Magnesium sulphate is it necessary to prevent eclampsia?

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ABSTRACT

Background: Preeclampsia was reported to account for 15% of all antenatal hospitalization for pregnancy complications. It causes maternal as well as fetal death by developing eclampsia. Since the turn of the century, obstetrician have to decrease the incidence of eclampsia. Hypertension complicated with seizures in pregnant women by treating them magnesium sulfate in eclampsia. In our study we tried to find out Magnesium sulphate really helpful in prevention of eclampsia or not.

Methods: This prospective study was carried out by the department of Pharmacology with the help from department of obstetrics and gynecology, in rural hospital and medical college i.e Mahatma Gandhi Institute of Medical sciences Sewagram, Wardha, Maharashtra, India during January 2007 to January 2008. A total of 100 subjects registered in inpatient department were included in this study. Patients were divided in to two group one group receiving nifedipine (calcium channel blockers) and other group receive combination of nifedipine and magnesium sulfate. We compared the delivery outcome of both the group.

Results: Patients receiving nifedipine had good pregnancy outcome with less side effects than the patients receiving combination of nifedipine and magnesium sulphate.

Conclusions: Magnesium sulphate is not necessary drug for prophylaxis of eclampsia.

Keywords: Preeclampsia, Eclampsia, Nifedipine, Magnesium sulphate.

INTRODUCTION

Hypertensive disorder during pregnancy, (pregnancy induced hypertension/preeclampsia/eclampsia) is the most common mysterious and difficult to manage, predispose to potentially lethal complications such as abruptio placentae, acute renal failure, cerebral haemorrhage, disseminated intravascular coagulation, circulatory collapse and so on. The reported incidence of hypertension, including preeclampsia, eclampsia and superimposed preeclampsia and eclampsia in all pregnant women varies from approximately 3% to 10%.1,4 Hypertension was reported to account for 15% of all antenatal hospitalization for pregnancy complications.1,5 Preeclampsia is believed to be the third leading cause of maternal mortality and major cause of intrauterine growth retardation and perinatal morbidity and mortality. Eclampsia accounts for up to 13% maternal mortality and 10-28% perinatal mortality.6 Numerous efforts at prevention, early diagnosis and treatment are being made as hypertensive disorder are major cause of adverse maternal and foeto-neonatal outcome and prevention would have significant impact on pregnancy outcome worldwide.7

Pregnancy induced hypertension

Preeclampsia and eclampsia are multi system disorder of unknown cause unique to pregnancy. Mild PH/preeclampsia is typically asymptomatic but headache, visual disturbances, anxiety and epigastric pain are likely in severe cases. It is thought that in third
trimester, that the symptoms and signs of preeclampsia become apparent however, the underline pathophysiology occurs, by early second trimester, may be between 8-18 weeks. While established preeclampsia is easy to recognized; its onset may often be insidious which can make diagnosis in early stages difficult. Early detection is important as PIH/preeclampsia can progress quickly while antenatal care is intermittent. It is imperative that necessity of intervention is known early/easily.

There are different drugs available to treat preeclampsia, acting by different mechanism.

The compelling indication of antihypertensive drug use is

- Persistent rise of blood pressure especially where diastolic blood pressure is over 110 mmHg the use is urgent if associated with proteinuria.
- In severe preeclampsia, to bring down the blood pressure during the continued pregnancy and during the period of induction of labour.

The common oral drugs used are

- Methyl dopa (dose 250-500 mg tid or qid) it acts by central and peripheral anti-adrenergic action.
- Labetalol (dose 250 mg tid or qid) it acts by antagonizing adrenoceptor (α and β blockers)
- Nifedipine (dose 10-20 mg bid) calcium channel blockers.
- Hydralazine (Dose 10-25 mg bid) vascular smooth muscle relaxant.

If the patient is in hypertensive crisis then the intravenous infusion of drug till the diastolic pressure become < 110 mm Hg.

The common intravenous drugs used in hypertensive crisis are

- Labetalol (200 mg in 200 ml normal saline) at the rate of 20 mg/hour to be doubled every 30 minutes.
- Hydralazine 5 mg I.V. bolus to be followed by infusion 25 mg in 200 ml of normal saline, the rate being 2.5 mg/hour to be doubled every 30 minutes.
- Nitroglycerin 5 µg/ min I.V. or sodium nitroprusside 0.25-5 µg/kg/ min I.V

Once the pressure is under control, oral therapy is continued. Since the turn of the century, obstetrician have to decrease the incidence of seizures in pregnant women who develop preeclampsia or eclampsia by treating them magnesium sulfate. Loading dose of magnesium sulfate is 4 gm I.V over 3-5 min followed by 10 gm deep I.M (5 gm in each buttock) followed by maintenance of 5 gm I.M hourly in alternate buttock. However the efficiency of magnesium sulfate in preventing convulsions remains controversial. After considering above factor we decided to conduct above study.

METHODS

This prospective study entitled “magnesium sulphate is it necessary to prevent eclampsia?” was carried out by the department of Pharmacology with the help from department of obstetrics and gynecology, in rural hospital Mahatma Gandhi Institute of Medical science, Sewagram Wardha, Maharashtra, India during January 2007 to January 2008. This study was started after getting ethical clearance from local institutional ethical committee.

Subjects

A total of 100 subjects registered in inpatient department were included in this study. The detailed history of subject obtained after admission and general obstetrical examinations were carried out. Blood pressure in mm Hg was recorded using sphygmomanometer. The pregnant women are selected according to the inclusion criteria. Patients receiving nifedipine OR combination nifedipine and magnesium sulfate were interviewed once after admission and then after starting drug treatment for five days. After taking informed consent in local language, the study was started.

The interview is based on specially designed questionnaire. The interview was providing the information regarding drug utilization. The management and investigation chart was maintained to identify the complete coverage of study sample.

Inclusion criteria

- All pregnant women more than 20 weeks of gestation having blood pressure more than 140/90 mm Hg with proteinuria
- With or without swelling on body.

Exclusion criteria

- Patient is previously hypertensive
- Patient having Gestational hypertension i.e. the hypertension occurs before 20 weeks and without proteinuria
- Hypertensive and proteinuric patients complicated with convulsive disorder i.e. Eclampsia of pregnancy.

Drugs and doses

- Capsule nifedipine 10 mg thrice daily sublingually and SOS.
- Injection magnesium sulfate loading dose of magnesium sulfate is 4 gm I.V over 3-5 minutes followed by 10 gm deep I.M (5 gm in each buttock) followed by maintenance of 5 gm I.M hourly in alternate buttock.
All preeclampsia investigations: proteinuria, platelet count, liver function test, kidney function test, ultrasonography, along with routine investigation like: hemogram, blood grouping and typing, blood sugar, urine routine examination were carried out before admission of the patients.

Statistical analysis

Study result of above study was statistically analysed by using SPSS with the help of percentage, chi-square test.

RESULTS

Out of 100 subjects included in this study. As the preeclampsia is common in advance maternal age, but in our study group of 21-25 years (52%) (Table 1). Common in the primigravida (67%) in (Table 2), 88% and 91% of the patients do not have the past history and family history of preeclampsia (Table 3, 4).

While it is more common in the 36-40 weeks of gestational age (Table 5). Out of 50 patients receiving nifedipine 15 subjects (30%) were suffered from palpitation, followed by 10 patients (20%) were suffered from headache, 8 patients (16%) were suffered from vomiting, 7 (14%) patients suffered from constipation, 5 (10%) patients were suffered from nausea, generalized muscle weakness, breathing difficulty, while 1 (2%) suffered from lethargy, but no one was suffered from flushing, ankle edema, hypotension, pulmonary edema, respiratory arrest and drowsiness (Table 6).

While another 50 patients receiving combination therapy of nifedipine and intramuscular injection of magnesium sulfate (nifedipine+injection magnesium sulphate) 28 (56%) subjects were suffered from palpitation, 26 (52%) subjects were suffered from generalized muscle weakness and breathing difficulty, 18 (36%) of subjects were suffered from headache, 13 (26%) of subjects were suffered from nausea and vomiting, 8 (16%) of subjects were suffered from constipation, 2 (4%) of subjects were suffered from drowsiness and 1 (2%) was suffering from ankle edema while none of them suffered from flushing, hypotension, pulmonary edema, respiratory arrest (Table 6).

Nifedipine group here the outcome of pregnancy in terms of baby delivery was 31 (62%) subjects had vaginal delivery while 19 (38%) subjects had caesarean section in nifedipine alone group. While the group receiving combination of (nifedipine+injection magnesium sulfate) here the outcome of pregnancy in term of baby delivery was, 15 (30%) of subjects delivered by vaginal delivery while 35 (70%) of subjects had caesarean section.

This data is evaluated by the chi-square test considering degree of freedom was 1 and value of $X^2$ was 10.3, here the p value is <0.005. So this result is statistically significant (Table 7). In the group of $Ca^{++}$ channel blocker i.e. nifedipine. 19 subjects had caesarean section out of 50 subjects. In 10 (52.63%) subjects because of foetal distress, 3 (15.79%) subjects because of previous scar and inadequate pelvis, 1 (5.26%) because of transverse lie along with deteriorating maternal condition and twin with ABO Rh- negative blood group.

### Table 1: Distribution according to age.

| Age in years | No. of subjects | Percentage |
|--------------|-----------------|------------|
| 18-20        | 13              | 13%        |
| 21-25        | 52              | 52%        |
| 26-30        | 25              | 25%        |
| 31-35        | 10              | 10%        |
| Total        | 100             | 100%       |

### Table 2: Distribution according to gravida.

| Gravida       | No. of subjects | Percentage |
|---------------|-----------------|------------|
| Primi-gravida | 67              | 67%        |
| Multi-gravida | 23              | 23%        |
| Total         | 100             | 100%       |

### Table 3: Distribution according to past history.

| Past history | No. of subjects | Percentage |
|--------------|-----------------|------------|
| Present      | 12              | 12%        |
| Absent       | 88              | 88%        |
| Total        | 100             | 100%       |

### Table 4: Distribution according to family history.

| Family history | No. of subjects | Percentage |
|---------------|-----------------|------------|
| Present       | 9               | 9%         |
| Absent        | 91              | 91%        |
| Total         | 100             | 100%       |

### Table 5: Distribution according to gestational period.

| Gestational period (weeks) | No. of subjects | Percentage |
|----------------------------|-----------------|------------|
| 20                         | 0               | 0%         |
| 21-25                      | 1               | 1%         |
| 26-30                      | 2               | 2%         |
| 31-35                      | 12              | 12%        |
| 36-40                      | 85              | 85%        |
| Total                      | 100             | 100%       |
Table 6: Distribution of subjects according to adverse effects of drugs in both groups (multiple responses).

| Adverse effect          | Subjects on Ca++ blockers (nifedipine) | Subject (Ca++ blockers+MgSO4) |
|-------------------------|----------------------------------------|-------------------------------|
|                         | No. | %       | No. | %       |
| Flushing                | 0   | 0 %     | 0   | 0 %     |
| Nausea                  | 5   | 10 %    | 13  | 26 %    |
| Vomiting                | 8   | 16 %    | 13  | 26 %    |
| Palpititation           | 15  | 30 %    | 28  | 56 %    |
| Headache                | 10  | 20 %    | 18  | 36 %    |
| Lethargy                | 1   | 2 %     | 5   | 10 %    |
| Constipation            | 7   | 14 %    | 8   | 16 %    |
| Ankle edema             | 0   | 0 %     | 0   | 0 %     |
| Hypotension             | 0   | 0 %     | 0   | 0 %     |
| Pulmonary edema         | 0   | 0 %     | 0   | 0 %     |
| Generalize muscle weakness | 5   | 10 %    | 26  | 52 %    |
| Breathing difficulty    | 5   | 10 %    | 26  | 52 %    |
| Respiratory arrest      | 0   | 0 %     | 0   | 0 %     |
| Drowsiness              | 0   | 0 %     | 2   | 4 %     |
| Total                   | 50  | -       | 50  | -       |

Table 7: Distribution of subjects according to outcome of pregnancy of drugs in both groups.

| Outcome of pregnancy      | Ca++ Blocker (nifedipine) | Ca++blocker (nifedipine)+magnesium sulphate | Total |
|---------------------------|---------------------------|--------------------------------------------|-------|
|                           | No. | %       | No. | %       |       |
| Vaginal delivery          | 31  | 62 %    | 15  | 30 %    | 46    |
| Caesarean sec.            | 19  | 38 %    | 35  | 70 %    | 54    |
| Total                     | 50  | 100 %   | 50  | 100 %   | 100   |

Degree of freedom = 1 and x2 = 10.3; p<0.005 which is significant.

Table 8: Distribution of subjects in caesarean section according to indication of caesarean section in both the groups (n =54).

| Indication of C/S                  | Ca++ blocker (nifedipine) | Ca++ blocker (nifedipine)+magnesium sulphate |
|------------------------------------|---------------------------|---------------------------------------------|
|                                    | No. | %       | No. | %       |
| Fetal distress                     | 10  | 52.63 % | 20  | 57.14 % |
| Previous scar                      | 3   | 15.79 % | 3   | 8.57 %  |
| Transverse lie                     | 1   | 5.26 %  | 0   | 0 %     |
| Deteriorating maternal condition   | 1   | 5.26 %  | 7   | 20 %    |
| Inadequate pelvis                  | 3   | 15.79 % | 4   | 11.43 % |
| Twin with ABO Rh-negative          | 1   | 5.26 %  | 0   | 0 %     |
| Antipartum hemorrhage              | 0   | 0 %     | 1   | 2.26 %  |
| Total                              | 19  | 100 %   | 35  | 100 %   |

Table 9: Distribution of subjects according to socioeconomics classes according to modified Prasad BC socioeconomics scale in both the groups.46

| Socioeconomic classes | Ca++ blocker (nifedipine) | Combination (nifedipine+MgSO4) | Total |
|-----------------------|---------------------------|---------------------------------|-------|
|                       | No. | %       | No. | %       |       |
| I                     | 1   | 2 %     | 1   | 2 %     | 2     |
| II                    | 5   | 10 %    | 3   | 6 %     | 8     |
| III                   | 3   | 6 %     | 14  | 28 %    | 17    |
| IV                    | 21  | 42 %    | 3   | 6 %     | 24    |
| V                     | 13  | 26 %    | 13  | 26 %    | 26    |
| VI                    | 7   | 14 %    | 16  | 32 %    | 23    |
| Total                 | 50  | 100 %   | 50  | 100 %   | 100   |
Table 10: Quality of life affected (n=100, multiple responses).

| QOL Questions                          | Ca** Blocker (nifedipine) | Combination (nifedipine+MgSO4) |
|----------------------------------------|--------------------------|-------------------------------|
| Pain during drug administrated         | 00                       | 00 %                          |
| Affecte daily routine                  | 00                       | 00 %                          |
| Mental tension about baby’s health     | 16                       | 32 %                          |
| Afford drug cost                       | 43                       | 86 %                          |

Table 11: Complications in relation with drugs regimen.

| Complications               | Drug regimen CCB+MgSO4 |
|-----------------------------|------------------------|
| Foetal                      | IUD 04 05              |
|                             | IUGR 04 02             |
|                             | Asphyxia 00 01         |
|                             | Pre-maturity 00 05     |
| Maternal                    | Eclampsia 03 05        |
|                             | Shock 00 00            |
|                             | Postpartum haemorrhage 00 00 |

Abbreviations- CCB: Calcium channel blocker i.e. Nifedipine, MgSO4: magnesium sulfate, IUD: Intrauterine death, IUGR: Intrauterine growth retardation.

While in the combination group i.e. Ca** channel blocker (nifedipine) and magnesium sulfate there were 35 caesarean section, out of this 20 (57.14%) subjects because of foetal distress, 7 (20%) subjects because of deteriorating maternal condition, 4 (11.43%) subjects because of inadequate pelvis, 3 (8.57%) subjects because of previous scar, and in 1 (2.86%) subject because of antipartum haemorrhage (Table 8). We also consider the socioeconomics of the patients because the combination therapy also increases the cost of the drugs also (Table 9). Most of the women in both the groups IV, V, VI as per the modified Prasad BC socioeconomics classification. We also consider the drug related quality of life in both the groups (Table 10) it is better in Ca** blocker (nifedipine) group.

The complication occurring in both i.e maternal and foetal complications. In calcium channel blocker i.e. Nifedipine four subjects babies were having intrauterine growth retardation and intrauterine death while no one having asphyxia and premature birth, while three subjects gone into eclampsia (Table 11). And in the combination group (calcium channel blocker i.e. nifedipine and magnesium sulfate) two subject’s babies were having intrauterine growth retardation and in five subjects reported intrauterine death, one baby suffered from asphyxia and five delivered premature, while five subjects had eclampsia (Table 11).

In the both group not a single subject suffering from shock and postpartum haemorrhage.

DISCUSSION

Hypertensive disease occurs in approximately 12-22 % of pregnancies, and it is directly responsible for 17.6 % of maternal death in United States. While the worldwide incidence about 5-10 %. In India among hospitalized patient 5-15 % suffering from preeclampsia.

The study of preeclampsia is very important because, it leads to complication like reduced utero placental blood and causes infarct, placental abruption, intrauterine growth retardation, and signs of foetal asphyxia during labour and can lead to maternal and foetal death.

According to the criteria established by the national high blood pressure education program working group (referred as the “working group”) in pregnant women, hypertension is define as systolic blood pressure level of 140 mmHg or higher or a diastolic blood pressure level of 90 mmHg or higher that occurs after 20 weeks of gestation in a women with previously normal blood pressure. As many as one quarter of women with pregnancy induced hypertension will develop proteinuria, i.e. preeclampsia.

So many women are affected by this dangerous disease but the etiology continues to be an enigma.

Various hypotheses to explain pathogenesis of preeclampsia are:

- Vasospasm and pathologic vascular lesion in various organs including utero placental arterial bed.
- Endothelial cell injury.
- Altered prostacyclin-thromboxane ratio.
- Increased platelet activation with platelet consumption and subsequent activation of coagulation system in microvasculature.
- Other hypotheses: a) Immunological b) Genetic predisposition.

With so much knowledge, prevention and starting pharmacotherapy is almost lacking so the disorder continues to be rampant globally due to non-specificity of risk factors. So it has remained a constant challenge to obstetrician.
Pregnancy induced hypertension, preeclampsia and eclampsia continues to be multisystem disorders of unknown etiology unique to pregnancy. However, during past several years major advances have been made regarding the pathogenesis, early detection, potential prevention, and the management of this syndrome. Traditionally, these disorders have been known to occur late in pregnancy. This is true for the majority of the cases, both clinicians and researchers have been known to be aware that preeclampsia can occur as early as 20 week, gestation from early utero placental vascular damage due to abnormal interaction between foetal maternal tissues, between 8-18 week. Though the cause of preeclampsia is unknown, it seems to represent the clinical end point of multiple contributory factors, and it is unlikely that any single cause will found. No doubt the delivery of foetus and placenta safely remains the only effective treatment so the good pharmacological treatment is important to correct /reverse pathophysiological changes as preeclampsia can progress quickly. So present study was taken. Keeping in view that pharmacological treatment play a major role in the management of preeclampsia, present study was prospective and open label study.

Since the turn of the century, obstetrician have to decrease the incidence of seizures in pregnant women who develop preeclampsia or eclampsia by treating them with magnesium sulfate. The efficiency of magnesium sulfate in preventing convulsions remains controversial. So by this study we were trying to find out the drug related quality of life in the preeclampsia treated by calcium channels blocker i.e. nifedipine and combination of calcium channel blocker i.e. nifedipine and magnesium sulfate considering the points i.e. freedom from the pain and distress, physical mobility, capacity for self-care and treatment compliance of the patients, as well as pharmacoeconomics of these drugs. And by this study we tried to find out that, is the magnesium sulfate necessary of the prevention of convulsion in the preeclampsia patients?

As the maternal age is one of the risk factor for the development of preeclampsia, according to the literature condition is common in extremities of the child bearing ages i.e. <20 years of age and >30 of age. But most of the studies have shown that But most of the studies have shown that incidence of hypertensive disorder is more in 27-29 years. In our study incidence differ and was more in 21-25 years of age group. It may be due to early marriages as the study is carried out in rural area (Table 1). As many as one quarter of women with pregnancy induced hypertension will develop proteinuria, i.e., preeclampsia. Common gestational age of patients presenting preeclampsia in our study was 36-40 weeks this may reflect social neglect of this disease (Table 2). Nifedipine has recently been used for the reduction of blood pressure in severe preeclampsia (calcium channel blocker) it causes peripheral arterial vasodilatation. Pharmacokinetics and pharmacodynamics indicate that nifedipine is associated with a 25% reduction in systolic blood pressure, diastolic blood pressure and mean arterial pressure in 98% of cases. Even though all the treatment regimens are still empiric, the standard therapy of preeclampsia includes three. The prevention of maternal convulsions Control of severe hypertension Delivery of foetus and placenta safely.

Magnesium sulfate has been a standard therapy for preeclampsia and eclampsia to prevent convulsions since the 1925 publication of study conducted by Edmond Lazard. However the efficacy of magnesium sulfate in preventing convulsions remains controversial. In this study we are trying to find out that whether magnesium sulfate was essential to prevent convulsions along with their comparing the side effects in both the groups i.e. one group received only nifedipine and other groups received combination of nifedipine and magnesium sulfate.

We were found that out of 50 patients received nifedipine 30% subjects were suffered from palpitation, followed by 20% patients were suffered from headache. This finding support the other reports, 16% patients were suffered from vomiting, 14% patients suffered from constipation, 10% patients were suffered from nausea, generalized muscle weakness, breathing difficulty, while 1 (2%) suffered from lethargy, but no one was suffered from flushing, ankle edema, hypotension, pulmonary edema, respiratory arrest and drowsiness. Frequent side effects of nifedipine are palpitation, flushing, ankle edema; hypotension, headache, drowsiness and nausea. Reflex tachycardia, hypotension. While another 50 patients receiving combination therapy of nifedipine and magnesium sulfate. 56% subjects were suffered from palpitation, 52% subjects were suffered from generalized muscle weakness and breathing difficulty, 36% of subjects were suffered from headache, 26% of subjects were suffered from nausea and vomiting, 16% of subjects were suffered from constipation, 4% of subjects were suffered from drowsiness and 2% was suffering from ankle edema while none of them suffered from hypotension, this finding support the other reports, flushing, pulmonary edema, respiratory arrest.

Initial results for magnesium sulfate were encouraging but wider use revealed more serious adverse effects, Flushing, nausea, chest tightness and lethargy, which are all directed to high serum magnesium concentration. In addition, magnesium may interfere with working memory and attention in women which may have implications on gaining informed consent.

Maternal side-effects are mainly association with the cardiovascular (e.g. Cardiac conduction effects, ischemia, arrest, hypotension) and respiratory symptoms (e.g. Respiratory depression) may be due to magnesium ions applied directly to the brain and spinal cord and depresses the central nervous system and acts as a sedative. And several cases of pulmonary edema have been reported.
In addition, one recent case of respiratory arrest attributed to acute hypermagnesemia required rescue therapy with calcium gluconate. Prolonged treatment may result in neuromuscular blockade causes generalized muscle weakness may be due to blocks transmission in sympathetic ganglia by the inhibition of the release of acetylcholine, and it is more severe if magnesium sulfate administrated together with nifedipine. Osteoporosis also has been reported after prolonged therapy.

Incidence of caesarean section was more in combination therapy i.e. nifedipine and magnesium sulfate group 70% while in only nifedipine group it was only 38% this finding support the other report, which was highly significant p value <0.005. Indications of caesarean section in combination group were foetal distress 57.14% may be due to maternal serum concentration exceed 6 m Eq/l, previous scar 8.57%, deteriorating maternal condition 20% may be due to high serum magnesium concentration, inadequate pelvis 11.43%, antipartum hemorrhage 2.26 %. While the indication of caesarean section in nifedipine alone group were foetal distress 52.63%, previous scar 15.79%, transverse lie 5.26%, deteriorating maternal condition 5.26%, inadequate pelvis 15.79%, twin with ABO Rh negative 5.26%.

We distributed patients according to their socio economics status with the help of modified Prasad BC socio economics scale. We found that most of the patients was in class VI i.e very poor or below poverty line (per capita income <500 Rs.), followed by class III (per capita income 3000-4999 Rs.) and class V (per capita income 500-1499 Rs.) in combination group while in nifedipine only group most of patients belongs to class IV (per capita income 1500-2999 Rs.) followed by class V (per capita income 500-1499 Rs.), class VI (very poor or below poverty line) and class II (5000-9999 Rs.).

In nifedipine group intrauterine death of foetus occurred in 3 cases, 4 foetuses suffered from intrauterine growth retardation may be due to the total neglect of the condition by the patient and started late treatment, and 3 patients developed eclampsia.

In combination group intrauterine death occurred in 5 cases, 2 cases of intrauterine growth retardation occurred may due to the total neglect of the condition by the patient and started late treatment, premature delivery occurred in 5 cases because foetal distress may be due to maternal serum concentration exceed 6 m Eq/l, while 5 cases of eclampsia occurred. So that the drug related complication was more if the magnesium sulfate is added with nifedipine.

In combination group nifedipine is effective for longer time along with it achieves good BP control and required few doses (5-10 mg TDS). The magnesium sulfate dose is- loading dose of magnesium sulfate is 4 gm IV over 3-5 minutes followed by 10 gm deep IM (5 gm in each buttock) followed by maintenance of 5 gm IM hourly in alternate buttock, due to deep IM administration make it very painful. All patients suffered from pain during drug administration and patient suffered from more mental tension about their baby’s health and trauma, affect daily routine of the patient by increasing side effect like generalized muscle weakness, palpitation, headache, breathing difficulty and lethargy. In this group patient had to pay for both the drugs daily 3 rupees for nifedipine. One tablet of 10 mg nifedipine costing one rupee (Cipla-Nifelan), and 200 rupees for magnesium sulfate on first day and 100 rupees after second day because 500 mg of injection magnesium sulfate costing five rupees (Rathi laboratories Hindustan pvt. Ltd) which is so expensive and patients took treatment in government hospital was mostly poor patients not afforded the cost of these drugs.

Nifedipine is effective for longer time along with it achieves good BP control and required few doses (5-10 mg TDS), safe for mother and foetus have fewer side effects so the effects on daily routine was less as compared to combination of magnesium sulfate and conveniently and easy administered via sublingual route so it is painless administration of drug, so that patient has less mental tension and trauma. Cost wise it is cheaper i.e. one cap. Of 10 mg nifedipine costing around one rupees. So the daily patient has to spend only three rupees per day so that patients below poverty line can afford the drug and after seeing the result of this study, it is sure that magnesium sulfate does not seem to be necessary therapy and may actually even to be a bad choice for preeclampsia because it worsens the quality of life as per A. Williams of the patients by increasing pain, incidence of caesarean section, deteriorating maternal condition, mental tension and trauma, affecting daily routine by increasing side effects, economical trauma also and no benefited over the nifedipine therapy alone.

CONCLUSIONS

- Magnesium sulfate increase incidence of caesarean section due to foetal distress may be due to maternal serum concentration exceed 6 m Eq/l and deteriorating maternal condition may be due to high serum magnesium concentration.
- Magnesium sulfate causes high incidence of maternal adverse effect like palpitation, generalized muscle weakness, breathing difficulty, constipation, vomiting, nausea, lethargy and affect patient’s daily routine.
- The outcome of pregnancy was good in only nifedipine therapy.
- After seeing the result of this study it is sure that magnesium sulfate does not seem to be necessary therapy and may actually even to be a bad choice for preeclampsia because it worsens the quality of life of the patients by increasing pain, incidence of caesarean section, deteriorating maternal condition, mental tension and trauma, affecting daily routine, economical trauma also. And no benefited over the nifedipine therapy alone.
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REFERENCES

1. MacKay, Cynthia JB, Atrash HK. Pregnancy related mortality from preeclampsia and eclampsia. Obstet Gynecol. 2001;97:533-8.
2. Safflas AF, Olson DR, Franks AL, Atrash HK, Pokras R. Epidemiology of hypertension in United Sates 1979-1986. Am J Obstet Gynecol. 1990;163:460-5.
3. Burrows RF, Burrows EA. The feasibility of control population for a randomized control trial of seizure prophylaxis in the hypertensive disorder of pregnancy. Am J Obstet Gynecol. 1995;173:929-35.
4. Cunningham FG, MacDonald PC, Gant NF, McDonald PC, Leveno KJ, Gilsstrap LC, et al. Williams obstetrics. 20th ed. Norwalk, Connecticut: Appleton and Lange; 1997.
5. Scott CL, Chaves GF, Atrash HK, Taylor DJ, Shah RS, Rowlay D. Hospitalizations for severe complications of pregnancy 1987-1992. Obstet Gynecol. 1997;90:225-9.
6. Sibai BM. Pitfalls in diagnosis and management of preeclampsia. Am J Obstet Gynecol. 1988;159:1:1.
7. Dekker GA, Sibai M. Early detection of preeclampsia. Am J Obstet Gynecol. 1991;165(1):160-72.
8. Robertson WB, Khong TV. Pathology of the uteroplacental bed. Sharp F, Symond EM, eds. Hypertension in pregnancy. Ithaca, New York: Perinatology press;1987:101.
9. Dutta DC. Text book of obstetrics, hypertensive disorder in pregnancy, Hiralal Korane, 6th edition; 2004:221-42.
10. Handwerker SM, Bella T, Altura, Dennis SC, Burton M, Altura. Serum ionized magnesium levels during intravenous MgSO4 therapy of pre eclamptic women. Acta Obstet Gynecol Scand. 1995;74:517-9.
11. Chesley LC, Tepper I. Plasma levels of magnesium attained in MgSO4 therapy for preeclampsia and eclampsia. Surg Clin North Am. 1957;353-67.
12. Chen FP, Chang SD, Chu KK. Expectant management in severe preeclampsia: does magnesium sulfate prevent the development of eclampsia? Acta Obstet Gynecol Scand. 1995;74:181-5.
13. Larry CG, Gilstrap III, Susan MR. Diagnosis and management of preeclampsia and eclampsia. ACOG Practice Bulletin. 2002;90(1):159-67.
14. Walker LM. Preeclampsia. Lancet. 2000;356:1260-5.
15. Koonin LM, MacKay AP, Berg CJ, Atrash HK, Smith JC. Pregnancy related mortality surveillance-United States, 1987-1990. Mor Mortal Wky Rep CDC Surveill Summery. 1997;46(4):17-36.
16. Chen XK, Wen SW, Smith G, Yang Q, Walker M. Pregnancy induced hypertension is associated with infant mortality in preterm singletone. BJOG. 2006;113:544-51.
17. Gudmundsson S, Gennser G, Marsal K. Effect of hydralazine on placental and renal circulation in preeclampsia. Acta Obstet Gynecol Scand. 1995;74:415-8.
18. Naeye R, Friedman EA. Causes of perinatal death associated with gestational hypertension and proteinuria. Am J Obstet Gynecol. 1979;133:8-10.
19. Report of national high blood pressure education program working group on high blood pressure in pregnancy. Am J Obstet Gynecol. 2000;183:1-22.
20. Saudan P, Brown MA, Buddle ML, Jones M. Does gestational hypertension become pre-eclampsia? Br J Obstet Gynecol. 1998;105:1177-84.
21. Gant NF, Chrd S, Whalley PT, McDonald PC. The nature of pressor responsiveness to angiotensin II in human pregnancy. Obstet Gynecol. 1974;43:854.
22. Spitz B, Magness RR, Cox SM. Low dose aspirin I effect angiotensin II pressor responses and blood prostaglandin concentration in pregnant women sensitive to angiotensin II. Am J Obstet Gynecol. 1988;159(5):1035-43.
23. Massaro LD. Oxygen toxicity. Am J Obstet and Gynecol. 1980;69(1):117-26.
24. Walsh SW. Preeclampsia: an imbalance in placental prostacyclin and thromboxin production. Am J Obstet and Gynecol. 1985;152(2):335-40.
25. Pedersen EB, Aukjaer C, Christensen AJ. Renin, angiotensin-II, aldosteron, catecholamine, prostaglandins and vasopressin: the importance of pressor and depressor factors for hypertension in pregnancy. Scand J Clin Lab Invest Suppl. 1984;44:169-248.
26. Zeeman GG, Dekker GA. Pathogenesis of preeclampsia: a hypothesis. Clin Obstet Gynecol. 1992;35(2):317-37.
27. Redman CWG. Platelets and the beginning of preeclampsia. N Eng J Med. 1990;323:478.
28. Dekker GA, Sibai BM. Etiology and pathophysiology of preeclampsia: current concept. Am J Obstet Gynecol. 1998;179(8):1359-75.
29. Boer DK, Cate-ten JM, Sturk A, Borm JJJ, Treffers PE. Enhanced thrombin generation in normal and hypertension patients. Am J Obstet Gynecol. 1989;160(1):95-100.
30. Sibai BM. Immunologic aspects of preeclampsia. Clin Obstet Gynecol. 1991;34(1):27.
31. Arngrimson R, Bjornsson S, Geissron RT, Geissron H, Walker JJ, Snaedal G. Genetic and familial predisposition to eclampsia and preeclampsia in a defined population. Br J Obstet and Gynecol. 1990;97(9):762-9.
32. Chesley LC, Cooper DW. Genetics of hypertension in pregnancy: possible single gene control of preeclampsia and eclampsia in the descendants of eclamptic women. Br J Obstet and Gynecol. 1986;93(9):898-908.
33. Norwitz RE, Robinson JN, Repke JT. Prevention of preeclampsia: is it possible? Clin Obstet Gynecol. 1999;42(3):436-55.
34. Williams A. In: Smith GT (ed) Measuring the social benefits of medicine. Office of Health economics, London; 1983.
35. Dekker GA. Risk factors for preeclampsia. Clin Obstet Gynecol. 1999;42(3):422-35.
36. Aali BS, Nejad SS. Nifedipine or hydralazine as a first line agent to control hypertension in severe preeclampsia. Acta Obstet Gynecol Scand. 2002;81:25-30.
37. Tripathi KD. Essentials of medical pharmacology. Antianginal and other anti-ischemic drugs, M. Tripathi, 5th edition; 2004:486-503.
38. Ingemarsson I, Lamont RF. An update on the controversies of tocolytic therapy for the prevention of preterm birth. Acta Obstet Gynecol Scand. 2003;82:1-9.
39. Elliot JP. Magnesium sulfate as a tocolytic agent. Am J Obstet Gynecol. 1983;147:277-84.
40. Ghia N, Spong CY, Starbuck VN, Scialli AR, Ghidini A. Magnesium sulfate affect attention and working memory in patient undergoing preterm labour. Am J Obstet Gynecol. 1982;142:840-6.
41. Elliot JP, O’Keefe DF, Greenberg P, Freeman RK. Pulmonary edema associated with magnesium sulfate and betamethasone administration. Am J Obstet Gynecol. 1979;134:717-9.
42. Semchyshyn S, Zuspan FP, O’Shughnnessy R. Pulmonary edema associated with the use of hydrocortisone and a tocolytic agent for management for preterm labour. J Reprod Med. 1983;28:47-52.
43. Cao Z, Bideau R, Vald R, Elin RJ. Acute hypermagnesemia and respiratory arrest following infusion of MgSO4 for tocolysis. Clinica Chimica Acta. 1999;285:191-3.
44. Canez MS, Reed KL, Shenker L. Effect of maternal magnesium treatment on fetal heart rate variability. Am J Perinatol. 1987;4:167-9.
45. Peaceman AM, Meyer BA, Thorp JA, Parisi VM, Creasy RK. The effect of magnesium sulfate tocolysis on the fetal biophysical profile. Am J Obstet Gynecol. 1989;161:771-4.
46. Agarwal AK. Social classification: need to update in the present scenario. Indian Journal of community medicine. 2008;33(1):50-1.

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