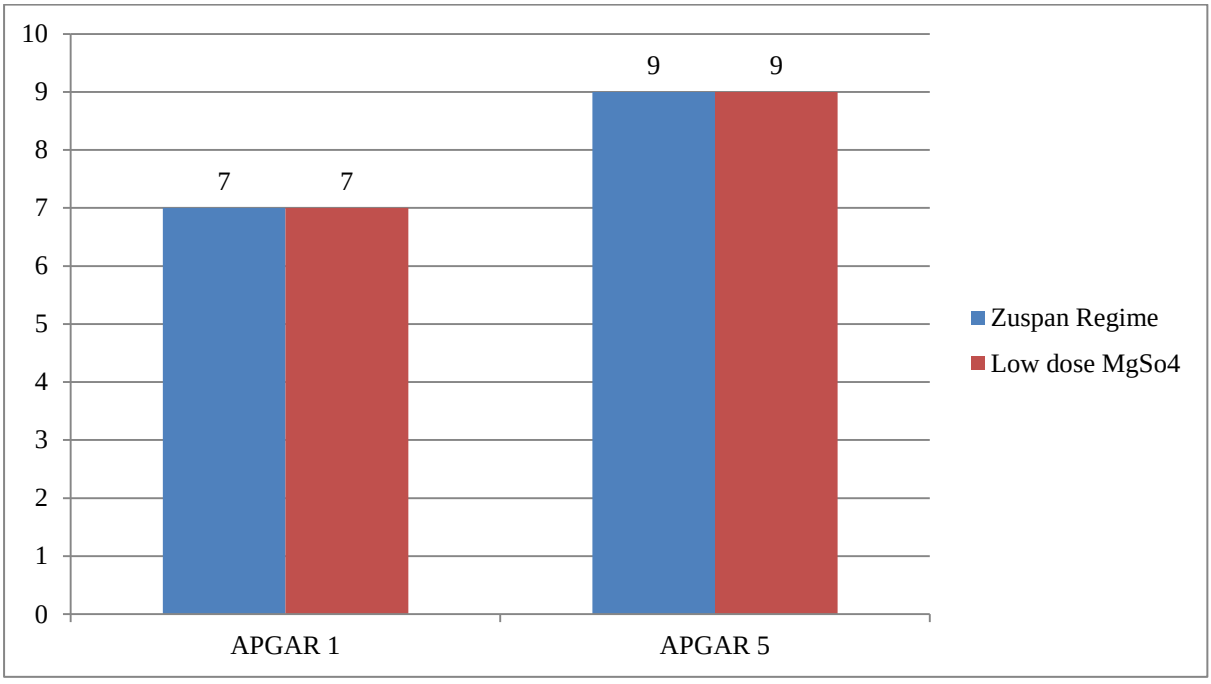
Graph 19: Mean convulsion delivery interval between both the groups

Neonatal Outcomes in the study

Table 23: APGAR score comparison between two groups at 1 min and 5 min

	Group	
	Zuspan Regime	Low dose MgSo4
	Median	Median
APGAR 1	7	7
APGAR 5	9	9

No difference in APGAR score between two groups.



Graph 20: Bar diagram showing APGAR score comparison between two groups at 1 min and 5 min

Table 24: Association between Gestational age and need for NICU admissions in both the groups

		Group					
		Zuspan Regime					
		Need For NICU					
		NA		No		Yes	
		Number	%	Number	%	Number	%
Gestational age	<32 weeks	7	100	0	0	2	11.8
	32w 0d to 36w 6d	0	0	0	0	8	47.1
	>37 weeks	0	0	6	100	7	41.2

$\chi 2 = 28.73$, df = 4, p <0.001*

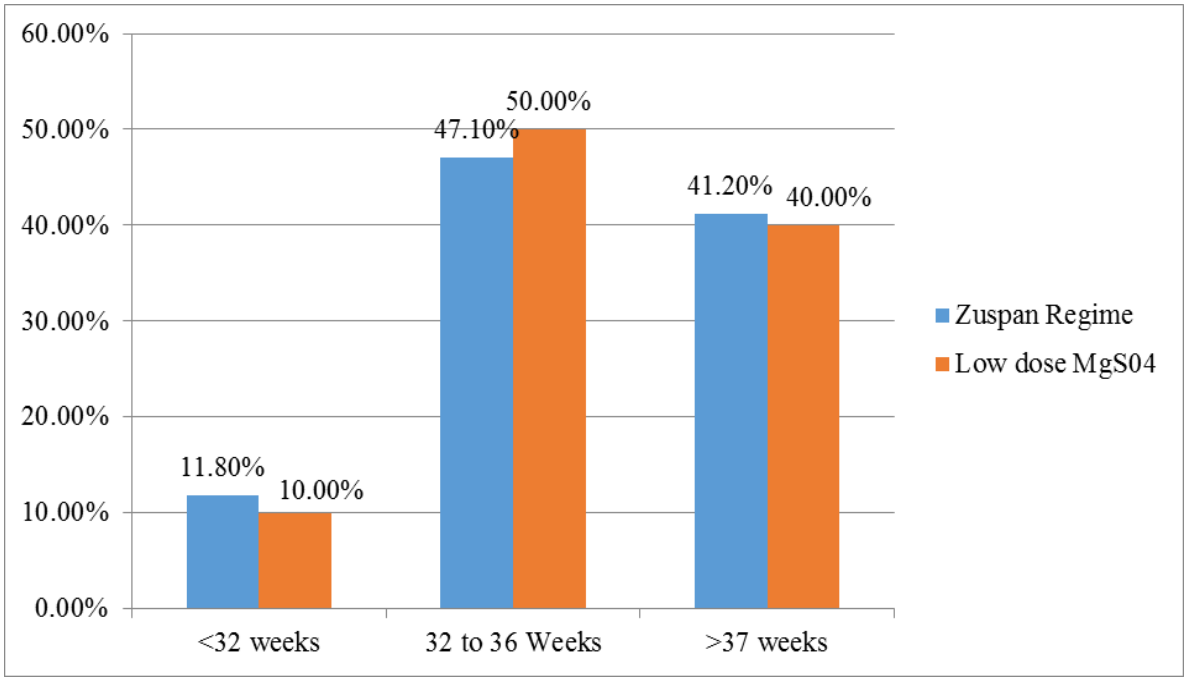
In the study significant association was observed in Group A between gestational age and Need for NICU admission. Subjects who were not placed in ICU, 100% of them were >37 weeks of GA, were as in subjects placed in NICU, 11.8% were <32 weeks, 47.1% were 32 to 36 weeks and 41.2% were >37 weeks.

Table 25: Association between gestational age and need for NICU admissions in both the groups

		Group					
		Low dose MgS04					
		Need For NICU					
		NA		No		Yes	
		Number	%	Number	%	Number	%
Gestational age	<32 weeks	4	80	1	6.7	1	10
	32w 0d to 36w 6d	1	20	3	20.0	5	50
	>37 weeks	0	0	11	73.3	4	40

χ 2 = 17.16, df = 4, p= 0.002*

In the study significant association was observed in Group B between gestational age and Need for NICU admission. Subjects who were not placed in ICU, 6.7% of them were <32 weeks, 20% were in 32 to 36 weeks and 73.3% were in >37 weeks of GA, were as in subjects placed in NICU, 10% were <32 weeks, 50% were 32 to 36 weeks and 40% were >37 weeks.



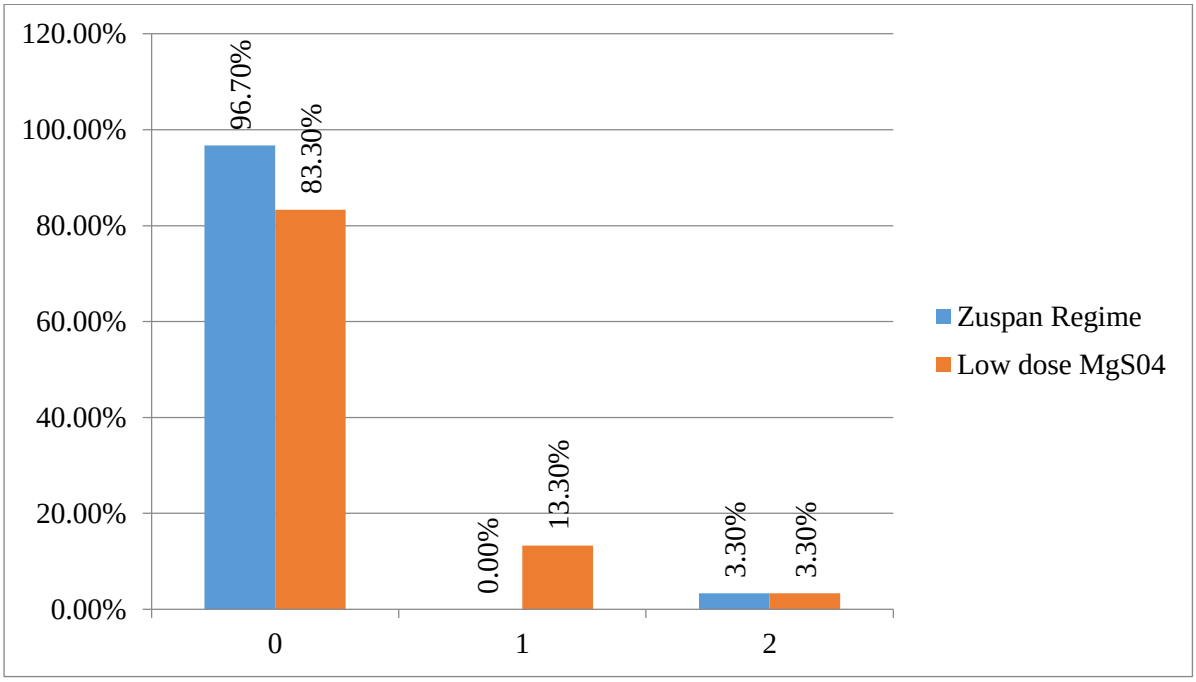
Graph 21: Gestational age and need for NICU admission in both the groups

Table 26 : Association between number of recurrence of convulsions and two groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
No. of Convulsions	0	29	96.7	25	83.3
	1	0	0.0	4	13.3
	2	1	3.3	1	3.3

$\chi 2 = 4.29$, df = 2, p= 0.117

In Group A, 3.3% had 2 episodes of convulsions and in group B, 13.3% had one episode and 3.3% had 2 episodes of convulsions. There was no significant difference in no of convulsions between two groups.

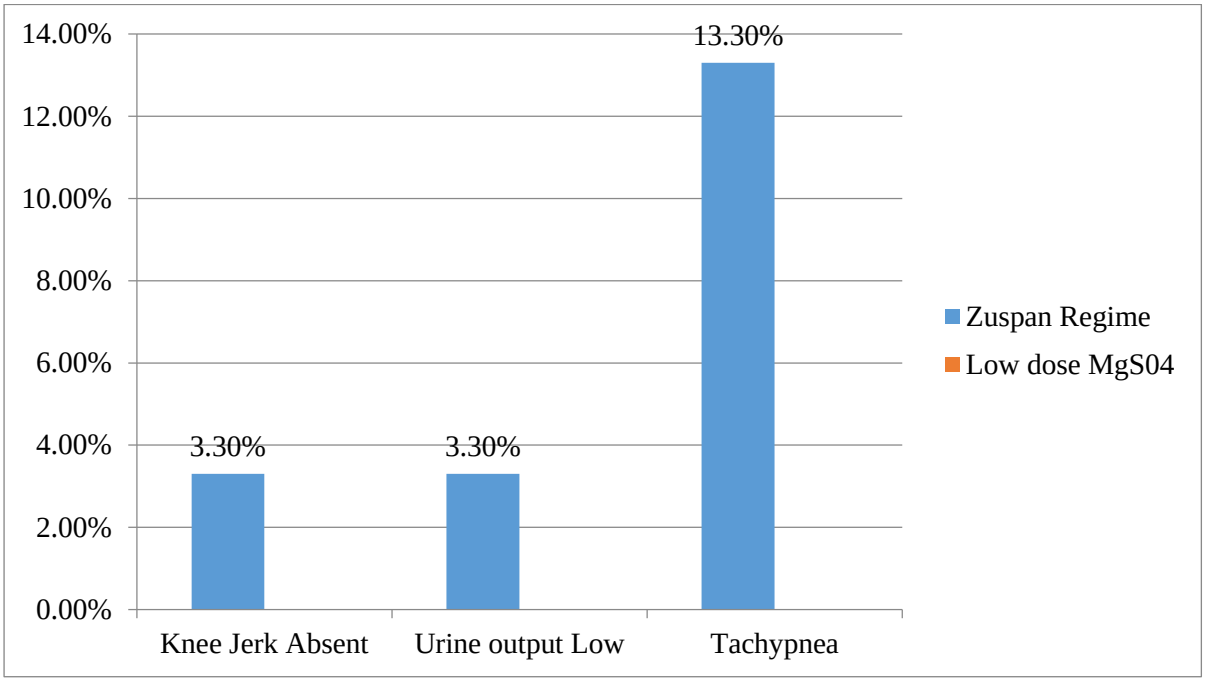


Graph 22: Association between the recurrence of convulsions between both the groups

Table 27: Magnesium toxicity signs between two groups

		Group				P value
		Zuspan Regime		Low dose MgS04		
		Number	%	Number	%	
Knee Jerk	Absent	1	3.3%	0	0.0%	0.313
Urine output	Low	1	3.3%	0	0.0%	0.313
Respiratory Rate	Tachypnea	4	13.3%	0	0.0%	0.038*

In Group A, 3.3% knee jerk was absent and low urine output and in 13.3% of subjects 13.3% had Tachypnea. There was significant difference in incidence of Tachypnea between two groups.

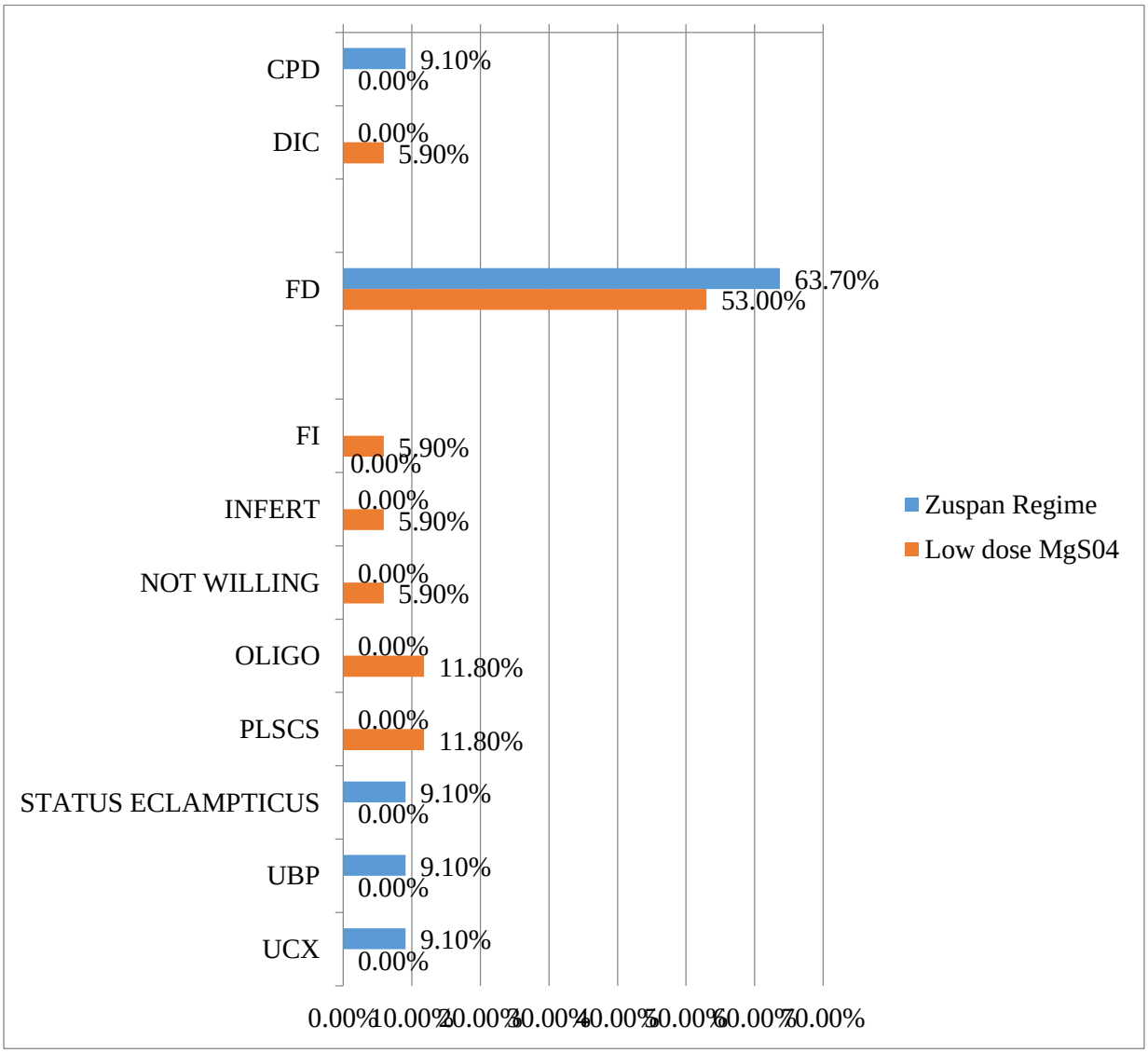


Graph 23: Bar diagram showing signs of magnesium toxicity

Table 28 : Comparison of Indication for LSCS between two groups

		Mode of delivery			
		Zuspan Regime		Low dose MgS04	
		Count	%	Count	%
INDICATION	CephaloPelvic Disproportion	1	9.1%	0	0.0%
	Disseminated Intravascular Coagulopathy	0	0.0%	1	5.9%
	FD	7	63.7%	9	53%
	Failed Induction	0	0.0%	1	5.9%
	Infertility	0	0.0%	1	5.9%
	Not willing	0	0.0%	1	5.9%
	Oligohydramnios	0	0.0%	2	11.8%
	Previous LSCS	0	0.0%	2	11.8%
	Status Eclampticus	1	9.1%	0	0.0%
	Uncontrolled BP	1	9.1%	0	0.0%
	Unfavorable cervix	1	9.1%	0	0.0%
P value		<0.001*		<0.001*	

In Group A and Group B Most common indication for LSCS was fetal distress 45.5% and 47.1% respectively. There was significant difference in indications for LSCS between two groups.



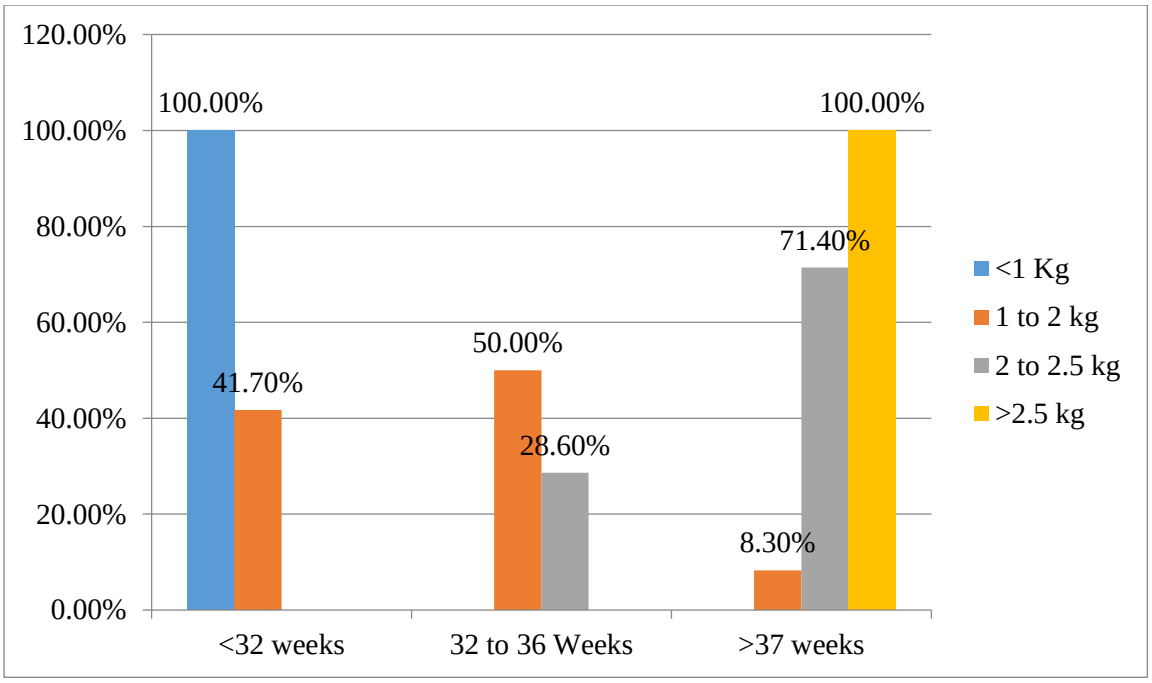
Graph 24: Indications for LSCS

Table 29: Association between Gestational age and birth weight in Zuspan regimen

		Group							
		Zuspan Regime							
		Birth weight							
		<1 Kg		1 to 2 kg		2 to 2.5 kg		>2.5 kg	
		Number	%	Number	%	Number	%	Number	%
Gestational age	<32 weeks	4	100.0%	5	41.7%	0	0.0%	0	0.0%
	32 to 36 Weeks	0	0.0%	6	50.0%	2	28.6%	0	0.0%
	>37 weeks	0	0.0%	1	8.3%	5	71.4%	7	100.0%

$\chi 2 = 28.25$, df = 6, $p<0.001$*

In Zuspan group there was significant association between birth weight and gestational age. Infants with >2.5 kg, 100% of them were >37 weeks of gestational age. Were as in subjects with birth weight 2 to 2.5 kg 28.6% were in 32 to 36 weeks of gestation, subjects with birth weight 1 to 2 kg, 41.7% were in <32 weeks and 50% were in 32 to 36 weeks of gestation.



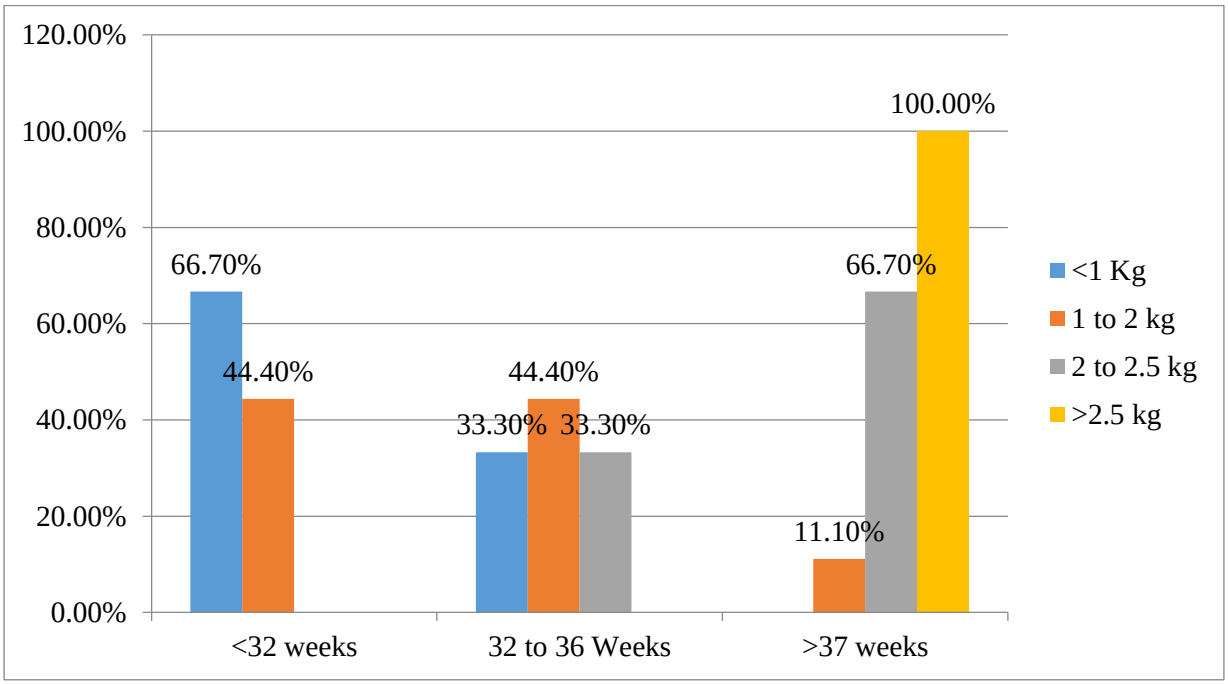
Graph 25 : Bar diagram showing Association between Gestational age and birth weight in Zuspan group

Table 30: Association between gestational age and birth weight in low dose magnesium sulphate regimen

		Group							
		Low dose MgS04							
		Birth weight							
		<1 Kg		1 to 2 kg		2 to 2.5 kg		>2.5 kg	
		Number	%	Number	%	Number	%	Number	%
Gestational age	<32 weeks	2	66.7%	4	44.4%	0	0.0%	0	0.0%
	32w 0d to 36 W 6d	1	33.3%	4	44.4%	4	33.3%	0	0.0%
	>37 weeks	0	0.0%	1	11.1%	8	66.7%	6	100.0%

χ 2 = 19.92, df = 6, p= 0.003*

In MgSo4 group there was significant association between birth weight and gestational age. Infants with >2.5 kg, 100% of them were >37 weeks of gestational age. Were as in subjects with birth weight 2 to 2.5 kg 33.3% were in 32 to 36 weeks of gestation, subjects with birth weight 1 to 2 kg, 44.4% were in <32 weeks and 32 to 36 weeks of gestation gestation.



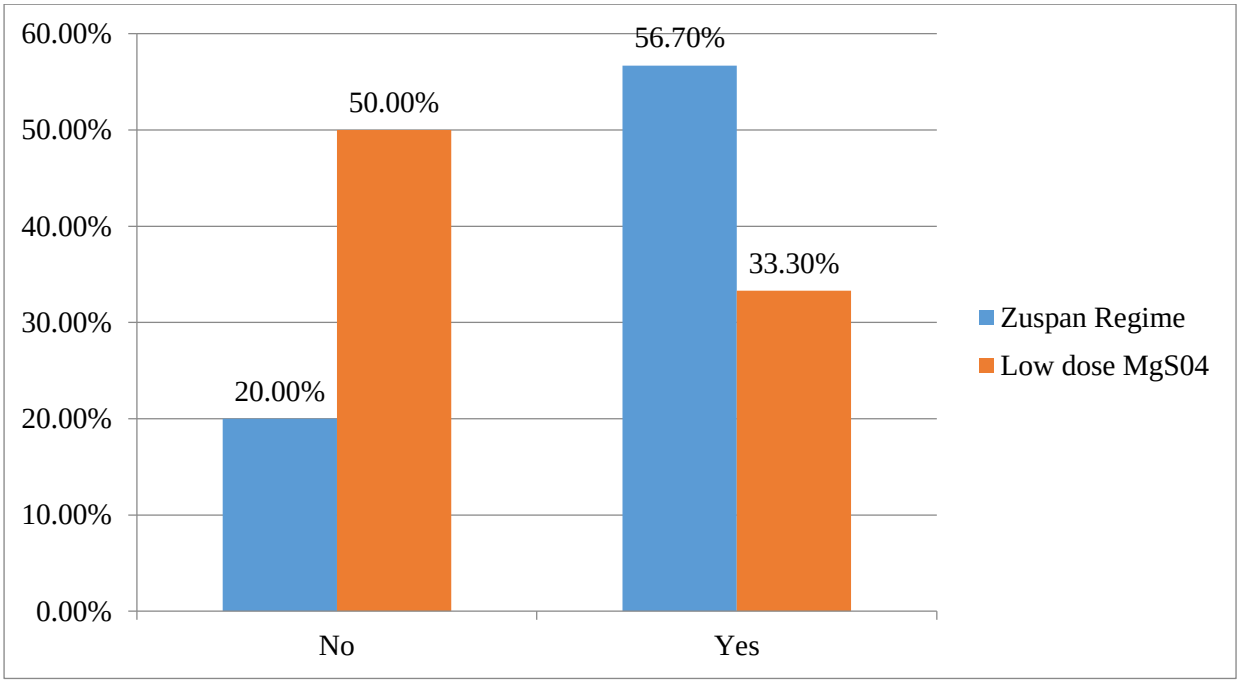
Graph 26: Association between gestational age and birth weight in low dose magnesium sulphate reigmen

Table 31: Association between Need for NICU admission between two groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
Need For NICU	No	6	20.0%	15	50.0%
	Yes	17	56.7%	10	33.3%

$\chi 2 = 5.59$, df = 1, p= 0.01*

In Zuspan group 56.7% required NICU admission were as in MgSo4 group 33.3% required NICU admission. This difference in NICU admission between two groups was statistically significant.



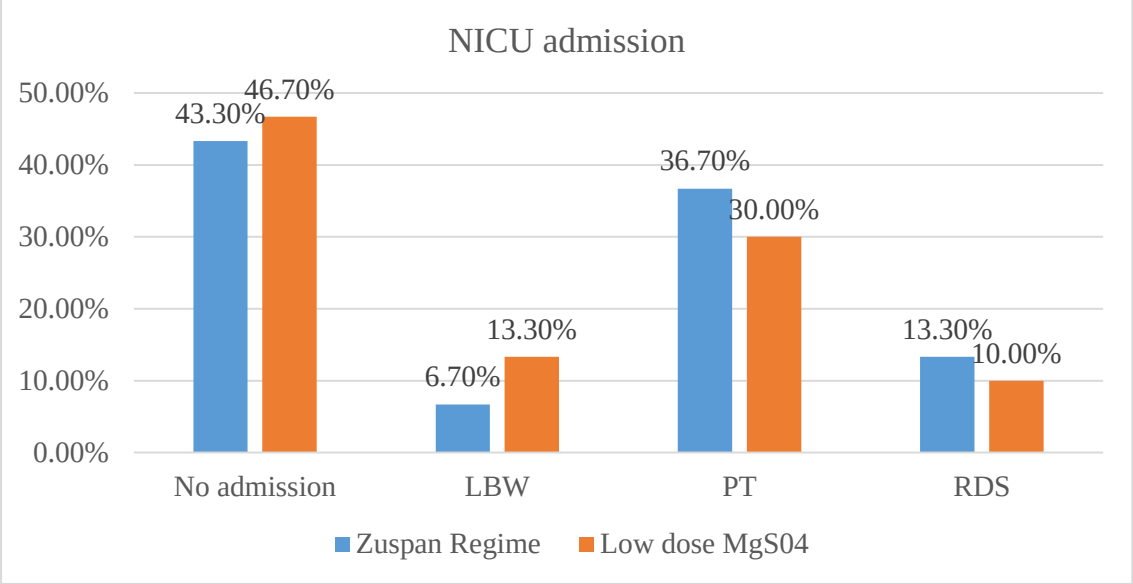
Graph 27: Bar diagram showing Association between Need for NICU admission between two groups

Table 32 : Association between reason for NICU admission and groups

		Group			
		Zuspan Regime		Low dose MgS04	
		Number	%	Number	%
Reason	No admission	13	43.3%	14	46.7%
	LBW	2	6.7%	4	13.3%
	PT	11	36.7%	9	30.0%
	RDS	4	13.3%	3	10.0%

χ 2 = 7.904, df = 3, p = 0.790

In Zuspan group, 6.7% admitted due to LBW, 36.7% admitted due to preterm and 13.3% admitted due to Respiratory distress and in MgSo4 group, 13.3% admitted due to LBW, 30% due to preterm and 10% due to RDS. There was no significant association between reasons for NICU admission between two groups.



Graph 28: Bar diagram showing Association between reason for NICU admission and groups

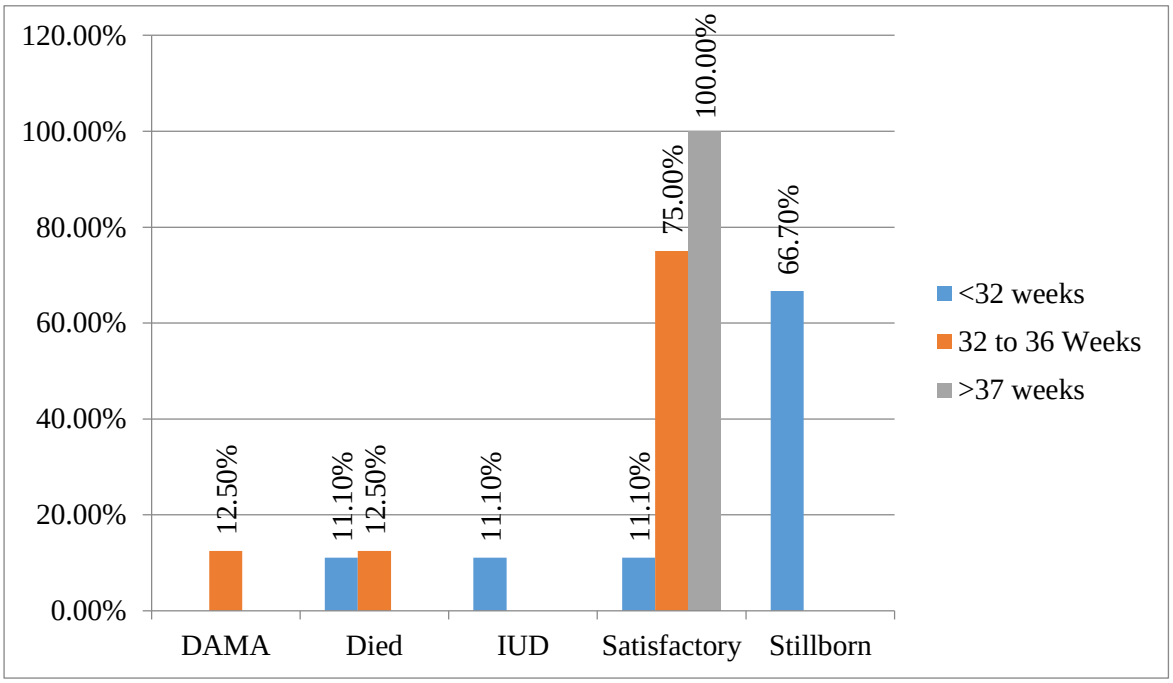
Table 33 : Association between Outcome and gestational age in Zuspan group

		Zuspan Regime					
		Gestational age					
		<32 weeks		32 to 36 Weeks		>37 weeks	
		Number	%	Number	%	Number	%
Outcome	DAMA	0	0.0%	1	12.5%	0	0.0%
	Died	1	11.1%	1	12.5%	0	0.0%
	IUD	1	11.1%	0	0.0%	0	0.0%
	Satisfactory	1	11.1%	6	75.0%	13	100.0%
	Stillborn	6	66.7%	0	0.0%	0	0.0%

χ 2 = 27.04, df = 8, p= 0.001*

Significant association was observed between outcome and gestational age in Zuspan group.

When gestational age was <32 weeks, majority of them had still born (66.7%), In Gestational age group 32 to 36 weeks, 75% of them had satisfactory outcome and when gestational age was >37 weeks, 100% of them had satisfactory outcome.



Graph 21: Bar diagram showing Association between Outcome and gestational age in Zuspan group

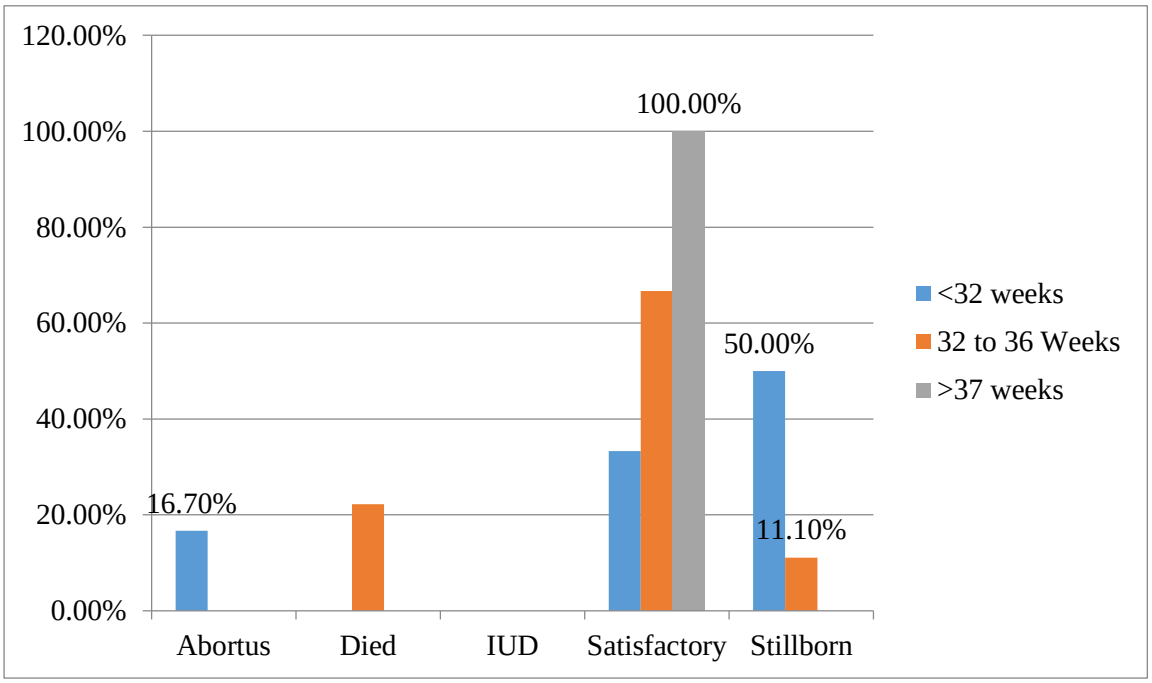
Table 34: Association between gestational age and outcome in low dose group

		Low dose MgS04					
		Gestational age					
		<32 weeks		32 to 36 Weeks		>37 weeks	
		Number	%	Number	%	Number	%
Outcome	Abortus	1	16.7%	0	0.0%	0	0.0%
	Died	0	0.0%	2	22.2%	0	0.0%
	IUD	0	0.0%	0	0.0%	0	0.0%
	Satisfactory	2	33.3%	6	66.7%	15	100.0%
	Stillborn	3	50.0%	1	11.1%	0	0.0%

$\chi 2 = 19.92$, df = 6, p= 0.004*

Significant association was observed between outcome and gestational age in MgSo4 group.

When gestational age was <32 weeks, majority of them had still born (50%), In Gestational age group 32 to 36 weeks, 66.7% of them had satisfactory outcome and when gestational age was >37 weeks, 100% of them had satisfactory outcome.



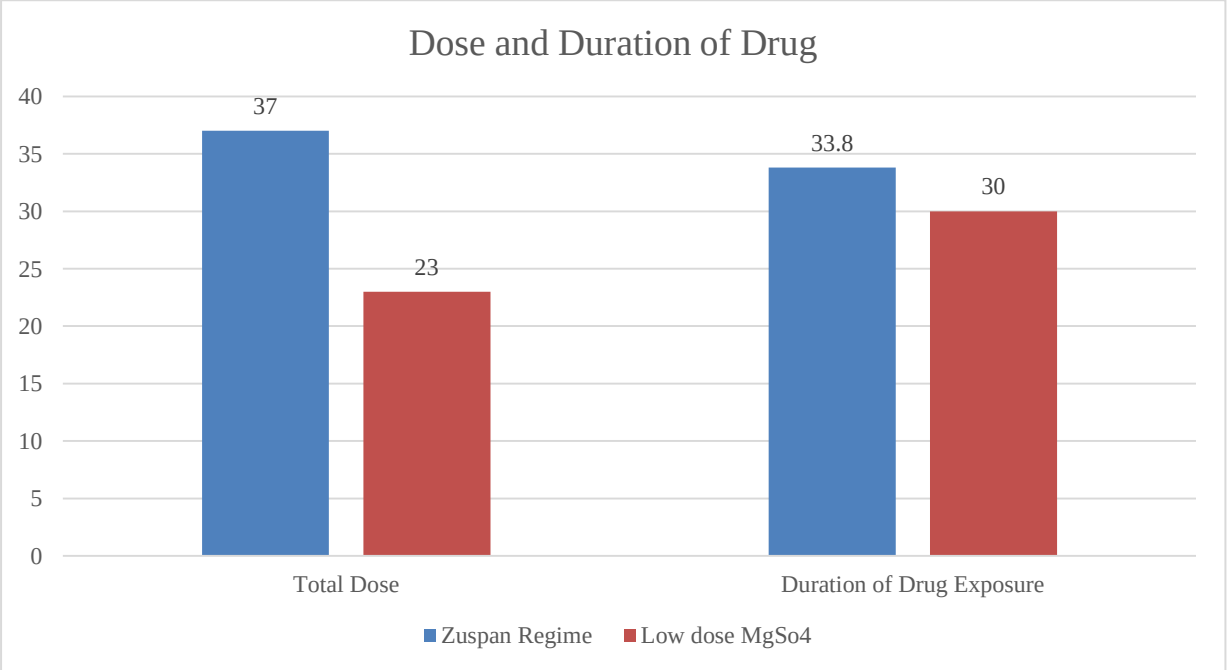
Graph 30 : Bar diagram showing Association between Outcome and gestational age in low dose MgSO4 group

Table 35: Total dose of drug used in both the groups

	Group				P value
	Zuspan Regime		Low dose MgSo4		
	Mean	SD	Mean	SD	
Total Dose	37.0	9.2	23.0	5.0	<0.001*
Duration of Drug Exposure	33.8	8.5	30.0	7.6	0.073

Mean dose of drug required in group B was lesser compared to group A. This difference was statistically significant.

No difference was observed in duration of drug exposure between two groups.

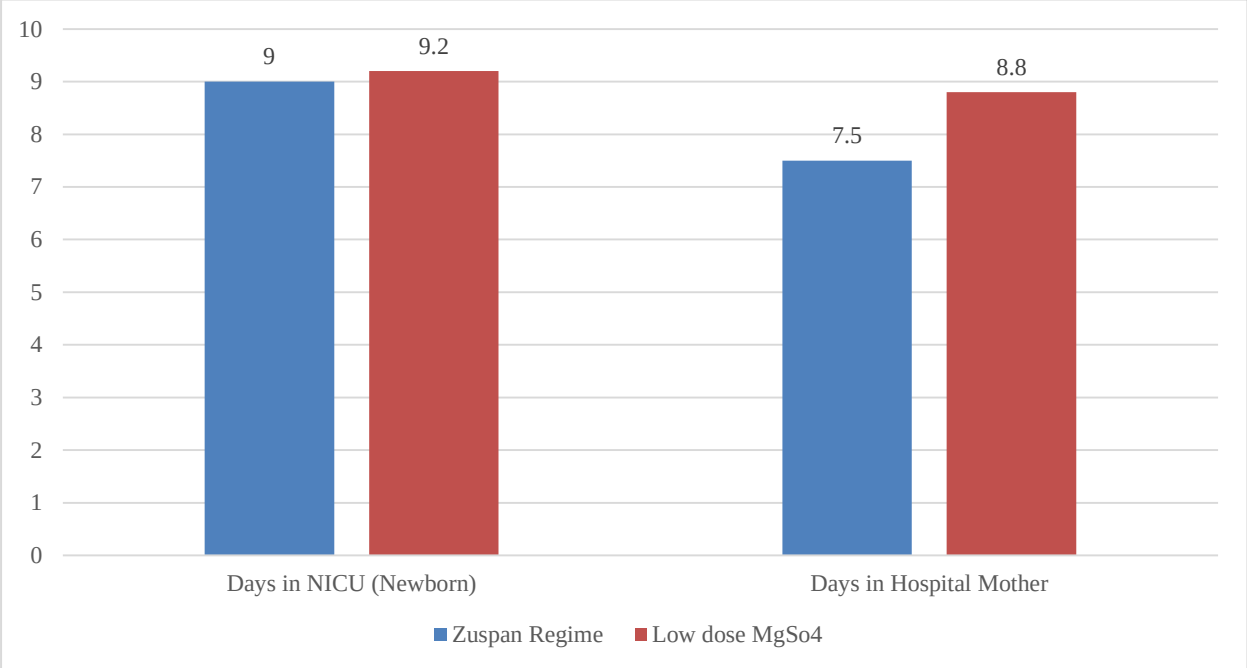


Graph 31: Bar diagram showing Total dose of drug used and duration of drug exposure in both the groups

Table 36: Days in NICU among infants and Days of Hospital stay of Mother between two groups

	Group				P value
	Zuspan Regime		Low dose MgSo4		
	Mean	SD	Mean	SD	
Days in NICU (Newborn)	9.0	5.2	9.2	5.2	0.914
Days in Hospital Mother	7.5	1.9	8.8	2.8	0.03*

No significant difference in no of days in NICU b/w two groups. Significant difference was observed in day of hospital stay of mothers. Group A mothers stayed for lesser duration compared to group B.



Graph 32: Bar diagram showing Days in NICU among infants and Days of Hospital stay of Mother between two groups

Discussion

DISCUSSION

Eclampsia is one of the direct causes of maternal mortality. The eclampsia related mortality can be reduced by an early referral and an effective institution of anticonvulsant therapy. But there are many barriers that come in between access of proper healthcare facilities and availability of magnesium especially in developing nations. A study done in Zambia assessed retrospectively the barriers in regulation/ supply, procurement, distribution, health facility and health professional levels. The assessment was done in Lusaka District in Zambia. They found that the major barrier was the lack of procurement by the Ministry of Health. Other barriers included a lack of demand by healthcare professionals and lack on in service training on the use of magnesium sulphate. There was a lack of dissemination of national standard treatment guidelines in health facilities and pharmacies as well.[66]

Magnesium sulphate therapy for treatment of eclampsia is cited as one of the 56 essential evidence based interventions that together could potentially eliminate the ultimate deaths of 358,000 women and 7.6 million children in low and middle income countries.[67]

The present study included 60 cases of eclampsia and imminent eclampsia in which 30 patients received Zuspans Regimen and 30 patients received low dose magnesium sulphate.

Patients/ patients attenders history was taken into account whether they had increased Blood Pressure (BP) readings in the past along with other imminent signs such as headache, vomiting, blurring of vision or pedal edema.

They were all assessed for GCS on admission and vitals were taken into account before starting on any hypertensive. Systemic examination was done. A cardiotocograph was connected and a bedside scan done.

Magnesium sulphate was immediately administered as per randomization and investigations such as Complete blood count, blood grouping with Rh typing, Viral serology, Random blood sugar, Liver function tests , renal function tests and coagulation profile was sent.

The patient was monitored for any magnesium toxicity signs like absent knee jerk, any tachypnea, decreased urine output (25ml/hr) The total dose of drug administered was studied along with mode of delivery whether spontaneous , induced or any need for emergency LSCS and the indications for the same.

The condition of the baby was studied whether there was any asphyxia or hypotonia with any need for resurcitation, need for NICU admission along with number of days in NICU and when the baby was handed motherside. Any IUDs and still borns were taken into account with respect to gestational age.

Both groups had comparable education status. Most of the patients had a primary school education with the Zuspan group having 56.7% and low dose magnesium sulphate group having 36.7% with just a primary level education.

The socioeconomic status between the two groups was comparable according to Modified BG Prasad Classfication. Majority of patients in both the groups belonged to Socioeconomic class 3. A systematic review done in 2014 studied magnesium sulphate dosing in low and middle income countries for the management of preeclampsia and eclampsia. About 753 publications were reviewed in World Bank classified low and

middle income countries. They studied the following income groups because treatment has been well documented in the high income countries previously. Rates of eclampsia were usually < 5% (median 3.0%, range 0.0% to 26.5%) even when MgSO4 was administered for eclampsia. The dosage varied from the standard regimens like Pritchard or Zuspan almost all (n = 22) reduced the dose or duration of treatment, most commonly because of concerns about maternal safety, cost, or resource availability. Four trials of a loading dose only (4 g IV + 10 g IM) versus loading plus maintenance dosing of 5 g/4 hr IM found no difference in eclampsia recurrence (RR 1.64; 95% CI 0.48 to 5.65, n = 396). One study documented less eclampsia recurrence associated with community administration of a MgSO4 loading dose before referral to a care facility versus treatment in a care facility.[68]

Preeclampsia and eclampsia are regarded as a disease of the first pregnancy The protective effects of long term sperm exposure with the same partner might explain the high risk of eclampsia in women younger than 20 years.[61] In the present study similarly most patients were primigravida with 60% in the Zuspans Regime and 53.3% in the Low dose regime. The mean age in both the groups was 23 years with Zuspan having 23.5 ± 3.8 years and in low dose magnesium sulphate group having 23.3 ± 3.3 years.

In the age group of 21-25years with 43.3% in the Zuspans Regime and 56.7% in the low dose magnesium sulphate regime. Only 30% and 23.3% ended up being below 20 years of age in Zuspans Group and Low dose Magnesium sulphate group respectively. This was similar to study done by Sahu L[69] where they compared a low dose and standard dose of magnesium sulphate in 50 patients (25 in each group). The median age in years

was 23.6 for the low dose group and 22.6 for the standard dose group with most patients that is 80% and 76% respectively being primigravidas. Sardesai et al. also reported 79% cases being primigravida .[42]

Most patients in the study were term gestations with 43.3% and 50% in the Zuspans Regime and Low dose regime respectively. There was no statistical significance between both the groups. The mean gestational age was 33 weeks im Zuspan Regimen whereas 35 weeks in low dose this was similar to a study done by Sahu L[69] who reported most patients having a mean gestational age of 34 weeks in the study. It was also similar to a study done by Bhatacharjee N[48] which also has most patients being above 37 weeks gestation with mean gestational age being 34weeks.

In this study 70% Cases were Antepartum eclampsia and 30% were imminent eclampsia in the Zuspan Regimen and 60% Antepartum eclampsia and 40% imminent eclampsia in the low dose group. This was similar to a study done by Asani[56] et al. where the antepartum eclampsia patients accounted for 80% of the patients. Murthy O[70] et al also had a higher incidence of antepartum eclampsia compared to imminent eclampia in their study. Antepartum eclmapsia was also common in studies done by Sardesai et al[42] and Menon et al[71] . TS Savitha et al[57] however had more cases of impending eclampsia with 90% in the study group and 83% in the control group.

In respect to imminent symptoms at presentation according to history given by the patient or the attenders , headache was the most common imminent symptom (63.3%) in the Zuspan group whereas history of increased BP readings prior to admission(66.7%) was more common in the Low dose regimen group. Where as in Asnani et al[56] study they

found vomiting to be the most common predominant imminent symptom in both the study (70%) and control groups (56.67%).

Patients with antepartum eclampsia most commonly had one convulsion prior to admission to the Hospital. Around 57.7% in the Zuspan Group and 50% in the low dose magnesium sulphate regimen had just one convulsions whereas only 4.8% had four or more convulsions in the Zuspan group whereas none of the low dose magnesium sulphate group patients had more than 3 convulsions prior to admission. In Regmi et al[49] study the mean convulsions prior to admission was 7 in the Prichard group and 5 in the low dose group. Murthy O[70] had comparable number of convulsions prior to admission i.e 51.7% had around 1-5 convulsions prior to admission. Sahu[69] et al and Bangal V[47] observed 72% of cases had less than 3 convulsions prior to admission in the hospital. Jana N[72] however observed that the number of seizures before admission varied from 1 to more than 10.

Patients level of consciousness was assessed by a Glasgow Coma Scale[65]. In this study the mean GCS in the Zuspan group was 13 and 14 in the low dose magnesium sulphate group. The levels of consciousness was comparable in both the groups. The GCS in Regmi et al[49] study was also comparable between the two groups that is 10 in Group A and 11 in group B.

Mean systolic by diastolic blood pressure on admission was slightly higher in the Zuspan group (164/110mmHg) compared to the low dose magnesium sulphate group (152/104 mmHg)

This is comparable to the study done by Savitha et al[57] where the mean blood pressure was 164/104mmHg in both the groups. Bhattachajee at al[48] also reported most patients having a blood pressure of 160/110mmHg in both the groups.

When body weight was taken before pregnancy or after delivery it shows that compared to western populations , Indian women have a lower BMI. In this study BMI assessed in both the groups showed the mean BMI in the Zuspan regimen to be 22.1 kg/m^2 and 20.3 kg/m^2 in the low dose group. Bangal et al. observed that 70% of women had a body weight of less than 50 kilograms at the time of admission.[47] Asnani[56] reported a similar mean BMI of 22 kg/m^2. Sahu et al had taken pre pregnancy maternal weight in her study and found mean BMI in Dhaka regimen 20.75+/- 1.33 and Prichard regimen is 20.64+/- 1.24.[68] Jana N et al measured weight after three to four days of delivery and when patient was ambulatory showed most women were of small stature with the mean height being 151+/- 7cm, a mean weight being 41.7 +/- 5.3kgs and a mean body mass index of 19.3+/- 2.1.[72] Gortzak-Uzen et al, says levels of magnesium in amniotic fluid increase with duration of maternal infusion and has small but significant effects on the fetal heart rate pattern. Specifically beat to beat variability. So measuring body weight before delivery helps in evaluating perinatal outcome.[73]

The Zuspan regimen had 63.3% vaginal deliveries while just 36.7% LSCS and low dose having 43.3% vaginal deliveries with a slightly higher percentage of LSCS being 56.7% . This was however not statistically significant. The most common indication for emergency LSCS was fetal distress in the form of non resassuring NST. Vailaya et al also reported that the most common indication for LSCS in all three groups was non reassuring NST.[58] Bhattacharjee et al reported a higher LSCS rate than a vaginal delivery rate in both the groups.[48]

The first convulsion to delivery interval for the patients in this study was comparable in both the groups with 15 hours in the Zuspan group and 13 hours in the low dose magnesium sulphate group. With Vailaya et al[57] study two patients delivered within the first six hours and two more within the first twenty four hours and just one after 48 hours.

There was no significant difference between both the groups in respect to the investigations such as platelets, renal function test (RFT) and Liver function test (LFT). In Zuspan Group and Low dose magnesium sulphate group, majority of subjects 43.3% and 46.7% had grade 3 proteinuria. Devarmani M[52] study 92% of patients had proteinuria. Protienuria is feature of glomerular dysfunction and its presence with hypertension doubles the risk of perinatal death.

The Zuspan group had 10% of subjects and in Low dose magnesium sulphate had 13.3% had abnormal RFT. In Zuspan group 36.7% had abnormal LFT and in Low dose group 16.7% had abnormal LFT. There was no significant difference in LFT between two groups.

With respect to magnesium levels Zuspan group had 13.3% increased magnesium levels, were as none of them had Mg toxicity in the low dose group. This difference in magnesium toxicity between two groups was statistically significant. In Zuspan group, 3.3% knee jerk was absent and low urine output in 13.3% of subjects 13.3% had Tachypnea. There were no signs of magnesium toxicity in the low dose magnesium group. There was significant difference in incidence of Tachypnea between two groups. Devarmani M[51] reported no signs of magnesium sulphate toxicity while using a low dose magnesium sulphate regimen. Ranganna et al reported that there was a significant reduction in toxicity in their study with use of low dose magnesium sulphate there was a difference seen in between the two groups in terms of absent knee jerk (0.93% vs 0.98%) and oliguria (2.26% vs 2.93%).[53] Omakara M[70] In patients with eclampsia loss of knee jerk was seen in 16% of group I patients and 8% of group II patients and this was not statistically significant. Respiratory depression was seen in 2% of group I patients and

none in group II. In patients with imminent eclampsia loss of knee jerk was seen in 8.6% of patients of Group I and 2.9% of Group II and this was also not statistically significant. There were no cases of respiratory depression in any of the groups with imminent eclampsia. Vailaya et al[58] knee jerk was lost in 7 patients including all patients who had been given therapy and magnesium sulphate on and off.

In the Zuspan group, 3.3% had 2 episodes of convulsions and in group low dose, 13.3% had one episode and 3.3% had 2 episodes of convulsions. There was no significant difference in no of convulsions between two groups. The recurrent convulsions lasted for lesser than 45 seconds in both the groups. The following table shows various studies comparing the recurrence to the maternal mortality. The present study had no maternal mortality.

Table 37: Table comparing the recurrence and maternal mortality in various studies

Regimen	Recurrence	Maternal Mortality	Author
Single dose magnesium sulphate[50]	9.16%	3.3%	Joshi et al.
Prichard[3]	12%	0.4%	Prichard et al
Low dose magnesium sulphate[42]	7.8%	2.6%	Suman Sardesai
Eclampsia trial group[38]	5.3-13.2%	3.8-5.2%	Eclampsia trial group
Dhaka regimen[40]	1.53%	8.6%	Begum et al
Padhar regimen[41]	1.05%	_	Mahajan
Low dose maintenance[74]	2%	3.3-5%	Chowdary

The total dose of drug given in the Zuspan group was 37g where as that given in the low dose magnesium sulphate group was just 23g to control convulsions and this was statistically significant. The duration of drug exposure in both the groups was 33 hours and 30 hours respectively and was hence comparable.

Significant association was observed between outcome and gestational age in Zuspan group.

When gestational age was <32 weeks, majority of them had still born (66.7%), In Gestational age group 32 to 36 weeks, 75% of them had satisfactory outcome and when gestational age was >37 weeks, 100% of them had satisfactory outcome. Significant association was observed between outcome and gestational age in low dose magnesium

sulphate group. When gestational age was <32 weeks, majority of them had still born (50%), In Gestational age group 32 to 36 weeks, 66.7% of them had satisfactory outcome and when gestational age was >37 weeks, 100% of them had satisfactory outcome.

The mean birth weight in this study in the magnesium group was 1.8 kgs where as low dose magnesium sulphate was 2.2kgs. At the Rotunda Hospital in Dublin[74] and the Yorkshire region[75] of the UK involving 16 maternity units using a common guideline of MgSO 4 therapy for pre-eclampsia for a 5-year prospective study there were no maternal deaths but about 72% of these women were delivered by lower segment caesarean section and the mean birth weight was 2.54 kg due to intra-uterine growth restriction and preterm delivery.

Ther perinatal outcome when the low dose magnesium sulphate regimen was used in our hospital according to the Sardesai regimen was lower 22.2% compared to the study done by Sardesai et al.[42]

Table 37: table comparing the recurrence of convulsions maternal and perinatal mortality in various studies

Study	Recurrence of convulsions (%)	Maternal Mortality (%)	Perinatal Mortality(%)
Pritchard et al[3]	12.1	0.4	15.7
Sibai et al[39]	14.1	0.4	11.8
Magpie Trial[4]	0.8	2.6	11.4
Sardesai et al[42]	7.8	0.2	28.5
Vailaya et al[58]	14.3	0	14.9
Present study	16.6	0	22.2

Magnesium sulphate therapy in pre-eclampsia has not been associated with improved neonatal outcome in the short-term. There are many confounding factors that contribute to adverse neonatal outcome, and therefore make the evaluation of the neonatal outcome after magnesium sulphate therapy difficult, such as primigravidity (52%), preterm delivery in 56 and 53% of preeclamptic and eclamptic women, respectively, and intrauterine growth restriction among 30.2% of the women in a study done by Omu A.E.[77]

Another study aimed to study the effects of magnesium sulphate on newborns. It was a prospective study where subjects were newborn infants delivered at > or = 34 weeks of gestation whose mothers received a minimum of 12 hours of intravenous MgSO4 therapy before delivery. Control infants were the next born infants of similar gestational age. Outcome recorded at delivery included Apgar scores, whether resuscitation was required, and whether respiratory depression or decreased tone were noted by the physician in attendance. Pneumocardiograms on magnesium-exposed and control infants, obtained within 6 to 18 hours after delivery, were analyzed post discharge by a single investigator who was blinded to group. The nursery course, feeding patterns, time to first stool, and time to first void were recorded. They concluded that Infants born to mothers treated with MgSO4 were more likely to be hypotonic and have lower Apgar scores at birth. Beyond the immediate post delivery period, there were no additional complications in this cohort attributable to prenatal MgSO4 exposure. [78]

The mean APGAR score in both the groups was 1 minute -7/10 and 5'-9/10

Pruett et al[79] studied magnesium sulphate effects on APGAR score. For 30 patients they gave 6g of loading dose of magnesium sulphate and then 2g/hr as continuous infusion .

They observed that 29 neonates had APGAR score at 1 minute and 5 minutes of >7 . They observed that low APGAR was not due to hypotonia but due to a colour factor and concluded that mother who received magnesium sulphate with intravenous dose maintaining magnesium levels within the therapeutic range had no adverse effects on APGAR score.

In Zuspan group 56.7% required NICU admission were as in MgSo4 group 33.3% required NICU admission. This difference in NICU admission between two groups was statistically significant.

In Zuspan group, 6.7% admitted due to LBW, 36.7% admitted due to preterm and 13.3% admitted due to Respiratory distress and in MgSo4 group, 13.3% admitted due to LBW, 30% due to preterm and 10% due to RDS. There was no significant association between reasons for NICU admission between two groups.

Greenberg et al[80] studied the incidence of neonatal intensive care unit admission rate and care needs among term and late preterm neonates who were exposed to antenatal magnesium sulphate. They conducted a retrospective cohort study of all singleton neonates >35 weeks of gestation who were exposed immediately antenatally to magnesium sulphate for eclampsia or imminent eclampsia. Fifty one of 242 neonates (21.1%) who at >35 weeks gestation had been exposed to antenatal magnesium were admitted to NICU.

There was no maternal mortality in this study.

Conclusion

CONCLUSION

There is without a doubt that magnesium sulphate is the first line drug for imminent eclampsia and ecalmpsia but what is the minimum effective dose needs to be still understood clearly.

The pioneers of magnesium sulphate therapy like Pritchard and Sibai have come up with protocols more suitable to their own hospital and patients. The fact that magnesium sulphate has a very narrow therapeutic range also mandates that we must give a minimum dose required to avoid any toxicity and control convulsions and to improve maternal and fetal outcome.

This comparative study shows the efficacy of intravenous low dose magnesium sulphate regimen compared to the Zuspan regimen in respect to recurrence rate of convulsion, chance of toxicity and maternal and perinatal outcome. There was also a significantly lower dose administered in the low dose group compared to the Zuspan group.

Since there is less associated toxicity magnesium sulphate treatment is likely to become more acceptable to peripheral health centres where there are no resources , manpower and facilities to monitor magnesium infusion .Taking this into consideration, the above results and lower BMI of the Indian population, dose modification of magnesium sulphate in eclampsia and imminent eclampsia maybe recommended in our set up.

The major limitations of this study was the smaller sample size. This study has included only Antepartum and Imminent eclampsia. Cases of postpartum eclampsia were not taken. In cases where pre pregnancy weight was not available the patients weight on admission after stabilizing the patient or post pregnancy weight has been taken into

account. Serum magnesium levels were not estimated for all patients due to financial constraints and has been estimated only in cases of magnesium toxicity.

The present study suggests that low dose magnesium sulphate is as effective as Zuspan regimen.

Summary

SUMMARY

- The present study had 60 patients of eclampsia and imminent eclampsia . A low dose regimen (Suman Sardesai regimen[42]) was compared to the standard Zuspan regimen and assessed for maternal and perinatal morbidity and mortality.
- Both groups had comparable baseline demographics. Most patients were Primigravida with a mean age of 23 years belonging to socioeconomic class 3.
- Although majority patients were booked cases they had not been booked in our Hospital.
- Most cases of antepartum eclampsia presented with history of a single convulsion on admission.
- The mean BMI in the low dose group was slightly lower than in the Zuspan group. ($22.1 kg/m^2$ versus $20.3 kg/m^2$)

- With respect to maternal variables we observed that the dose given to the mother was significantly lower in the low dose magnesium sulphate group compared to Zuspan regimen. There was no signs of magnesium toxicity in the low dose group but the Zuspan regimen was associated with signs of magnesium toxicity.With the most common sign of magnesium toxicity being tachypnea. When serum levels were estimated in these patients all the patients in the Zuspan group showed signs of toxicity and increased serum magnesium levels.
- There was no significant difference between the recurrence of convulsions between both the groups.
- The mean convulsion to delivery interval measured was lower in the low dose magnesium sulphate group that was 13.8 hours compared to the Zuspan group which was 15.2 hours.

- There was no maternal mortality . But two cases of abruption placenta and one case admitted to the ICU in view of status eclampticus.
- The total dose of drug administered was significantly lower in the low dose group compared to the Zuspan regimen
- With respect to the fetal outcome there were lesser admissions to NICU in the low dose magnesium sulphate group than Zuspan group with the most common reason for NICU admission being preterm care followed by low birth weight.
- Perinatal mortality was 22.2% in the low dose group . The number of days spent in NICU was similar in both the groups.
- Hence low dose magnesium sulphate regimen can be used in our hospital compared to the conventional Zuspan regimen.

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Annexures

ANNEXURE -1

CASE PROFORMA

NAME: AGE: Yrs

IP NO :

OCCUPATION:

DOA:

ADDRESS:

DOD:

EDUCATION:

HUSBANDS OCCUPATION:

SOCIOECONOMIC STATUS:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

OBSTETRIC HISTORY:

Marital life:

Consanguinity:

Obstetric formula:

Details of previous pregnancy:

Details of present pregnancy:

MENSTRUAL HISTORY

Last menstrual period: Age of menarche:

Expected delivery date:

Past menstrual cycles:

Period of gestation:

Period of gestation according to early scan:

PAST HISTORY:

HTN/DM/BA/RHD/TB/DENGUE/MALARIA/BLOOD DYSCRASIAS/EPILEPSY

H/O blood transfusions:

Others: H/O Surgeries

PERSONAL HISTORY:

Sleep and appetite: Diet:

Bowel and bladder:

FAMILY HISTORY:

DRUG HISTORY:

GENERAL EXAMINATION:

General condition: Fair/ moderate/ Poor

GCS:

Built: Nourishment:

Ht: cms Wt: kgs BMI:

Pallor: Icterus: Cyanosis: Clubbing: Lymphadenopathy:

Pedal oedema:Grade1/2/3/4

VITALS:

Pulse rate:

Respiratory rate:

Blood pressure

Temperature:

Urine output:

SYSTEMIC EXAMINATION:

Cardiovascular system:

Respiratory system:

Central nervous system:

PER ABDOMEN:

PER VAGINUM:

PROVISIONAL DIAGNOSIS:

INVESTIGATIONS:

Blood group and Rh typing:

CBC: HB:	RBS:
PCV:	HIV:
RBC:	Urine albumin +1/+2/+3/+4
VDRL:	HbsAG:
WBC:	APTT
PLT:	PT
	INR

SERUM MAGNESIUM:

SIGNS OF MAGNESIUM LEVEL TOXICITY:

OBSTETRICS SCAN:

FETAL DOPPLER:

MODE OF DELIVERY:

INDICATION:

DELIVERY DETAILS:

Date: APGAR SCORE:

Time: I min:

Sex: 5 min:

Birth weight:

MATERNAL COMPLICATIONS: FETAL COMPLICATIONS:

No. of convulsions: Asphyxia:

Duration of convulsions (if any): Hypotonia:

Need for neonatal resurcitation:

Admission to NICU:

TREATMENT GIVEN:

TIME OF STARTING TREATMENT

REGIMEN: LOW DOSE REGIMEN/ ZUSPANS REGIMEN

TOTAL DOSE OF DRUG GIVEN:

DURATION OF EXPOSURE OF THE DRUG:

CONDITION AT DISCHARGE:

Mother: Baby:

PATIENT INFORMATION SHEET

Study title: Comparative study of the obstetric outcome in eclamptic and imminent eclamptic patients treated with low dose magnesium sulphate versus Zuspan's regime.

Study location: R L Jallappa Hospital and Research Centre attached to Sri Devraj Urs Medical College. Tamaka, Kolar

Details-

In patients presenting with eclampsia and imminent eclampsia after 20 weeks gestation age in the inpatient department will be administered magnesium sulphate according to two different protocols.

Patients will be assigned the protocol based on randomization.

Magnesium sulphate is used as the first line of treatment and control of convulsions in eclampsia. Patients in this study will have to undergo routine blood investigations such as a complete blood count, viral serology, Renal function test, Liver function tests , serum magnesium levels. To assess the fetal wellbeing a cardiotocograph and an obstetric ultrasound with biophysical profile and fetal Doppler will also be done.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the

Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

Dr Aditi C Ramachandra

Post graduate

Department of obstetrics and gynecology

SDUMC , Kolar

INFORMED CONSENT

Date:

Obstetrician:

I / We the attenders of the patient were told the condition of the patient i.e

_____

_____

_____

and the need for therpuetic intervention. I/we the attenders of the patient agree to participate in the study. The nature and purpose of the study and its potential risks / benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail in my own understandable language. I /we understand that my participation is voluntary and that I/we are free to withdraw at any time, without giving any reason, without my medical care or legal right being affected. I/ we give permission for these individuals to have access to patient records. And we here by give consent to the treating doctors for pharmacological intervention and we donot claim any responsibility on to the treating doctors,staff or hospital for any maternal and fetal complications and patient condition.

Signature of patient /attenders

Time

KEYS TO MASTERCHART

GA- Gestational age

BMI- body mass index

LSCS- lower segment caesarean section

Hb- Hemoglobin

Plt- Platelets

FD- Fetal distress

VD- Vaginal delivery

BOV- blurring of vision

Epi pain- Epigastric pain

IUGR- Intrauterine growth restriction

MIVD- Misoprostrol induced vaginla delivery

OFD- Outlet forceps delivery

IDI- Induction delivery interval

Foley- Foleys catheter induced

ADEQ-Adequate

KJ- Knee Jerk

RR- respiratory rate

RFT- Renal function test

LFT –liver function test

Mg- Magnesium

PT- Pre term

RDS- Respiratory distress syndrome

LBW- Low birth weight

CDI- convulsion delivery interval

PPH- Post partum hemorrhage