ASSESSMENT OF PAIN ASSOCIATED WITH INTRAMUSCULAR INJECTION OF MAGNESIUM SULPHATE WITH OR WITHOUT LIGNOCAINE IN WOMEN WITH SEVERE PREECLAMPSIA AND CONSCIOUS ECLAMPTIC WOMEN– A RANDOMIZED CONTROL TRIAL

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This is to certify that this dissertation entitled **"ASSESSMENT OF PAIN ASSOCIATED WITH INTRAMUSCULAR INJECTION OF MAGNESIUM SULPHATE WITH OR WITHOUT LIGNOCAINE IN WOMEN WITH SEVERE PREECLAMPSIA AND CONSCIOUS ECLAMPTIC WOMEN– A RANDOMIZED CONTROL TRIAL "** is a bonafide research work done by **REG.NO.BJ0113005.**

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LIST OF ABBREVIATIONS USED

ACOG	-	The American Congress of Obstetricians and Gynecologists
BBB	-	Blood brain barrier
BMI	-	Body Mass Index
Ca^{2+}	-	Calcium
CONSORT	-	Consolidated Standards of Reporting Trials.
CTRI	-	Clinical Trials Registry- India
DRG	-	Dorsal root ganglion
g	-	Gram
g/h	-	gram per hour
g/min	-	Gram per minute
hrs	-	Hours
IM	-	Intramuscular
IV	-	Intravenous
Meq/dl	-	Milliequivalent per liter
mg	-	Milligram
Mg^{2+}	-	Magnesium
MgS04	-	Magnesium Sulphate

ml	-	milliliter
MLC	-	Myosin light chain
mmHg	-	Millimeters of mercury
NICE	-	The National Institute for Health and Care Excellence
NIPC	-	National intiative on pain control
NMDA	-	N-methyl-d-asparate
NO	-	Nitric Oxide
PAG	-	Periaqueductal grey matter
PGI_2	-	Prostaglandin I_2
PRES	-	Posterior reversible encephalopathy syndrome
RCT	-	Randomized Control Trial
SD	-	Standard Deviation
SNOSE	-	Sequentially Numbered Opaque Sealed Envelope
VOCC	-	Voltage operated calcium channel
WHO	-	World Health Organization

ABSTRACT

Assessment of pain associated with intramuscular injection of Magnesium Sulphate with or without Lignocaine in women with severe preeclampsia and conscious eclamptic women– A Randomized Control Trial.

Background

World wide Magnesium Sulphate (MgSO4) is the drug of choice for the management severe preeclampsia and eclampsia, used parentrally by intravenous (IV) and intramuscular route(IM). Most common side effect of intramuscular Magnesium Sulphate is pain at the site of injection seen in majority of the patients due to large volume(10ml) and multiple injections practiced in Asian countries. WHO 2006 guidelines recommend addition of 1ml 2% Lignocaine to IM injection of MgSO4. This recommendation is consensus based. There is lack of sufficient data on whether addition of Lignocaine reduces pain at the site of injection.

Objective

To find out whether addition of 1ml of 2% Lignocaine with MgSO4 in IM injection reduces the injection site pain, when used in severe preeclampsia and conscious eclamptic women using visual (faces) analogue scale of 0 to 10.

Methodology

This Randomized control trial was done at labour room of department of Obstetrics and Gynaecology, teaching hospital attached to KLE university's, J N medical college, Belagaum. Total sample size of 90 eligible women were randomized into 2 groups by using sequentially numbered opaque sealed envelop technique (SNOSE)-

Group A Magnesium Sulphate with 1ml of 2% Lignocaine .

Group B Magnesium Sulphate alone.

Injection was given deep IM at upper outer quadrant of alternate buttocks.

Pain assessment was done by using visual (faces) analogue scale in both the groups with in 5minutes of 1st injection , at the end of 4 hours of giving 1st injection and at end of 24 hours or 4hours of the last dose which ever is later.

Results

As per the CONSORT flow diagram, 101women were approached to participate in the study of which 96 women were eligible, of them 90 women consented and were randomized into 2 groups by SNOSE method. 46 women received MgSO4 with 1ml of 2% Lignocaine and 44 women received MgSO4 alone. Of these, 73 women completed planned course of Pritchard's regimen and 17 were given partial regimen but were included in analysis of the result (6 were assesed after 1st dose of injection and 11 were available for 2nd assessment.

The pain scores were evaluated using Visual(faces) analog scale within 5minutes of injection of 1st dose, 4hours after injection of 1st dose and at the end of 24 hours or 4hours of last dose of injection. There was no statistical significance in mean pain scores between 2 groups within 5minutes of 1st injection(P value 0.897), 4hours after 1st injection(P value 0.138) and the end of 24hours or 4 hours of the last dose of injection(P value 0.423). There was no difference between minimum 4,2,0 and maximum 8,4(Group A) and 6(Group B),4 mean pain scores between the groups at different intervals respectively.

Conclusion

We conclude that the addition of 1ml of 2% Lignocaine in IM injections of 50% $MgSO_4$ is not beneficial in reducing pain.

Keywords

Magnesium Sulphate; Lignocaine/ Xylocaine; Intramuscular injection; Pain.

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INTRODUCTION

Hypertensive disorders of pregnancy contribute to significant maternal and perinatal morbidity and mortality in both developed and developing countries. Pre-eclampsia and eclampsia affects 5-10% of all the pregnancies and contributes to 18% of maternal deaths worldwide. Estimated case fatality rate due to eclampsia is 14 times higher in developing countries compared to developed countries [1,2].

Preeclampsia is a multi-system disorder whose pathophysiology remains unclear. Preeclampsia is defined as a blood pressure of at least 140 mmHg systolic pressure and 90 mmHg diastolic pressure measured on two occasions 6 hours apart, accompanied by proteinuria of at least 300 mg per 24 hours, or at least 1+ on dipstick testing after 20 weeks[3].

Eclampsia refers to the onset of convulsions/coma in a woman with preeclampsia that cannot be attributed to other causes. The seizures are generalized and may appear antepartum, intrapartum or postpartum. It's a serious manifestation that is associated with increased risk of mortality and morbidity in the pregnant women and poor perinatal outcomes.

In 2 to 3 percent of severely preeclamptic women eclamptic seizures were known to occur in women who are not receiving anti-seizure prophylaxis. The seizure rate is estimated to be between 0 - 0.6 percent in women with preeclampsia without severe features (previously referred to as "mild" preeclampsia) [4].The incidence of eclampsia is found to be relatively stable at 1.6 to 10 cases per 10,000 deliveries in developed countries [5-10] . However in developing countries, the incidence varied widely from 6 to 157 cases per 10,000 deliveries [11-13] .

In preeclamptic women, Magnesium sulfate (MgSO4) is considered to be superior to phenytoin, nimodipine, diazepam and placebo as an eclamptic seizure prophylactic[14-18] . In the multinational Collaborative Eclampsia Trial, MgSO4 is found to reduce the risk of recurrent seizures in eclamptic women by 52% when compared to diazepam and by 67% when compared to phenytoin [19].

Since 20th century MgSO4 has been considered as drug of choice for prevention of eclamptic seizures[20-24]. Empirical evidence supports the effectiveness of MgSO4 in preventing and treating eclamptic seizures [18,24-28].

Magnesium sulfate is considered to be very effective in reducing maternal and perinatal mortality and morbidity. It has been proved superior to diazepam with low seizure recurrence, quick recovery from coma and with improved fetal salvagability[30].

Magnesium sulfate can be administered parenterally by intramuscular(IM) or intravenous (IV) routes. Though IV regimen is more efficacious in achieving stable serum levels of magnesium but requires the use of an infusion pump for safe delivery of drug and has a greater potential for inadvertent overdose. But in low resource setting or developing countries like India the use of IV infusion set is not uncommon. So IM regimen is the standard of care used in most hospitals in India. Though it is potentially safer it requires repeated IM injections which are painful.

To reduce the pain at injection site due to repeated injections, WHO recommends addition of 1ml of 2% Lignocaine to 2.5mg(5ml)/ 5mg(10ml) of Magnesium Sulphate during IM use. This recommendation is consensus based and not evidence based[31].

However no or limited information is available about the use of Lignocaine in reduction of pain at intramuscular injection site with IM MgSO4 injections due to the scarcity of data in the literature . Hence the present study was undertaken to provide evidence either in favour of or against the use of lignocaine with IM Magnesium Sulphate.

OBJECTIVE

The objective of the present study is

- To assess the benefit of Lignocaine in IM injection of MgSO4 for pain relief in severe preeclamptics and conscious eclamptic women using visual(faces) analogue scale.

REVIEW OF LITERATURE

Preeclampsia is a hypertensive disorder of pregnancy. It involves multi-system causing multi organ failure which significantly contributed to maternal and fetal/neonatal morbidity and mortality[3].

Hippocrates stated that during pregnancy presence of a headache accompanied by heaviness and convulsions is considered bad[32].

McMillen was the first to describe eclampsia and to note that primigravida were at a greater risk for convulsions compared to multigravida[33]. Mauriceau described the cause of convulsions during pregnancy was due to lochial flow abnormality or intrauterine fetal death. When there is supressed lochial flow it would cause inflammation, headache, convulsions, suffocation and death can occur. In a case wherein intrauterine fetal death had occurred a retained dead fetus caused foul-smell and cadaverous humours in the womb which predisposed a woman to convulsions[34] .

The word “eclampsia” first appeared in Varandaeus’ treatise on gynecology in 1619[34].

Treatment

Two to three phlebotomies during pregnancy was recommended by Mauriceau in an attempt to decrease cerebral congestion and prevent eclampsia[35-36].

Theories on Disease Causation

According to Denman, uterus was enlarged as the pregnancy advances which created a greater pressure upon the descending blood vessels. Such an increase in pressure in the vessels led to the regurgitation of blood in the head and which further resulted in an overload of the cerebral vessels and subsequent convulsions[37].

In 1849 Dr. William Tyler Smith challenged the theory of cerebral congestion. He believed that pregnancy was a state of hyperdynamic circulation. The contractions which were present during the second stage of labor normally, interfered with the circulation of blood. And also he believed that the number of cases of convulsions were increased if such congestion of vessels were observed. In contrast, Smith described various causes for puerperal convulsions such as: (1) Excess of either mechanical or emotional stimulus applied to the spinal centre; (2) bloodletting; (3) Any variations in temperature, wind and other atmospheric changes; (4)Irritation of uterus, uterine passages, intestinal canal, and the stomach; and (5) toxic elements. According to Smith's theory on "toxic" elements, he believed that during pregnancy maternal health was depended on the exponential increase in the elimination of wastes (e.g., secretions of the bowels) and debris from the maternal and fetal systems. Any failure to do so resulted in a "toxemia" in which toxic elements were accumulated in the blood which resulted in irritation of the nervous system[38].

Treatment

During the early 1800's blood-letting was one of the important methods in the prevention and treatment of preeclampsia-eclampsia. Depending on strength of the patient and severity of the disease the amount and frequency of blood-letting was decided. Intially bleeding from the arm was attempted, but if convulsions continued,

bleeding was repeated. In some cases if the convulsions didn't get controlled then the jugular vein or temporal artery were opened in an attempt to stop the convulsions [37].

Denman recommended the usage of opiates to decrease irritability of the female constitution. If blood-letting and the opiates failed, splashing of cold water over the women's face or warm bath was given to women in an attempt to stop the convulsions. In cases where all treatments failed then the physician had to choose between either hastening delivery or allowing natural labor to occur. According to Denman, progress of delivery was hastened only if the woman was physiologically ready (cervix fully dilated, absence of membranes and station of fetus has descended) as any intervention if attempted in the early stage of labor increased maternal mortality rate[37].

Treatment was directed against the elimination of overabundant toxins as the theory of disease causation was shifted to the toxin theory in late 1800's .And those who believed that preeclampsia-eclampsia was caused by meat toxins, they restricted the consumption of meat and started on diets of fruits, vegetables, and milk products[35]

The association between edematous women and eclampsia was noted by Denmanet in 1979 [35]. Presence of albumin in the urine of eclamptic women was discovered by John Lever in 1843 [39]. The premonitory symptoms included headache, blurring of vision, epigastric pain, and edema of the hands, arms, neck, and face[40]. In 1897, Vaquez and Nobecourt were credited with the discovery of eclamptic hypertension. Since then, physicians were aware that whenever there is presence of edema, proteinuria, and headaches to think about the possibility of convulsions [41].

Treatment

Earlier morphine and chloral hydrate were administered to keep the women sedated and to decrease frequency of convulsions. Oxygen was administered to restore the respiratory function. To restore cardiac function, digitalis was administered if the pulse was found to be rapid and weak after a seizure. Labor was allowed to progress naturally and once cervix is dilated to six centimeters or more, the membranes were ruptured artificially.

Introduction of magnesium sulfate was done to manage preeclampsia-eclampsia in 20th century. The first usage of magnesium sulfate to manage preeclampsia and eclampsia was done by Horn in 1906. The parenteral use of magnesium sulfate in the treatment of preeclampsia and eclampsia was popularized by Lazard and Dorsett in 1920's. They also demonstrated that treatment with intravenous magnesium sulfate was both safe and effective[36].

For prevention and control of seizures in severe eclamptics and eclamptics, MgSO4 is superior to phenytoin, nimodipine, diazepam and placebo[14-18]. In the multinational Collaborative Eclampsia Trial, MgSO4 reduced the risk of recurrent seizures in eclamptic women by 67% when compared to phenytoin and by 52% when compared to diazepam[19].

Mechanism of action of MgSO4 remains unclear. Several possible mechanisms have been proposed such as vasodilatory action both peripherally and in the cerebral circulation, acts on the blood-brain barrier (BBB) to decrease the cerebral edema formation, and it also acts as a central anticonvulsant. All these possible mechanisms of actions are being discussed below.

Magnesium-induced Vasodilatation

Magnesium is an calcium antagonist which act on calcium channels in vascular smooth muscle to decrease intracellular calcium. Due to decreased intracellular calcium it would lead to inactivation of calmodulin dependent myosin light chain kinase activity and decreased contractions, causing arterial relaxation which subsequently lowers cerebral and pheripheral vascular resistance, relieve vasospasm, and thereby decrease arterial blood pressure[42]. However, the importance of magnesium-induced vasodilatation in the treatment and prevention of eclampsia is not understood completely.

Similar to hypertensive encephalopathy, eclampsia is considered to be a form of posterior reversible encephalopathy syndrome (PRES) in which there is acute elevations in blood pressure which caused force dilatation of the myogenic vasoconstriction of cerebral arteries and arterioles which in turn increased BBB permeability and edema formation[43-45].

MgSO4 acts as an eclamptic seizure prophylaxis by reducing peripheral vascular resistance and lowering of systemic blood pressure rather than having a direct effect on cerebral blood flow (CBF).

Magnesium also act by stimulating the production of prostacyclin from the endothelial cells causing vasodilatation, or by inhibiting platelet aggregation[46, 47]. MgSO4 treatment significantly decreased circulating levels of angiotensin-converting enzyme in patients with pregnancy induced hypertension [48]. This may lead to attenuation of the endothelial dysfunction associated with preeclampsia[49, 50].

As a result of disruption of the BBB resulted in vasogenic edema formation which is an important sign of eclampsia[51, 52]. MgSO4 is found to be effective in eclampsia treatment may be through protection of the BBB and there by decreased cerebral edema formation.

Vascular Effects of Magnesium Sulfate.

Cellular Target	Mode of Action	Possible Mechanism(s)
Smooth Muscle Uterine +++ Mesenteric +++ Aorta +++ Cerebral +	Relaxation ↓ Vasodilation ↓ Decreased Vascular Resistance	Calcium Antagonism Decreased Voltage-operated Calcium Channel (VOCC) Activity Decreased $[Ca^{+2}]_i$ Release From Sarcoplasmic Reticulum
Endothelium	Decreased Platelet Aggregation	Increased Prostaglandin I_2 (PGI_2)
	Vasodilation	Increased Nitric Oxide (NO, Gestation Dependent)

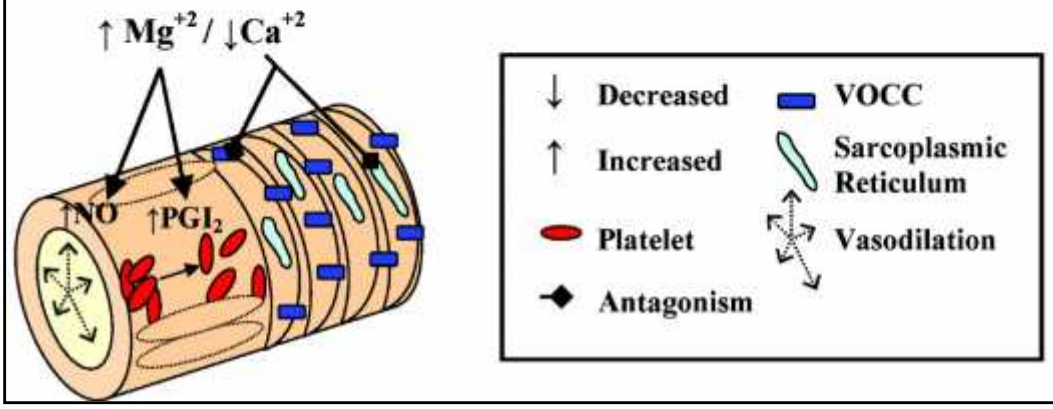


Figure 1. Vascular effects of magnesium sulfate. Picture courtesy-Anna G. Euser, and Marilyn J. Cipolla. Magnesium Sulfate for the Treatment of Eclampsia. American Heart Association; 2009;40:1169-1175

Neuroprotective effects of MgSO4

Magnesium is an calcium antagonist that acts both intracellularly and extracellularly and acts directly on cerebral endothelial cells. At the level of the endothelial cell actin cytoskeleton Magnesium Sulphate acts as an calcium antagonist. MgSO4 prevents the paracellular movement of solutes through the tight junctions .

Various studies supported this hypothesis which demonstrate that the inhibition of myosin light chain (MLC), phosphorylation decreases the agonist induced permeability by inhibiting actin stress fiber contraction[53-55].

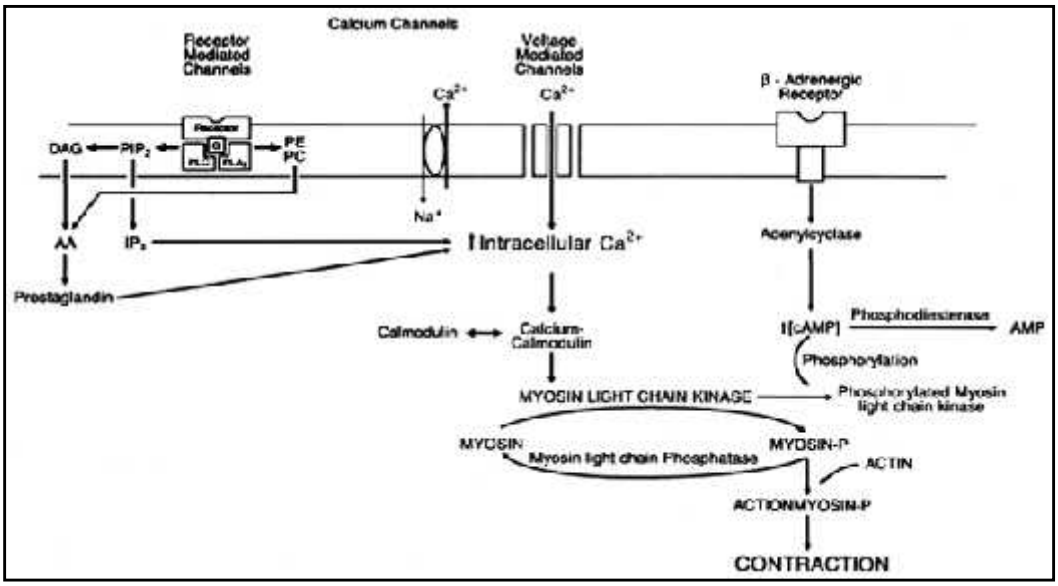


Figure. 2. Diagrammatic representation of the cellular regulatory mechanisms controlling myometrial contractility. Picture courtesy; Frederiksen M.Labor inhibition. The Global Library of Women's Medicine; 2008

Alternatively, acute hypertension caused pinocytosis which may contribute to raised BBB permeability during elevated intravascular pressure[56]. MgSO4 treatment may therefore decrease pinocytosis caused by acute hypertension which resulted in restriction of the movement of factors like water and solutes into the brain by transcellular transport, thereby limiting cerebral edema formation and the seizure activity.

Anticonvulsant activity of Magnesium Sulphate

Seizures are thought to be mediated due to stimulation of glutamate receptors, like the N-methyl-d-aspartate (NMDA) receptor when the neuronal network of these are over-activated[57, 58]. Magnesium sulphate acts as an NMDA receptor antagonist and there by reduces epileptic seizure activity.

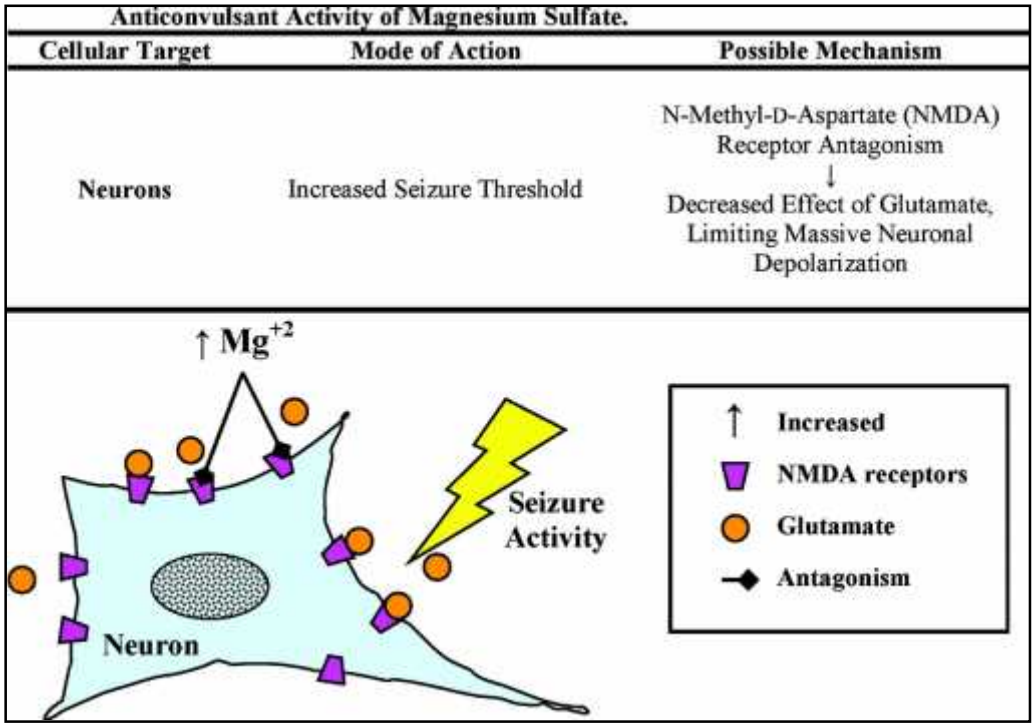


Figure 3. Anticonvulsant activity of magnesium sulfate.
Picture courtesy-Anna G. Euser, and Marilyn J. Cipolla. Magnesium Sulfate for the Treatment of Eclampsia. American Heart Association; 2009;40:1169-1175

Although MgSO4 is thought to be more effective in treatment and prevention eclampsia, questions still exist regarding its safety. There are many concerns regarding the possibility of hyper-magnesemia toxicity in eclampsia treatment. The adverse effects of it occur more due to it, acting as a smooth muscle relaxant.

Normal serum concentrations of Mg^{2+} are 1.5-2.5 mEq/L, of which one-third to half of it is bound to plasma proteins. Total serum magnesium concentration required for the treatment of eclamptic convulsions are 3.5-7 mEq/L, which can be obtained by administering it intramuscularly (6 g loading dose followed by 2 g/h), intravenously (2-4 g dose up to 1 g/min) or a combination of both. Absence of deep tendon reflexes(patellar tendon reflex) is one the important earliest sign has been observed at serum magnesium levels of 8-10 mEq/L, and respiratory paralysis seen at >13 mEq/L. Progressively higher serum magnesium levels can ultimately lead to cardiac arrest at serum magnesium levels greater than 15mEq/L. According to This

dose response relationship the clinical monitoring should ensure the toxicity and adverse effects are to be avoided. Hence there is no need to monitor the serum magnesium levels to check for its toxicity. It can be ensured clinically by checking for deep tendon reflexes and the respiratory rate.

SIDE EFFECTS OF MAGNESIUM SULPHATE

Approximately 25% of women experience side effects from MgS04. These may include:

- Sensation of pain and warmth in arms
- Disruption to sensation, particularly in extremities
- Flushing of face, neck and hands
- Thirst, headache, dizziness, itching
- Nausea and vomiting
- Loss of patellar reflexes- absent well before toxic serum levels are reached
- Muscle weakness, slurring of speech, drowsiness and visual disturbances
- Irritation at the injection site
- Respiratory depression which may lead to respiratory/cardiac arrest(major side effect).

Mechanism of Action of Lignocaine

Lignocaine is a membrane stabilizing drug it reversibly decrease the rate of depolarization and repolarization of excitable membranes. Lignocaine act mainly by inhibiting sodium influx through sodium-specific ion channels in the neuronal cell membrane, specifically the voltage-gated sodium channels. By interrupting the influx of sodium an action potential cannot arise and thereby signal conduction is inhibited[59].

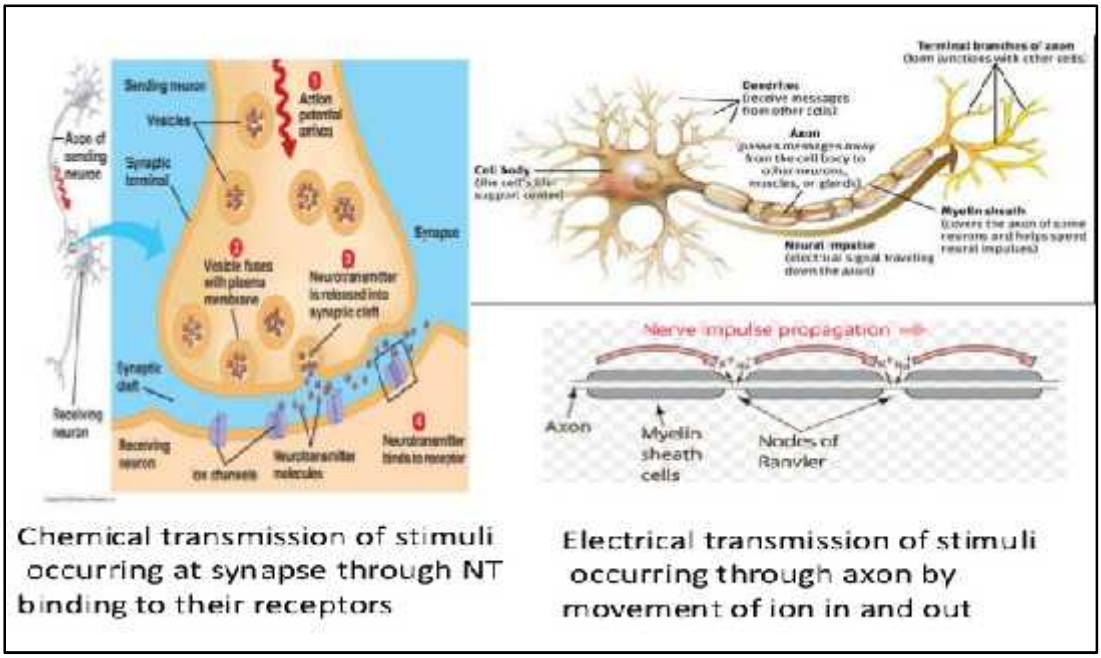
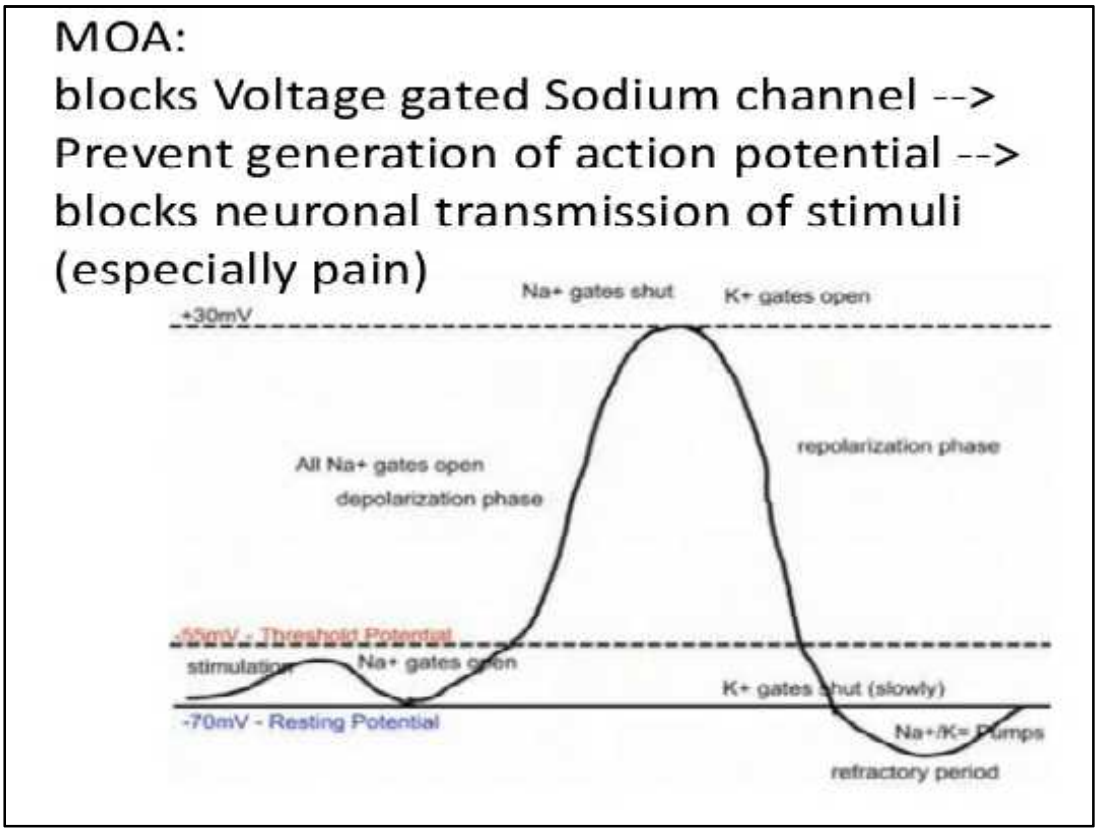


Figure 4: Chemical transmission of stimuli occurring at synapse through NT binding to their receptors.Electrical transmission of stimuli occurring through axon by movement of ion in and out



Mechanism and pathways of pain

Nociceptors are one of the specialised sensory receptors which are responsible for the detection of noxious (unpleasant) stimuli. These are the free nerve endings of primary afferent Aδ and C fibres which are mainly distributed throughout the body (skin, viscera, muscles, joints, meninges) which can be stimulated by mechanical, chemical or thermal stimuli.

Aδ and C fibers synapse with secondary afferent neurons in the dorsal horn of the spinal cord. The primary afferent terminals release a number of excitatory neurotransmitters like substance P and glutamate.

Secondary afferent neurones decussate within a few segments of the level of entry into the spinal cord and ascend in the contralateral spinothalamic tract to nuclei within the thalamus. Third order neurones ascend to terminate in the somatosensory cortex. There are also few projections to the periaqueductal grey matter (PAG). This spinothalamic tract which transmits signals is important for pain localization[60].

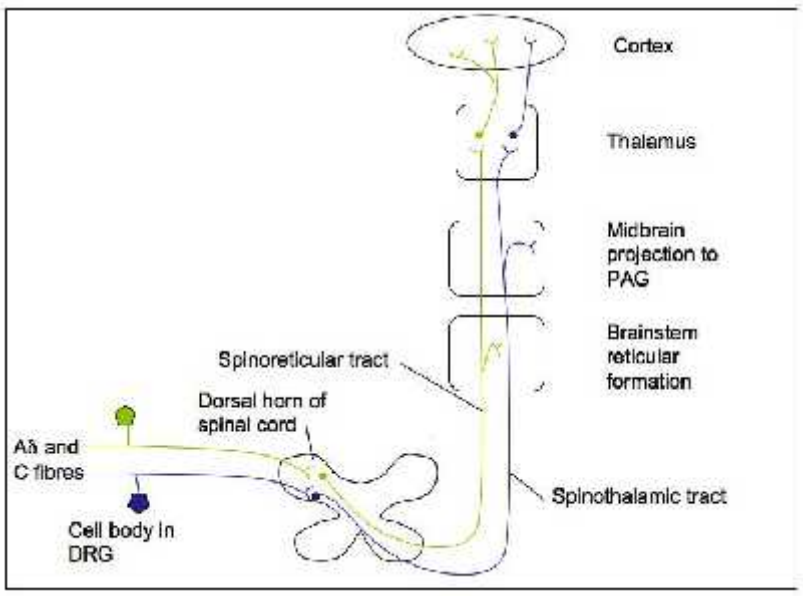


Figure 5: Ascending pain pathways. DRG dorsal root ganglion, PAG periaqueductal grey matter

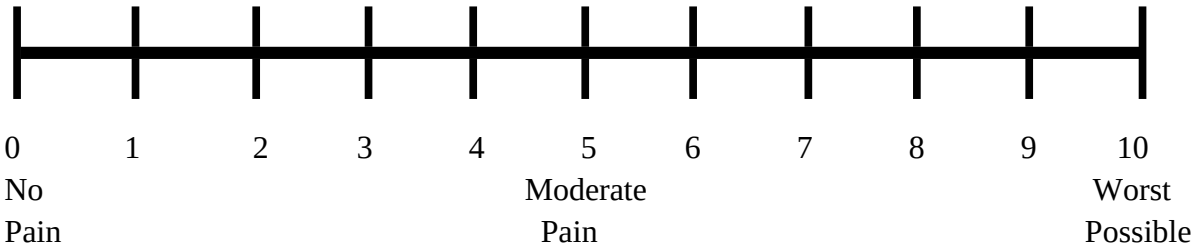
Intramuscular injections are painful due to-

- Stimulation of skin due to sharp needle.
- Volume of the drug injected
- Tissue reaction due to the concentration of the drug.
- 'Potassium' released from the damaged cells.
- Prostaglandins and histamine from immune cells that invade the area during any injury.
- Substance-P from nearby nerve fibres.

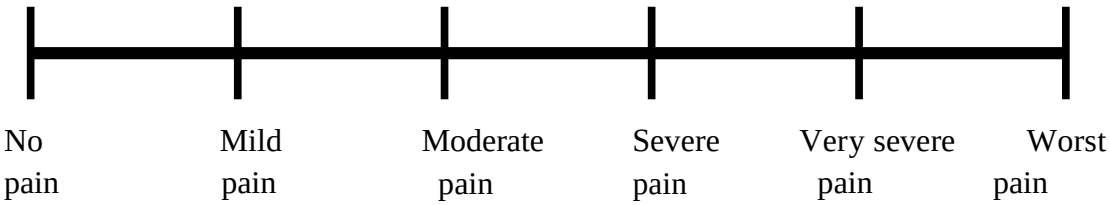
Different types of pain scale

The National Initiative on Pain Control (NIPC) provided the diagnostic tools to assist in assessing the severity and quality of pain experienced by patients. Various types of pain scales available are described below

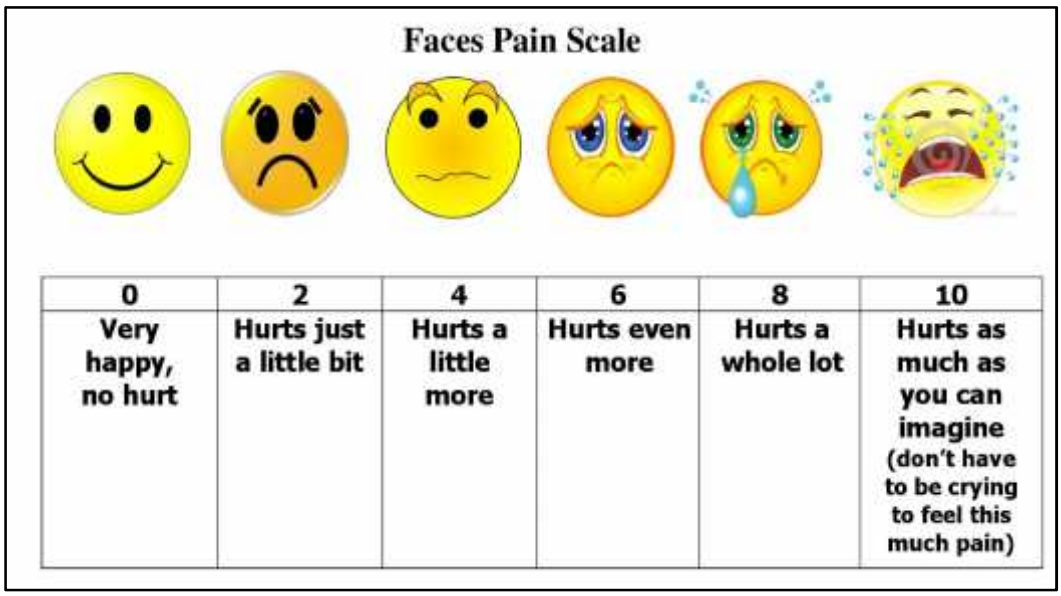
0–10 Numeric Pain Rating Scale:



Verbal Pain Intensity Scale:



Wong-Baker FACES Pain Rating Scale[61]:



Pain is one of the most common side effects IM MgSO4 injections. Though Who guidelines recommend to give Magnesium Sulphate injection with Lignocaine to reduce pain at the site of injection but this is only consensus based not evidence based.

WHO guidelines recommend to give:

Loading dose-

20ml of 20%Magnesium Sulphate intravenous slowly over 10 min and 10ml of 50%Magnesium Sulphate deep IM in each buttock in the upper outer quadrant with 1ml of 2% Lignocaine in the same syringe.

Maintaince dose-

5grams of 50% Magnesium Sulphate with 1ml of 2% Lignocaine every 4 hours deep IM in alternate buttocks until 24 hours after birth or after last convulsion (whichever is later)[31].

Other guidelines –

NICE guidelines of 2006 recommend to give-

Loading dose of 4 grams given intravenously over 5 min, followed by infusion at the rate of 1gram/hour for 24 hours.

Further dose of 2-4 gram given over 5 minutes if recurrent seizures occur.

ACOG guidelines recommends to give:

4-6g IV Magnesium Sulphate as loading dose over 20 minutes followed by 2g/hr as continous infusion pump.

MATERIALS AND METHODS

The present study was conducted in the Department of Obstetrics and Gynaecology, KLE University's teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum.

Study design

The study design was a Randomized Controlled Trial.

Time line for the study

PHASE	TIME PERIOD	OUTLINE
I	June 2013 to October 2013	1.Identification of problem 2.Review of Literature 3.Development of data collection instrument 4.Submission of Synopsis
II	September 2014 to April 2015	1.Enrolment 2.Data Collection
III	May 2015 to August 2015	1.Analysis of collection data 2.Discussion
IV	September & October 2015	1.Submission of dissertation

Source of data

All women with severe preeclampsia and conscious eclamptics admitted to Labour room of Department of Obstetrics and Gynaecology, and willing to participate in the study at KLE university's teaching hospital attached to J.N.Medical College , Belgaum.

Sample size

Sample of 90 pregnant women were studied.

Sampling procedure

Minimum sample size required to perform a independent stundent's 't' test or for any randomized control trial according to rule of thumb is 30 in each group. 10% refusal and 10% including loss for follow up, a total sample size of 72 women were required.

Total sample of 90 women were enrolled who were randomly assigned to one of the two group using sequentially numbered opaque sealed and numbered envelopes.

Selection Criteria

Inclusion criteria

All cases of severe pre eclampsia and eclampsia-antepartum, intrapartum, postpartum (convulsion occurring within 48 hours of delivery).

Exclusion Criteria:

- Not willing to participate

Method of Collection of Data

Ethical clearance

The ethical clearance was obtained from institutional Review Board of KLE University's teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum. (MDC/DOME/17) dated on 30/11/2013 (Annexure I). This study is registered with Clinical trial registry of India CTRI /2014/03/004503.

Screening and Enrolment

All consenting women who were admitted to the labour room were screened for eligibility based on selection criteria. Informed consent was obtained at the time of enrolment into the study from the eligible women. The informed consent form was provided by the investigator to the patient to be enrolled. The investigator obtained a signature or left hand thumb impression from the consented participant. Adequate time was provided for describing the study and fielding questions from the participant and immediate family members. Fair balance was maintained while explaining the risks and benefits of participation in the study. No undue pressure was placed on the patient to enroll in the study.

It was further explained that lack of participation will not affect the usual and anticipated standard of care. The women were enrolled in the study only after taking their signature or left hand thumb impression on informed consent form (Annexure II).

Randomization

Women were randomized by using sequentially numbered opaque sealed envelope technique (SNOSE) into 2 groups.

Group A - Magnesium Sulphate with 1ml 0f 2% Lignocaine.

Group B – Magnesium Sulphate alone.

A unique subject ID was assigned to those women who consented for the study starting from 001. These numbers were allotted to the patient as and when they come to labour room.

Every time before giving Magnesium Sulphate, it was ensured that knee or other reflexes are present, respiratory rate was normal and urine output was more than 100ml in last 4 hours or greater than 25ml in last hour.

SNOSE (Sequentially Numbered Opaque Sealed Envelopes)

The primary aim of randomizing women into 2 groups is to prevent researchers from predicting and thus influencing, which patient will receive which treatment. Among the many methods described for allocation concealment (to omit selection bias), SNOSE is both simple and effective.

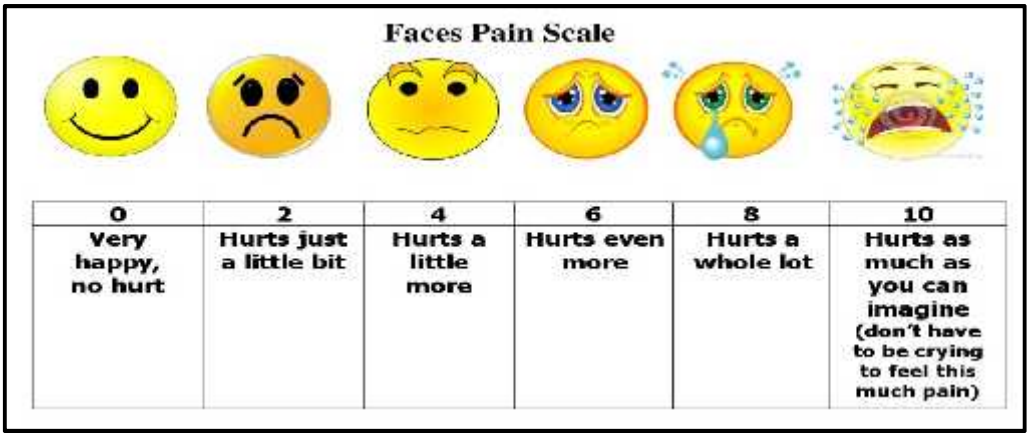
The materials required for preparing SNOSE were envelops(printed/ hand written), card paper, single sided carbon sheet and kitchen use aluminum foil. The card paper formed the core on which the intervention was encrypted. A carbon sheet of same size was placed on the card and the two were wrapped in aluminum foil(presence of aluminum foil prevented the investigator to predict the allocation). The mix was then placed in a proper size envelope and was sealed. These envelopes once formed were mixed thoroughly like a deck of cards and then numbered on the top sequentially. On randomizing a participant, the name of the participant and in patient number and date of enrollment was written on the envelope. This imprinted the details on the card and the envelope was opened to reveal the allocated group. This way investigator selection bias was avoided.

Administration of interventions

Women in Group A, Magnesium Sulphate with 1ml of 2% Lignocaine and in group B Magnesium Sulphate alone was given deep IM injection in upper outer quadrant of gluteal region.

Assessment of pain

Pain assessment was done using visual(faces) analogue scale (Warden V et al, 2011) in both the groups within 5minutes of 1st injection, at the end of 4 hours of giving 1st injection and 4hours of the last dose of injection or at the end of 24 hours of 1st injection whichever is later.



Statistical analysis:

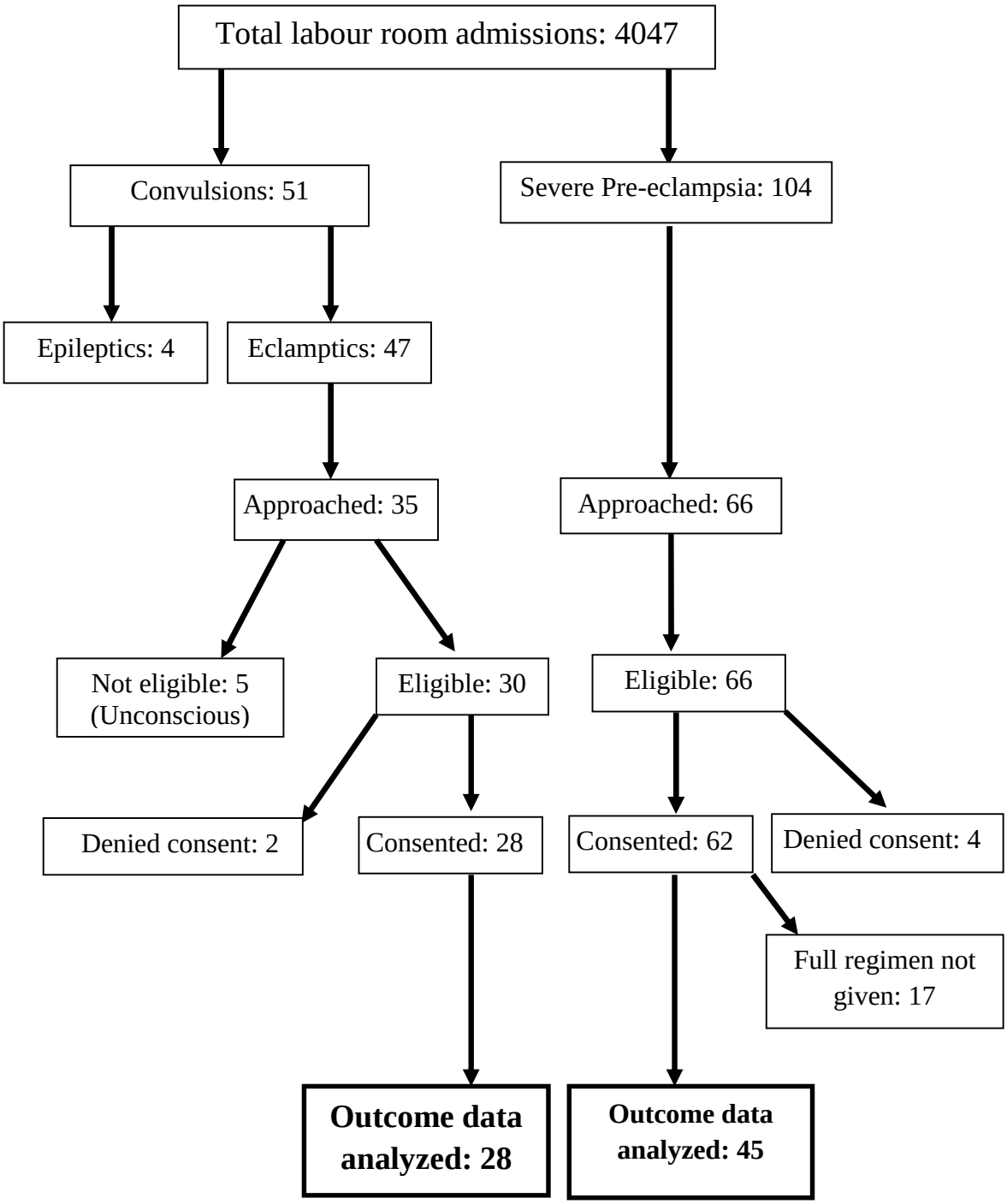
The data entered into data monitoring system and master chart (Annexure V) was prepared. The data was analysed as below:

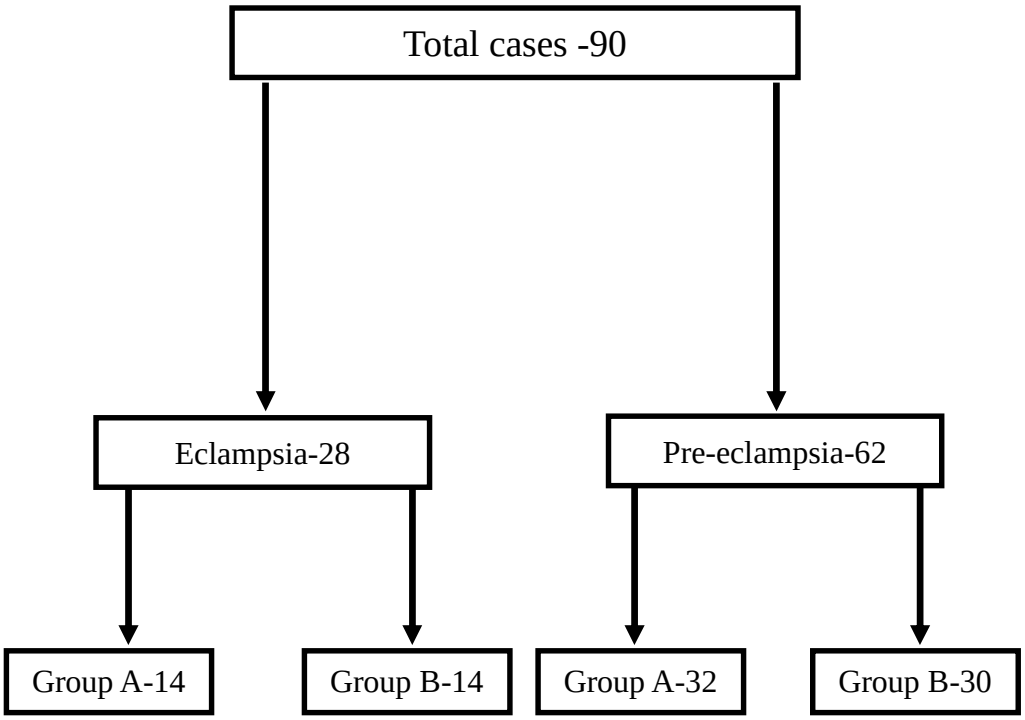
- Categorical outcome summarized by rate (percentage).
- Numerical outcome summarized by Mean and Standard Deviation.
- Main outcome of the study is the Mean pain score of 2 groups and that was compared by students unpaired‘t’ test.
- Significance level of statistical test kept at 0.05 level of probability.

RESULTS

This Randomised control trial was conducted in the labour room of Department of Obstetrics and Gynaecology at KLE University's teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum. Total labour room admissions were 4047 during my study period from September 2014 to April 2015. In this study, a total of 105 cases were screened, out of which 96 were eligible and 90 given consent for participating in the study. However, 73 women were enrolled in final outcome analysis as complete Pritchard's regimen was not given in 17 women.

Flow chart of study population





The data obtained was analysed and the final results and observations are tabulated as below.

Table 1. Demographic data

Variable	Sub-groups	Group A (n=46)		Group B (n=44)		'p' value
		No.	%	No.	%	
Education	Literate	42	91.30	41	93.18	0.525
	Illiterate	4	8.70	3	6.82	
	Total	**46**	**100.00**	**44**	**100.00**	
Socio	Green card	23	50.00	22	50.00	0.956
Economic	White Card	18	39.13	16	36.36	
Status	Yellow card	5	10.87	6	13.64	
	Total	**46**	**100.00**	**44**	**100.00**	
Age	Mean ± SD (Years)	23.00	3.29	23.11	2.32	0.850
Gravida	Mean ± SD	1.54	1.05	1.66	0.91	0.578
GA	Mean ± SD (Weeks)	34.72	5.31	35.07	4.73	0.741
BMI	Mean ± SD (Kg/m^2)	25.47	3.22	24.55	2.43	0.127

The demographic characteristics between both the groups are as shown in table 1.

They were well matched between the groups.

Table 2. Clinical presentation

Symptoms	Group A (n=46)		Group B (n=44)		'p' value
	No.	%	No.	%	
Gestational hypertension	26	56.52	16	36.36	0.061
Epigastric pain	7	15.22	5	11.36	0.759
Headache	33	71.74	33	75.00	0.813
Blurring of vision	11	23.91	15	34.09	0.355
Vomiting	19	41.30	30	68.18	0.012
Swelling of limbs	22	47.83	26	59.09	0.300
Convulsions	14	30.43	14	31.82	1.000

Most of the women presented with multiple symptoms like headache, blurring of vision, swelling of limbs, vomiting and hypertension. Convulsions were seen in 28 women (38%) of 90 women. There was no statistical significance between both the groups.

Table 3.Comparison of vitals

Characteristics	Group A (n=46)		Group B (n=44)		p value
	Mean	SD	Mean	SD	
Pulse rate (Per minute)	89.22	5.12	91.95	3.48	0.05
Systolic blood pressure (mm Hg)	151.74	10.31	149.95	8.60	0.374
Diastolic blood pressure (mm Hg)	98.35	6.68	98.18	8.20	0.917
Respiratory rate (Per minute)	18.20	0.88	17.82	0.95	0.054

Table 4. Pain score within five minutes of 1st injection

Parameters	Group A (n=46)	Group B (n=44)
Mean	5.26	5.23
Standard deviation	1.22	1.24
Median	6.00	6.00
Minimum	4.00	4.00
Maximum	8.00	8.00

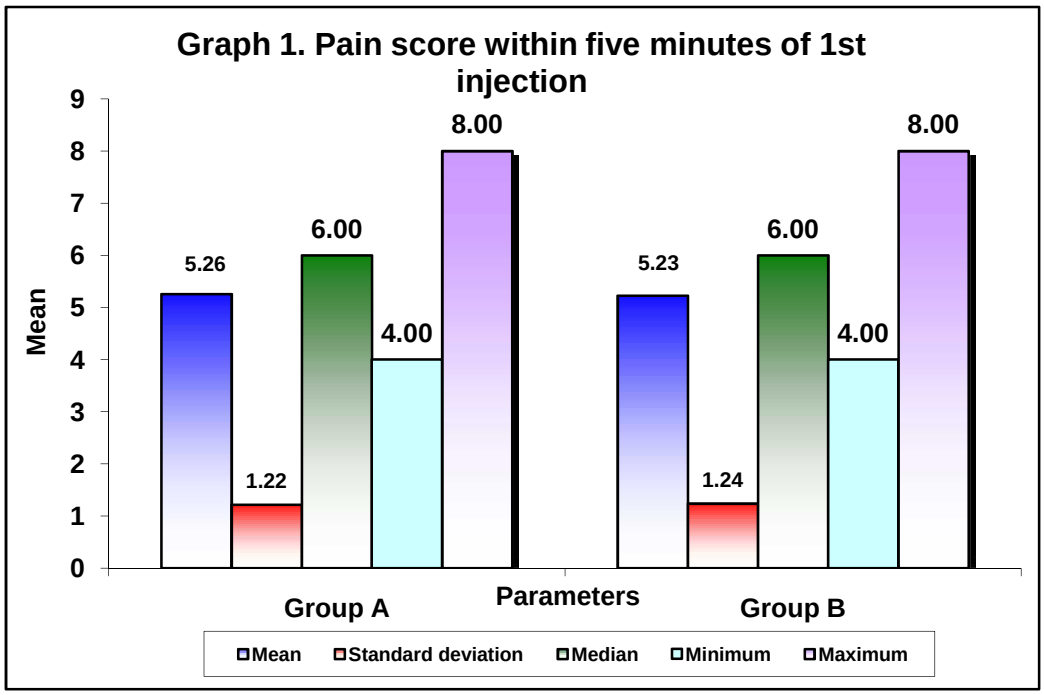


Table 5. Pain score after four hours of 1st injection

Parameters	Group A (n=40)	Group B (n=39)
Mean	2.13	2.55
Standard deviation	1.15	1.45
Median	2.00	2.00
Minimum	2.00	2.00
Maximum	4.00	6.00

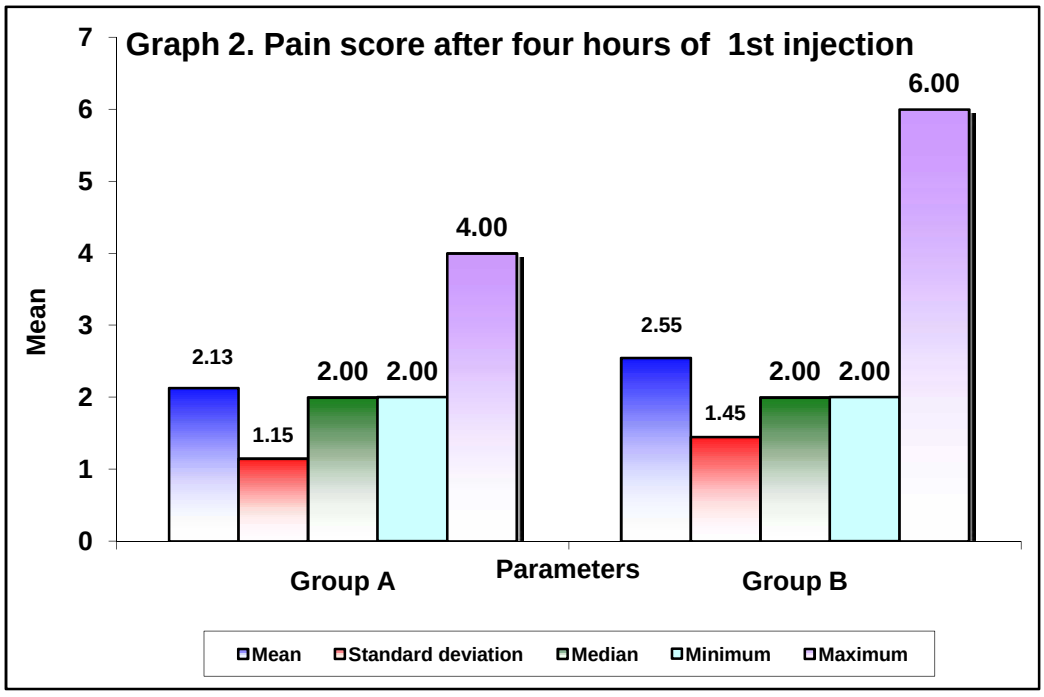


Table 6. Pain score after 4 hours of last dose of injection or at the end 24 hours whichever is later

Parameters	Group A (n=38)	Group B (n=35)
Mean	1.35	1.55
Standard deviation	1.20	1.13
Median	2.00	2.00
Minimum	0.00	0.00
Maximum	4.00	4.00

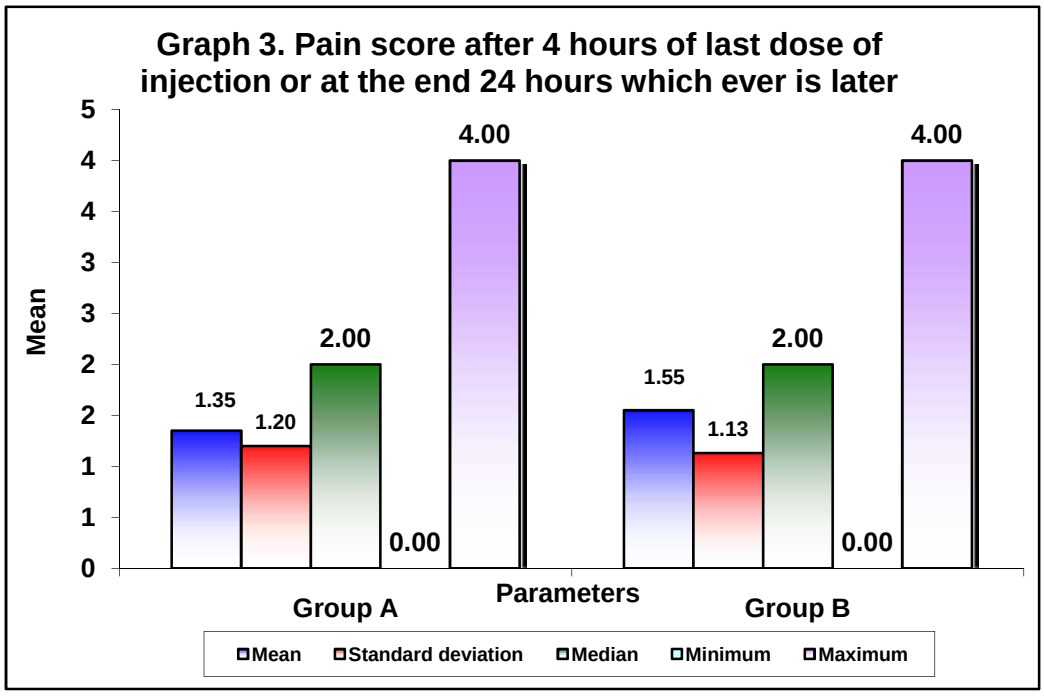
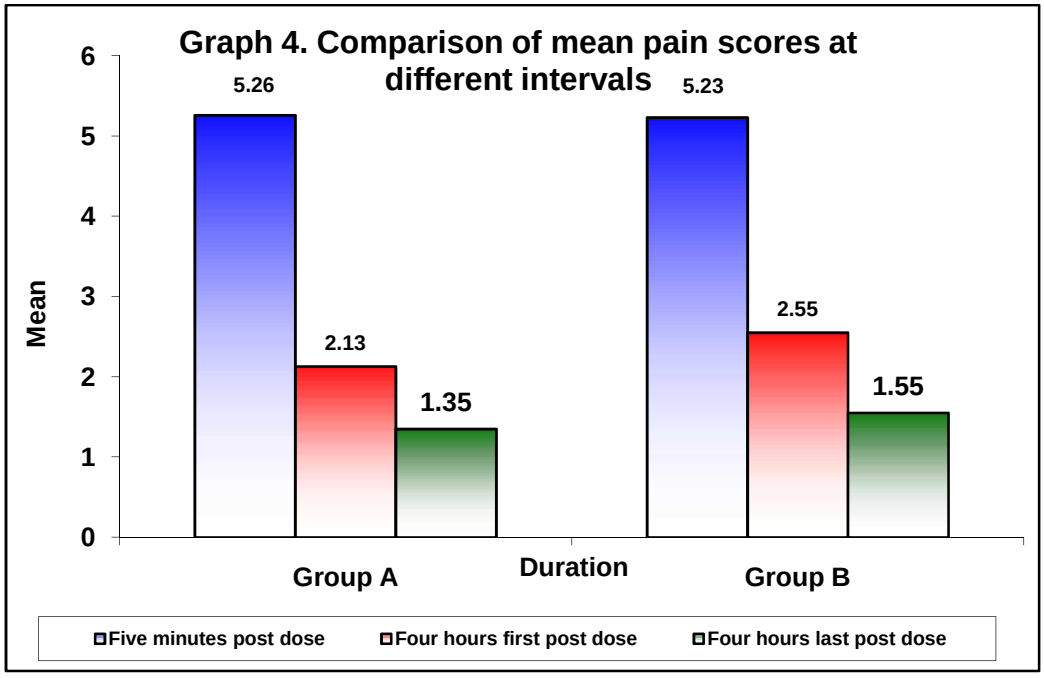


Table 7. Comparison of mean pain scores at different intervals

Duration	Group A		Group B		p value
	Mean	SD	Mean	SD	
Within five minutes of 1st injection	5.26	1.22	5.23	1.24	0.897
After four hours of 1st injection	2.13	1.15	2.55	1.45	0.138
After 4 hours of last dose of injection or at the end 24 hours whichever is later	1.35	1.20	1.55	1.13	0.423



The pain scores were evaluated using Visual(faces) analog scale within 5 minutes of 1st injection, 4hours after 1st injection and 4 hours after the last dose of injection or at the end of 24 hours later and compared between the groups (Table 4, 5 and 6). There was no statistical significance in mean pain scores between 2 groups within 5 minutes of 1st dose of injection(P value 0.897), 4hours after 1st injection(P value 0.138) and 4 hours after the last dose of injection or 24 hours later(P value 0.423) (Table 7). There was no difference between minimum 4,2,0 and maximum

8,4(Group A) and 6(Group B),4 mean pain scores between the groups at these intervals respectively. In Group A out of 39 women, 14 women (36.84%) and in Group B out of 35 women 14 women (40%) women had receive IM MgSO4 for more than 24 hours.

Table 8. Comparison of mean pain scores with eclampsia / pre eclampsia within Five minutes of 1st injection

Groups	Eclampsia		Preeclampsia		*p value
	Mean	SD	Mean	SD	
Group A (n=46)	4.71	0.99	5.50	1.24	0.030
Group B (n=44)	5.14	1.03	5.27	1.34	0.738
**p value	0.189		0.459		

*** Within group comparison**

**** Comparison between group A and group B**

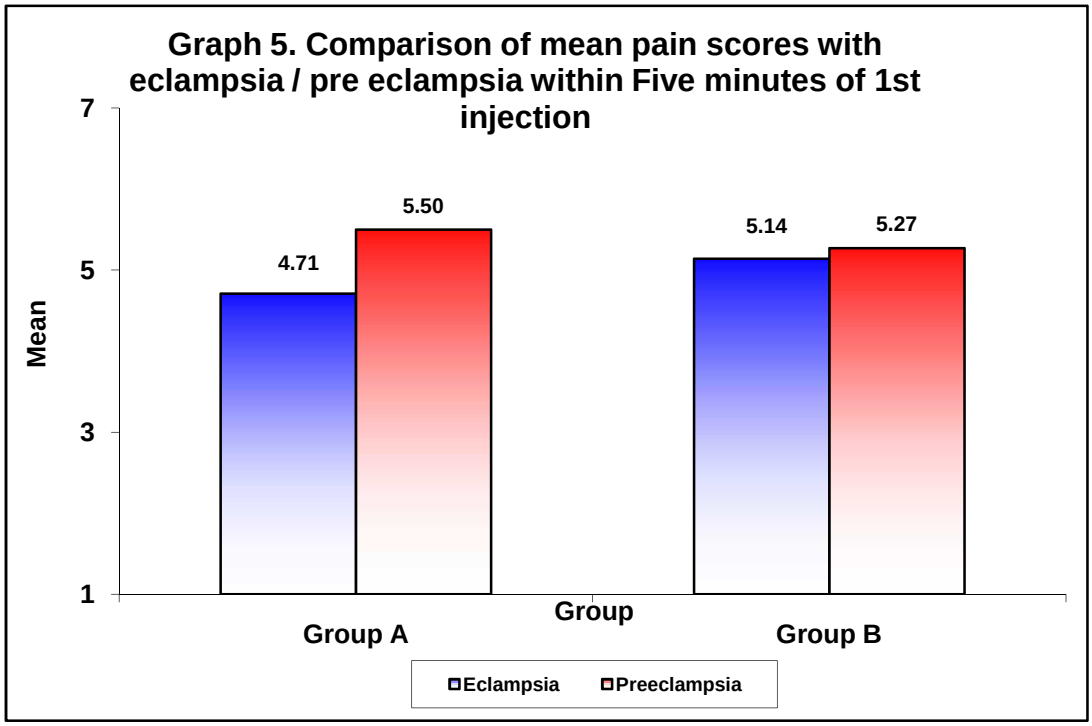


Table 8. Comparison of mean pain scores with eclampsia / pre eclampsia after Four hours of 1st injection

Groups	Eclampsia		Preeclampsia		*p value
	Mean	SD	Mean	SD	
Group A (n=40)	2.29	0.73	2.54	0.90	0.344
Group B (n=39)	3.00	1.04	2.80	1.29	0.601
**p value	0.055		0.417		

*** Within group comparison**

**** Comparison between group A and group B**

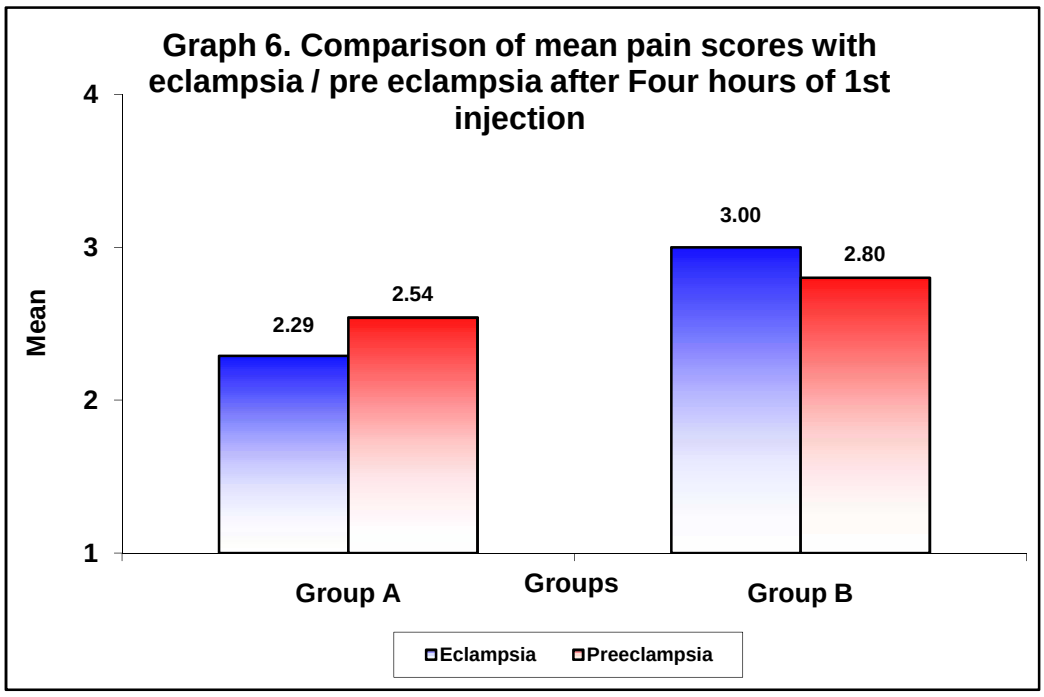
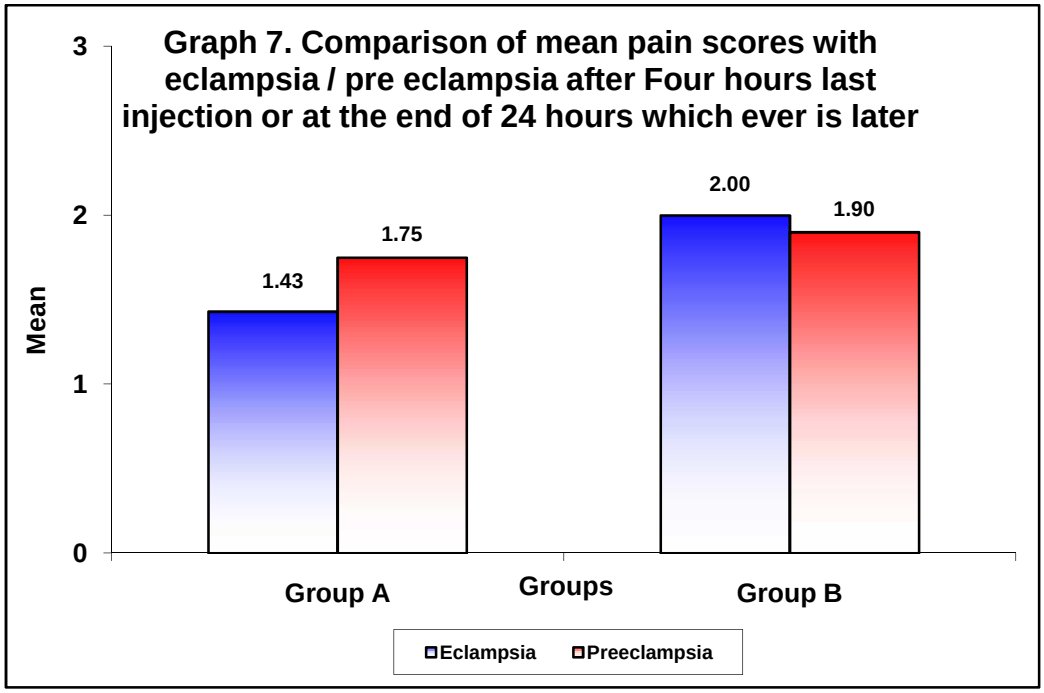


Table 9. Comparison of mean pain scores with eclampsia / pre eclampsia after Four hours last injection or at the end of 24 hours whichever is later

Groups	Eclampsia		Preeclampsia		*p value
	Mean	SD	Mean	SD	
Group A (n=38)	1.43	1.22	1.75	1.07	0.422
Group B (n=35)	2.00	0.78	1.90	1.00	0.754
**p value	0.104		0.540		

*** Within group comparison**

**** Comparison between group A and group B**



There was no statistical significant between mean pain scores between 2 groups in both severe pre-eclampsia and eclampsia within 5 minutes of 1st dose injection, 4hours after 1st injection and 4 hours after the last dose of injection or at the end 24 hours which ever is later (Table 8,9 and 10).

DISCUSSION

This Randomised control study was aimed to know whether the addition of Lignocaine reduces pain at intramuscular injection site with IM MgSO4 injections. Limited data is available on the reduction of pain with the usage of Lignocaine with IM injections of MgSO4.

As per the CONSORT flow diagram, 101women were approached to participate in the study of which 96 women were eligible, of them 90 women consented and were randomized into 2 groups by SNOSE method. 46 women received MgSO4 with 1ml of 2% Lignocaine and 44 women received MgSO4 alone. Total severe pre eclamptics and eclamptics were 62 and 28 respectively. Of these, 73 women completed planned course of Pritchard's regimen and 17 were given partial regimen but were included in analysis of the result(6 were assesed after 1st dose of injection and 11 were available for 2nd assessment). Both the groups were comparable with respect to demographic data, age, parity, gestational age, BMI and clinical/ Physical examination.

Pain score was assessed using visual (faces) pain analog scale within 5 minutes of 1st injection , at the end of 4 hours of giving 1st injection and 4hours of the last dose of injection or at the end of 24hours which ever is later, it was compared with intramuscular injection of Magnesium Sulphate alone.

There was no statistically significance and difference in mean pain scores between 2 groups within 5 min of 1st injection(P value 0.897), 4hours after 1st dose of injection(P value 0.138) and 4 hours after the last dose of injection or at the end of

24hours(P value 0.423). The minimum and maximum mean pain scores were also not satistically significant at different intervals between both the groups.

There was no statistical significance between mean pain scores of the 2 groups in both severe pre-eclampsia and eclampsia immediately after 1st dose injection, 4hours after the 1st dose of injection and 4 hours after the last dose of injection or at the end 24hours whichever is later.

It is evident from the present study that the addition of 1ml of 2% Lignocaine does not reduce pain in intramuscular injection of Magnesium sulphate at all intervals. Hence there is need to avoid the 1ml of Lignocaine which adds to extra volume without any benefit. However, the findings of this study need to be confirmed with a larger sample multicentric study.

The Strenghths of the present study are:

1. Randomization method by SNOSE eliminated the selection bias of the patient by the investigator
2. Multiple trained residents were involved in pain assessment.
3. Pain assessment was done by Visual (Faces) analog scale.

The limitations of the present study are:

1. Design of the study: Single blinded Randomised control Study.
2. Smaller sample size , but this sample size is actually more than those other studies which used the formula $n = \frac{2(Z\times+\square3)\square(S_1^2+S_2^2)}{(\square_1+\square_2)^2}$ by which the estimated sample size would be by considering pain scores at 2 and 4 minute are 2 and 4 in each group respectively[62].

CONCLUSION

It is evident from the present study that addition of 1 ml of 2% Lignocaine with 10 ml of Magnesium Sulphate (50%) does not reduce the pain at the intramuscular injection site. Hence there is need to avoid the 1ml of Lignocaine which adds to extra volume without any additional benefit.

The findings of the same study need to be confirmed by a larger multicentre trial.

SUMMARY

A Randomised control study(computer generated, randomized number sequence, block size of 2, blinding by SNOSE) was performed on 90 consenting women fulfilling eligibility criteria(all cases of severe pre eclampsia and conscious eclamptic women including antepartum, intrapartum and postpartum) at Department of Obstetrics and Gynaecology, KLE University's teaching hospital attached to Jawaharlal Nehru Medical College, Belgaum.

In this study, of the 101 women screened, 96 were eligible to participate in the trial of which 90 women consented and were enrolled. These 90 women were given either MgSO4 with 1 ml of 2% Lignocaine(46) or MgSO4 alone(44) by SNOSE technique. The final outcome was analysed in 73 women who completed planned course of Pritchard's regimen and 17 were given partial regimen but were included in analysis of the result(6 were assesed after 1st dose of injection and 11 were available for 2nd assessment).

Majority of the women (64.38%) were aged between 21 to 25 years. Most of the women (92.2%) were literate and engaged in agriculture related activities having green card (50%). Majority of the women were primigravida (64.38%) with term gestation (64%).Most of the women enrolled into the study were severe preeclamptics (68.88%). There was no significant difference between group A and group B with respect to age, literacy, socioeconomic status, gestational age and BMI. Most of the women presented with multiple symptoms like headache, blurring of vision, swelling of limbs, vomiting and gestational hypertension. Convulsions were seen in 31% of women.

There was no statistical significance in mean pain scores between 2 groups within 5 min of 1st dose of injection(P value 0.897), 4hours after 1st dose of injection(P value 0.138) and 4 hours after the last dose of injection or at the end of 24hours whichever is later(P value 0.423). There was no difference between minimum and maximum mean pain scores at different intervals between the groups.

There was no statistically significant difference between mean pain scores between 2 groups in both severe pre-eclampsia and eclampsia within 5 min of 1st dose of injection, 4hours after 1st dose injection and 4 hours after the last dose of injection or at the end of 24hours whichever is later.

From this study it is evident that, the addition of 1ml of 2% Lignocaine with 10 ml of Magnesium sulphate(50%) in intramuscular injections is not beneficial in reduction of pain at injection site. Hence there is need to avoid addition of 1ml of Lignocaine which adds to extra volume without any additional benefit.

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ANNEXURE-I

ETHICAL CLEARANCE LETTER

K.L.E.SOCIETY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELGAUM-590010 (KARNATAKA-INDIA)
(Affiliated to KLE University, Belgaum)

Website: http/www.jnmc.edu
E-Mail : domejnmc@sancharnet.in
: jnmc@sancharnet.in

Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 2470759

Ref: MDC/DOME/ | 7 **Date: 30/11/2013**

To,

PG student in M.S(OBG),
J.N.Medical College,
BELGAUM.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"Assessment of pain associated with intramuscular injection of management sulphate with or without lingocaine in women with severe preeclampsia and conscious eclamptic women – A randomized control trial "** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Hema Dhumale)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belgaum.

(Dr.Ganga Pilli)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belgaum.

ANNEXURE-II

INFORMED COSENT DOCUMENT

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mrs _____ we are requesting you to enroll yourself in study titled **"Assessment of pain associated with intramuscular injection of Magnesium Sulphate with or without Lignocaine in women with severe preeclampsia and conscious eclamptic women– A Randomized Control Trial"** conducted by Dr. _____, Post Graduate in M.S. Obstetrics And Gynaecology under the guidance of Dr._____ Professor , Department of Obstetrics And Gynaecology , J.N. Medical College, Belgaum under KLE university, Belgaum.

Respected Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

The purpose of research is to assess whether addition of Lignocaine with intramuscular injection of Magnesium Sulphate is beneficial or not.

Procedure Involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail and investigated accordingly. You will be allocated either into group A or and group B and

intramuscular injection of Magnesium Sulphate will be given accordingly.

Risks and Benefits:

The benefits of taking part in this research are that the intramuscular injection of Magnesium Sulphate when combined with 1ml of 2% Lignocaine would in actual reduce pain or not. There are no observable risks associated with the study.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E.S hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

In the event of injury related to the study, treatment will be made available through KLES Hospital & MRC, Belgaum. There is no compensation or payment for such medical treatment by law. If you are injured you may contact Dr. _____, at Department of Obstetrics And Gynaecology, KLES Hospital& MRC or by Ph. No: _____.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. _____, Department of Obstetrics And Gynaecology, KLES Hospital and MRC, Ph. No. 0831-2551292 or phone number: _____ or Dr._____, Professor, Dept. Of Obstetrics And Gynaecology, KLES Hospital and MRC, Belgaum Ph.: 0831-2551292 or phone number:_____

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Prof. & Head of Pathology as Chairman of J. N. Medical College Institutional Ethics Committee on Human Subjects Research, Phone No.0831 2473777 ext-1527 at J. N. Medical College, Belgaum or phone number: 9480275601.

Consent for participation in research trial

I, _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read form in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject :_____Date :

Witness Name : _____ Signature: _____ Date :

Investigators Name: _____Signature: _____Date :

Place : _____

INFORMED COSENT DOCUMENT - KANNADA

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳುವಿಕೆಗಾಗಿನ ಸಮ್ಮತಿಯ

ಶ್ರೀಮತಿ_____ನಾವು ಎಂಬ ಅಧ್ಯಯನದಲ್ಲಿ ನಮ್ಮನ್ನು ತೊಡಗಿಸಿಕೊಳ್ಳುವ ವಿನಂತಿಸುತ್ತಿದ್ದೇವೆ ಅಥವಾ ತೀವ್ರ ಪ್ರಿಕ್ಲಾಂಪ್ಸೀಯಾ ಮತ್ತು ಜಾಗೃತ ಪ್ರಸವಾನ್ಕಾರದ ಮಹಿಳೆಯರಲ್ಲಿ ಒಸಡು ಇಲ್ಲದೆ ಮೆಗ್ನೀಸಿಯಮ್ ಸಲ್ಫೇಟ್ ದೇಹಕ್ಕೆ ಇಂಜೆಕ್ಷನ್ ಮೂಲಕ ಸಂಬಂಧಿತ ನೊವು ಅಸೆಸ್ಮೆಂಟ್ women-ಒಂದು ಯಾದೃಚ್ಛಿಕ ನಿಯಂತ್ರಣ ಪ್ರಯೋಗ ಡಾ ಕೋಸ್ಸ ನಡೆಸಿದ ಎಂಎಸ್ ಪದವಿ Dr. ಪ್ರಸೂತಿ ಇಲಾಖೆ ಮತ್ತು ಗೈನಕಾಲಜಿ ಜವಾಹರಲಾಲ ವೈದ್ಯಕೀಯ ಕಾಲೇಜಿನ ಪ್ರಸೂತಿ ಮತ್ತು ಗೈನಕಾಲಜಿ KLE ವಿಶ್ವವಿದ್ಯಾಲಯ, ಬೆಳಗಾವಿ ಇದರ ಅಡಿಯಲ್ಲಿ ಆಗುತ್ತದೆ.

ಗೌರವಾನ್ವಿತ ಮೇಡಂ ನಾವು ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮ್ಮನ್ನು ತೊಡಗಿಸಿಕೊಳ್ಳುವುದು ನಮ್ಮ ಮನವಿ. ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮ ಪ್ರಸ್ತುತ ದೂರು ಬಗ್ಗೆ ಕೆಲವು ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲಾಗುತ್ತದೆ ಮತ್ತು ನಿಮ್ಮ ಜ್ಞಾನದಿಂದ ಅತ್ಯುತ್ತಮವಾಗಿ ಉತ್ತರಿಸಲು ಸೇರಬೇಕೆಂಯ, ಕೋರುತ್ತೇವೆ.

ಸಂಶೋಧನ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆ ವೈಯಕ್ತಿಕವಾಗಿದ್ದು, ಅಧ್ಯಯನದಲ್ಲಿ ಭಗವಹಿಸುವದು ಅಥವಾ ಇಲ್ಲವೋ ಎಂಬುದು ನಮ್ಮ ನಿರ್ಧಾರ ಜವಾಹರೆಕರರು ವೈದ್ಯಕೀಯ ಕಾಲೇಜು ಈ ಸಂಬಂಧ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ. ನೀವು ಭಗವಹಿಸಲು ನಿರ್ಧರಿಸಿದರೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹಿಂದಕ್ಕೆ ಸರಿಯಬಹುದು.

ಸಂಶೋಧನೆ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮೆಗ್ನೀಸಿಯಮ್ ಸಲ್ಫೇಟ್ ದೇಹಕ್ಕೆ ಇಂಜೆಕ್ಷನ್ ಮೂಲಕ ಜೊತೆ ಒಸಡು ಜೊತೆಗೆ ಅನುಕೂಲಕರ ಅದೆಯೋ, ಇಲ್ಲವೋ ಎಂಬ ಬಗ್ಗೆ ಮೌಲ್ಯಮಾಪನ ಮಾಡುವುದು.

ವಿಧಾನ ಒಳಗೊಂಡಂತೆ.

ನೀವು ನನ್ನ ಅಧ್ಯಯನದ ನಿಮ್ಮನ್ನು ಕೊಡಗಿಸಿಕೊಳ್ಳುವುದು ಒಮ್ಮತ್ತೀರಿ ವೇಳೆ, ನೀವು ನಂತರ ನೀವುಪ್ರಾಯೋಗಿಕವಾಗಿ ಏವರ ವಿಚಾರಣೆ ನಡೆಸಲಿದೆ ಮತ್ತು ತಕ್ಕಂತೆ ತನಿಖೆ. ನಿಮ್ಮ ವರ್ತಮಾನ, ಭೂತ ಮತ್ತು ಕುಟುಂಬದ ಇತಿಹಾಸದ ಬಗ್ಗೆ ಪಂದರ್ಶನ ನಡೆಯಲಿದೆ. ಗುಂಪು ಅಥವಾ ಅಥವಾ ಮತ್ತು ಗ್ರೂಪ್-ಬಿ ಮತ್ತು ಮೆಗ್ನೀಸಿಯಮ್ ಸಲ್ಫೇಟ್ ದೇಹಕ್ಕೆ ಇಂಜೆಕ್ಷನ್ ಮೂಲಕ ಒಳಗೆ ತಕ್ಕಂತೆ ನೀಡಲಾಗುವುದು ಎರಡೂ ನೀವು ಹಂಚಿಕೆಯಾಗುತ್ತವೆ.

ಅಪಾಯಗಳು ಮತ್ತು ಲಾಭಗಳು:

ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಭಗವಹಿಸಿದ ಪ್ರಯೋಜನಗಳನ್ನು 2% ಒಸಡು ಆಫ್ 1ml ಸಂಯೋಜಿಸಿ ಮೆಗ್ನೀಸಿಯಮ್ ಸಲ್ಫೇಟ್ ದೇಹಕ್ಕೆ ಇಂಜೆಕ್ಷನ್ ಮೂಲಕ ನಿಜವಾದ ನೋವು ಕಡಿಮೆ ಅಥವಾ ಎಂದು ಇವೆ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದ ಗಮನಿಸಬಹುದಾದ ಅಪಾಯಗಳಿವೆ.

ವಾಲಂಟರಿ ಭಾಗವಹಿಸುವಿಕೆ/ವಾಪಸಾತಿ.

ಅಧ್ಯಯನದಲ್ಲಿ ಭಗವಹಿಸುವದು ವೈಯಕ್ತಿಕವಾಗಿದ್ದು. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮನ್ನು ತೊಡಗಿಸಿಕೊಳ್ಳುವುದು ಹೌದು/ಇಲ್ಲ ಎಂಬ ಬಗ್ಗೆ ಸೇವೆ ಆಯ್ಕೆ ಮಾಡಬಹುದು. KLES ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ನಿಮಗೆ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೋಗ್ಯ ಸೇವೆಗಳ ಬದಲಾಗುವುದಿಲ್ಲ ನಿಮ್ಮ ನಿರ್ಧಾರ.

ಪರ್ಯಾಯಗಳು:

ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯನ್ನು ಇಳಿಕೆ. ನೀವು ನಿರ್ವಹಣೆಯ ದಿನನಿತ್ಯದ ಲೈನ್ ಪಡೆಯುತ್ತಾನೆ. ಗೌಪ್ಯತೆ ಮತ್ತು ರಹಸ್ಯವಾದ.

ಮಾತ್ರ ಜನರು ನೀವು ಸಂಶೋಧನಾ ತಂಡದ ಸದಸ್ಯರು ಸಂಶೋಧನಾ ವಿಷಯದ ಮಾಡಲಾಗುತ್ತದೆ ಎಂದು ತಿಳಿಯಲು. ನೀವು ಆಥವಾ ಸಂಶೋಧನೆಯ ಸಮಯದಲ್ಲಿ ನೀವು ನೀಡಿದ ಮಾಹಿತಿಯ ಬಗ್ಗೆ ಯಾವುದೇ ಮಾಹಿತಿ ಹೊರತುಪಡಿಸಿ ನಿಮ್ಮ ಲಿಖಿತ ಅನುಮತಿ ಇಲ್ಲದೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುತ್ತದೆ:

ತುರ್ತು 1. ನಿಮ್ಮ ಹಕ್ಕುಗಳು ಮಬಿವೃದ್ಧಿಗಾಗಿ ರಕ್ಷಿಸಲು.
2. ಕಾನೂನಿನ ಅಗತ್ಯ ವೇಳೆ.

ಅಧಿಕಾರ ಫಲಿತಾಂಶಗಳು ಪ್ರಕಟಿಸಿ ಗೆ:

ಸಂಶೋಧನೆಯ ಫಲಿತಾಂಶಗಳು ಪ್ರಕಟವಾದ ಅಥವಾ ಕುರಿತು ಚರ್ಚಿಸುವಾಗ, ಕಾನ್ಫರೆನ್ಸ್, ಯಾವುದೇ ಮಾಹಿತಿ ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಬಹುದು ಎಂದು ತೋರಿಸಲ್ಪಡುತ್ತದೆ. ನೀವು ಈ ಅಧ್ಯಯನದ ಸಂಬಂಧಿಸಿದಂತೆ ಪಡೆಯಲಾಗುತ್ತದೆ ಮತ್ತು ಗುರುತಿಸಬಹುದು ಯಾವುದೇ ಮಾಹಿತಿ ಗೌಪ್ಯವಾಗಿಡಲಾಗುವುದು.
ಭಾಹವಹಿಸುವಿಕೆ ಹಣಕಾಸು ಪ್ರೋತ್ಸಾಹ:

ಯಾವುದೇ ಹಣಕಾಸಿನ ಪ್ರೋತ್ಸಾಹ ನೋಂದಣಿಯಾದ ರೋಗಿಗಳಿಗೆ ನೀಡಲಾಯಿತು. ಅಷ್ಟಲ ಸಂಶೋಧನೆಯ ಯೋಚನೆ ಮಾಡಲಾಗಿದೆ ಮತ್ತು ಅಧ್ಯಯನದ ಏನೇ ಸಂಶೋಧಕ ಭರಿಸುತ್ತವೆ.

ಪರಿಹಾರ:

ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ಗಾಯಗಳಾದ, ಚಿಕಿತ್ಸೆ KLES ಆಸ್ಪತ್ರೆ ಮತ್ತು ಅಂಆರ್ಸಿ, ಬೆಳಗಾವಿ ಮೂಲಕ ಕೊಡಲಾಗುವುದು. ಕಾನೂನು ವ್ಯಾಪ್ತಿಯಲ್ಲಿ ವೈದ್ಯಕೀಯ ಚಿಕಿತ್ಸೆಗಾಗಿ ಯಾವುದೇ ಪರಿಹಾರ ಅಥವಾ ಪಾವತಿ ಇಲ್ಲ. ನೀವು ಗಾಯವಾಗಿದ್ದರೆ. ನೀವು ಪ್ರಸೂತಿ ಮತ್ತು ಗೈನಕಾಲಜಿ, KLES ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಂಆರ್ಸಿ ಇಲಾಖೆ ಆಥವಾ ದೂರವಾಣಿ ಮೂಲಕ ಡಾ ಸಂಪರ್ಕಿಸಬಹುದು ದಾಖಲಿಸಿಕೊಂಡು.

ಪ್ರಶ್ನೆಗಳು:

ಸಂದರ್ಭದಲ್ಲಿ ನೀವು ಭವಿಷ್ಯದಲ್ಲಿ ಅಥವಾ ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದ ಗಾಯದ ಅಥವಾ ಅನಾರೋಗ್ಯದ ಸಂದರ್ಭದಲ್ಲಿ ಅಧ್ಯಯನ ಸಂಬಂಧಿಸಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳನ್ನು ಹೊಮದಿದ್ದರೆ. ನೀವು ಸಂಪರ್ಕಿಸಬಹುದು ಡಾ ಪ್ರಸೂತಿ ಮತ್ತು ಗೈನಕಾಲಜಿ. ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಂಆರ್ಸಿದೂರವಾಣಿ ಇಲಾಖೆ ನಂ. 0831–2551292 ಅಥವಾ ಫೋನ್ ಸಂಖ್ಯೆ: ಅಥವಾ Dr ಪ್ರೊಫೆಸರ್, ಪ್ರಸೂತಿ ವಿಭಾಗ ಮತ್ತು ಗೈನಕಾಲಜಿ, KLES ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಂಆರ್ಸಿ ಬೆಳಗಾವಿ ದೂರವಾಣಿ.: 0831–2551292 ಅಥವಾ ದೂರವಾಣಿ ಸಂಖ್ಯೆ:

ನೀವು ಅಧ್ಯಯನ ವಿಷಯದ ನಿಮ್ಮ ಹಕ್ಕುಗಳ ಬಗ್ಗೆ ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳನ್ನು ಹೊಂದಿದ್ದರೆ. ನೀವು ಮಾನವ ವಿಷಯಗಳ ಮೇಲೆ ಜೆ.ಎನ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜು ನೈತಿಕ ಸಮಿತಿಯ ಅಧ್ಯಕ್ಷರಾಗಿ ಡಾ ಗಂಗಾ Pilli, ಪ್ರೋ ಪೆಥಾಲಜಿ ಮುಖ್ಯಸ್ಥರೆ ಮಾಡಬಹುದು ರಸರ್ಚ್, ಫೋನ್ ಕೊ. 0831 2473777 EXT-1527 ನಲ್ಲಿ ಜೆ. ಎನ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜು, ಬೆಳಗಾಅಥವಾ ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 9480275601.

ಸಂಶೋಧನೆ ಪ್ರಯೋಗ ಭಾಗವಹಿಸಲು ಸಮ್ಮತಿ

ನಾನು_____ ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಅಧ್ಯಯನದ ವಿಷಯವಾಗಿ ಭಾಗವಹಿಸುವಿಕೆ ಒಪ್ಪುತ್ತೇನೆ. ನನ್ನ ಹಕ್ಕುಗಳನ್ನು ಬಿಡಲಾಗುತ್ತಿದೆ ಇಲ್ಲ ಈ ಒಪ್ಪಿಗೆ ಪತ್ರಕ್ಕೆ ಸಹಿ ಮಾಡುವ ಮೂಲಕ, ಅಧ್ಯಯನ ಯಾವುದೇ ಹಂದಕ್ಕೆ ಮಾಡಬಹುದು. ನಾನು ಓದಿದ ಅಥವಾ ಅಪಾಯಗಳು ಮತ್ತು ಲಾಭಗಳು ಸೇರಿದಂತೆ ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿದ ನಂತರ, ದೇಶೀಯ ಭಾಷೆಯಲ್ಲಿ ರೂಪ ಓದಲು ಮಾಡಲಾಗಿದೆ ನಂತರ ಒಪ್ಪಿಗೆ ಪತ್ರಕ್ಕೆ ಸಹಿ ನಾನು.

ವಿಷಯ ಹೆಸರು:_____

ಸಹಿ ಅಥವಾ ವಿಷಯ ಎಡ ಹೆಬ್ಬೆರಳು ಮುದ್ರಣ:_____ ದಿನಾಂಕ:

ವಿಟ್ನೆಸ್ ಹೆಸರು:_____ ಸಹಿ: ದಿನಾಂಕ:

ಇನ್ವೆಸ್ಟಿಗೇಟರ್ಸ್ ಹೆಸರು: _____ಸಹಿ: _____ ದಿನಾಂಕ:

ಸ್ಥಳ:_____

INFORMED COSENT DOCUMENT – MARATHI

संशोधन अभ्यास क्रमात भाग घेणार असणारे सम्मती पत्रक

श्रीमती

.....आम्ही

आपल्याला विनंती करत आहे की, आपण ह्या अभ्यास क्रमात सहभागी व्हावे ज्याचे नांव आहे मॅग्नेशियम सल्फेट चे इंजेक्शन घेत असताना वेदना रहित बइंजेक्शन स्नायूमध्ये घेणे, की ज्याने करुन गर्भशयामध्ये असलेला रक्तदाब व त्यानंतर त्याचा झटका परिणाम कमी करण्याकरीता घेणारे औषध व त्याचा अंदाज परिणाम हा प्रकल्प डॉ. हीने उच्चशिक्षण विद्यार्थी एम- एस. हे स्त्रीरोग प्रसुति शास्त्रामध्ये - डॉ. स्त्री प्रशुती शास्त्र तज्ञ - ह्यांच्या मार्गदर्शनाखाली - उच्चशिक्षक असलेले (प्राध्यापक) जवाहरलाल तज्ञ - नेहरु वैद्यकिय महाविद्यालय बेळगांव - के. एल. ई विद्यापिठ .

महोदय श्रीमती आम्ही तुम्हाला विनंती करतो की, आमच्या अभ्यास क्रमात सहभागी होण्याकरिता कांही कांही प्रश्नांची उत्तर द्यावी लागतील जसे कीं, ह्या मध्ये भाग घेताना सध्या तुमच्या समस्या किंवा तुम्हाला कोणत्या प्रकारचा त्रास आहे त्याला तुम्ही योग्य उत्तर सहकार्य कराल ह्याची अपेक्षा आहे.

तुमचा सहभाग स्वखुशिने असेल. जरी तुम्ही सहभागी नसलात तरीही तुम्हाला इकडे जवाहरलाल नेहरु विद्यालयात कोणताही त्रास होणार नाही. पाहीजे तर सहभागी होऊ शकता किंवा कैव्हापण नांव नोंदवू शकता.

संशोधनाचा हेतु ऐवढाच आहे कीं, मॅग्नेशियम सल्फेट इंजेक्शनचा त्रास कमी होण्यासाठी त्या बरोबर लिब्नोकेन नांवाचे बधीर औषध वापरावे का नाही.

वापरणेची पध्दत : जर का तुंम्ही ह्या अभ्यासात यायला तयार असाल तर - वर्तमान काळातील - पूर्वीची व आत्ताची - पूर्ण कुटुंब इतिहास सांगावा लागेल तेसच पूर्ण आरोग्य तपासणी केली जाईल. व त्या प्रमाणे तुम्हांला विभाग अ किंवा ब मध्ये नोंद केले जाईल. व त्या प्रमाणे मॅग्नेशियम इंजेक्शन देण्यात येईल.

धोका व फायदा :

ह्याचा फायदा म्हणजे हे मॅग्नेशियम सल्फेट इंजेक्शन घेताना - लिग्नोकेन बरोबर घेतल्याने होण्याच्या वेदना कमी होणार का नाही ? अभ्यासात निरिक्षण करण्याचे धोका ह्यात काहीच नाही.

स्वइच्छेने सहभाग व सहभाग काढून घेणे :

अभ्यासात भाग घेणे हे स्वखुशिने केंव्हापण तुम्हाला भाग नको आहे अस सांगू शकता. आरोग्य तपासणीसाठी तुमचा सहभाग असुदे अगर नसुदे कांहीही परक पडणार नाही. के. एल. ई हॉस्पीटलमध्ये सर्व सुविधा मिळणारच.

पर्याय :

जरी तुम्ही नांव काढलात तरीही तुमच्या देखभालिमध्ये कांहीपण परिणाम होणार नाही.

गुप्तता व खाजगीपण राखले जाईल :

तुम्ही फक्त संशोधनात सहभागी आहे. येवढीच तुमची ओळख असेल त्या मध्ये दिलेली माहीती तुम्ही ती कोणालाही समजणार नाही कळणार नाही. तुमचे लेखी व्यक्तीमत्व केलेले जाईल. कारण १) कोणत्याही वेळी सुध्यता म्हणून लेखी परवानगी २ कायद्याने केंव्हा पण पाहिजे असल्यास परवानगी.

पत्रक प्रसिध्दी प्रयोगाचा परिणाम :

ह्या प्रयोगाचा निकाल किंवा परिणाम बाहेर येईल व प्रसिध्द होईल मोठ मोठ्या सभेमध्ये तुमच्या नावाचा कुठेही उल्लेख होणार नाही. व काहीपण माहीती देताना कुणाचाही उल्लेख न होता अगदी पूर्णपणे गुप्तता पाळण्यात येईल.

ह्या प्रयोगामध्ये आर्थीक सहाय्य :

रोगी किंवा सहभागीना आर्थीक लाभ कांहीपण मिळणार नाही- पूर्ण खर्च संशोधन केंन्द्रच करेल व मुख्य निर्देशकच त्याचा खर्चाचा भार उचलतील.

ह्या प्रयोगामध्ये आर्थीक सहाय्य :

रोगी किंवा सहभागीना आर्थीक लाभ काहींपण मिळणार नाही- पूर्ण खर्च संशोधन केन्द्रच करेल व मुख्य निर्देशकच त्याचा खर्चाचा भार उचलतील.

मोबदला : कांही अपघात झाला - अभ्यास क्रमात असताना तर त्यावर चिकित्सा पूर्णपणे के. एल. ई. संस्थेच्या दवाखान्यातच होईल. कायदा प्रमाणे चिकित्सा करण्यासाठी वेगळा पैसा उपलब्ध नाही- पण चिकित्सा मोफत मिळेल . डॉ.

- स्त्री प्रसुती विभाग . के. एल. ई दवाखाना व संशोधन केंन्द्र - फोन नंबर

प्रश्न :

अभ्यासाबद्दल पर का तुम्हाला कांही प्रश्न पडले असतील तसेच पुढे कांही आजार झाल्यास , जखम किंवा अपघात झाल्यास तुम्ही डॉ. स्वाती त्यांच्याबरोबर संपर्क करु शकता., डॉ. शास्त्र व प्रसुती विभाग, के. ऐल . ई. हॉस्पीटल व संशोधन केंन्द्र फोन नंबर 0831-2551292 किंवा मोबाईल -

किंवा डॉ. प्राध्यापक - स्त्रीरोग व प्रसुती विभाग के. ऐल. ई. हॉस्पीटल व संशोधन केंन्द्र - 0831 -2551292. व मो.

ANNEXURE - III

SCREENING FORM

"Assessment of pain associated with intramuscular injection of Magnesium Sulphate with or without Lignocaine in women with severe preeclampsia and conscious eclamptic women– A Randomized Control Trial"

I.SCREENING:

Id.No:

IP No:

Date:

Unit:

Patient's Name: _____

Age:

Address: H. No._____ Street _____ Place _____

Taluka _____ District_____

Tel No: _____

Mobile: _____

1) Is she eligible? [ ]

a) Yes b) No

If no why (specify) _____

2) Whether patients is willing to participate and give consent [ ]

a) Yes b) No

3) Is she enrolled ? [ ]

a) Yes b) No

ANNEXURE - IV

DATA COLLECTION INSTRUMENT

"Assessment of pain associated with intramuscular injection of Magnesium Sulphate with or without Lignocaine in women with severe preeclampsia and conscious eclamptic women– A Randomized Control Trial"

Screening ID. No :

☐ Group A

☐ Group B

I. Screening questions:

1) Is she known case of hypertensive ☐
   a) Yes b) No
2) If yes since how long
3) Does she has epigastric pain ☐
   a) Yes b) No
4) Does she has head ache ☐
   a) Yes b) No
5) Does she has blurring of vision ☐
   a) Yes b) No
6) Does she has vomiting ☐
   a) Yes b) No
7) Does she has pedal oedema ☐
   a) Yes b) No
8) Does she throw a convulsions ☐
   a) Yes b) No

9) If yes no of convulsions

10) 1st occurence of convulsion

Antepartum ☐

Intrapartum ☐

Postpartum ☐

II. Data Demographic:

1) Education: [ ]

a) Illiterate

b) Read

c) Write

d) Primary

e) Secondary

f) Graduate

g) Post graduate

2) What type of socio-economic card she has? [ ]

a) White

b) Green

c) Yellow

d) Red

e) Pan(income tax)

III. Menstrual History:

LMP- ☐☐ ☐☐ ☐☐☐☐ POG- ☐☐ Weeks ☐☐ Days

EDD- ☐☐ ☐☐ ☐☐☐☐

USG EDD- ☐☐ ☐☐ ☐☐☐☐

IV. Obstetric History:

Gravida ☐

Para ☐

Living ☐

Abortion ☐

Dead ☐

Still Birth ☐

V. Examination:

BMI (kg/m2): Pallor/ Icterus / Oedema

PR:

BP:

RR:

Respiratory System:

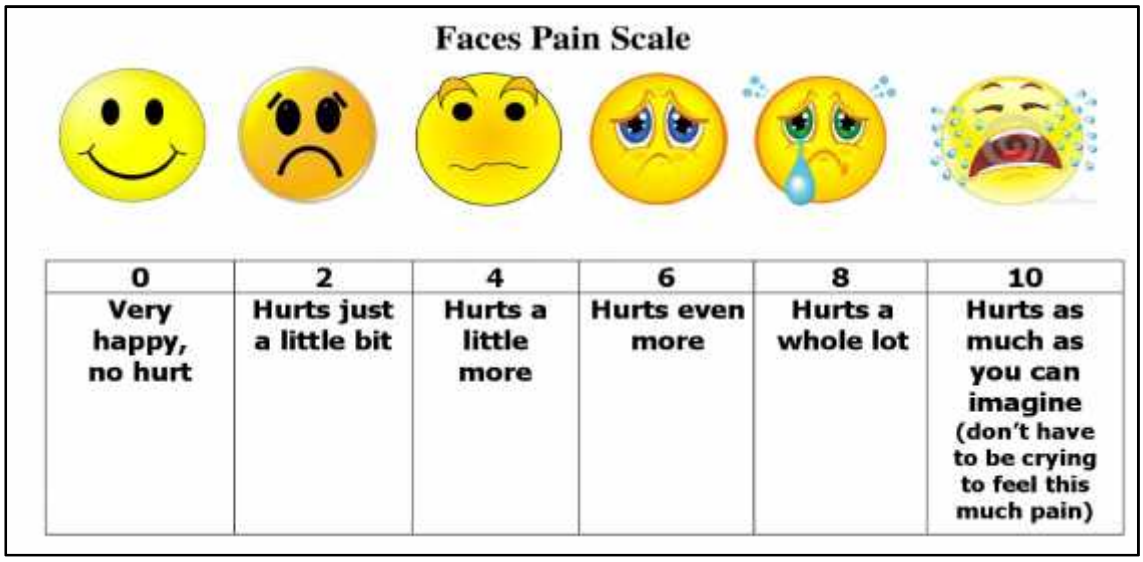
Per Abdomen:

$MgSO_4$ Regimen:

Pritchard ☐

Low Dose ☐

Faces Pain Scale



OBSERVATIONS:

PAIN ASSESSMENT		
Within five minutes of 1st injection	After four hours of 1st injection	After 4 hours of last dose of injection or at the end 24 hours whichever is later

ANNEXURE – V - KEY TO MASTER CHART

Group A – Magnesium sulphate with 1ml of 2% lignocaine.

Group B – Magnesium alone

Symptoms

Y- Yes

N- No

Convulsion

A- Antepartum

I- Intrapartum

P- Postpartum

Education

I- Illiterate

R- Read

W- Write

P- Primary

S- Secondary

G- Graduate

PG- Postgraduation

Socioeconomic Status

G- Green card

Y- Yellow card

W- White card

BMI- Body Mass Index

BP- Blood Pressure

mm Hg- Millimeter of mercury