Perinatal Outcomes of Magnesium sulphate and Diazepam use in Severe Pre-eclamptic and Eclamptic Mothers, Jimma University Specialized Hospital, Southwest Ethiopia

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Abstract

Currently the preferred anticonvulsant used to treat and prevent fits in eclampsia is magnesium sulphate. The main objective of this study was to evaluate the perinatal outcomes of magnesium sulphate and diazepam use in the management of severe pre-eclampsia and eclampsia in Jimma University Specialized Hospital. A retrospective hospital based cross-sectional comparative study was conducted using data collection format. Data was collected from the hospital delivery care register and patient chart records of all mothers who presented with the diagnosis of severe pre-eclampsia and eclampsia in two years and three months period from January, 2010 to April, 2012.

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Descriptive analysis such as frequency and percentage, Chi-square test, binary logistic regression and non parametric tests were analyzed by SPSS version 16.0. A P-value of <0.05 was considered statistically significant in all tests.

A total data of 343 births were included in this study. Two hundred seventeen from magnesium sulphate and one hundred forty from diazepam treated mothers group, were reviewed and analyzed. There were ninety eight still births yielding a stillbirth rate of 24.5% and 35.1% for the magnesium sulphate and diazepam groups respectively. Fewer newborns in the magnesium sulphate treated group had Apgar scores less than seven than in the diazepam treated group at first and fifth minutes. A higher proportion of babies from the diazepam group were admitted to the neonatal ward than from the magnesium sulphate group (31.8% versus 18.1%). Birth outcome, first minute Apgar score and admission to the neonatal ward had a statistically significant association with the type of anticonvulsant used.

Magnesium sulphate is more effective than diazepam in the management of severe pre-eclamptic and eclamptic mothers in terms of improving Apgar scores, reducing stillbirth outcome and admission to the neonatal ward. Therefore, its accessibility and wider use should be promoted.

Keywords: Magnesium sulphate; diazepam; Severe pre-eclampsia; Eclampsia; perinatal outcome

1. Introduction

Pre-eclampsia is a condition unique to pregnancy that is characterized by new onset of hypertension and proteinuria in a previously normotensive woman [1]. It is a relatively common complication of pregnancy, and can occur at any time during the second half of pregnancy or in the first few weeks after delivery for many women who have pre-eclampsia perinatal outcome is good, but severe disease can lead to death or serious problems for her baby [2].

Pre-eclampsia and eclampsia are not distinct disorders but the manifestation of the spectrum of clinical symptoms of the same condition. In pre-eclampsia, hypertension and proteinuria are present, and when convulsions occur after other causes of convulsion are excluded in addition to these signs, the condition is referred to as eclampsia [1]. Eclampsia, characterized by maternal seizures, is a serious complication increasing the risk of maternal and perinatal morbidity and mortality [3].

Preeclampsia can be mild or severe. The mild one is defined as a blood pressure (BP) of at least 140/90 mmHg on at least two occasions in a minimum of 6 hours apart after the 20th week of gestation in women known to be normotensive before pregnancy plus proteinuria (300 mg or more per 24-hour period). If 24-hour urine collection is not available, then a concentration of at least 30 mg/dL (at least 1+ on dipstick) in at least two random urine samples collected at least 6 hours apart is defined proteinuria. Severe preeclampsia is defined as sustained elevations in systolic BP to at least 160 mmHg and/or in diastolic BP to at least 110 mmHg for at least 6 hours in association with abnormal proteinuria or if there is hypertension in association with severe proteinuria (at least 5 g per 24-hour period). In addition, preeclampsia is severe in the presence of multiorgan involvement such as pulmonary edema, oliguria (less than 500 mL per 24-hour period), thrombocytopenia (platelet count less than 100,000/ mm3), abnormal liver enzymes

in association with persistent epigastric or right upper quadrant pain, or persistent severe central nervous system symptoms (altered mental status, headaches, blurred vision or blindness) [4, 5].

Pre-eclampsia has remained a significant public health threat in both developed and developing countries contributing to maternal and perinatal morbidity and mortality globally. However, the impact of the disease is felt more severely in developing countries, where, unlike other more prevalent causes of maternal mortality (such as haemorrhage and sepsis), medical interventions may be ineffective due to late presentation of the cases. The problem is confounded by the continued mystery of the aetiology and the unpredictable nature of the disease [6].

Eclampsia occurs when pre-eclampsia is complicated by seizures or coma and it develops in 1 of 200 patients with pre-eclampsia. Eclampsia is immediately life threatening for both the baby and the mother and can be fatal if untreated [7].

Current strategies for prevention of pre-eclampsia can be broadly classified as antenatal surveillance, modification of lifestyle, nutritional supplementation, and pharmacological therapy. Currently, standard care for women with severe pre-eclampsia/eclampsia is to use an anticonvulsant drug to control the immediate fit, and to continue maintenance treatment to prevent further seizures [8].

Currently, the preferred anticonvulsant is magnesium sulphate [9]. Large randomised trials in developing countries and systematic reviews have shown the usefulness of magnesium sulphate in treating recurrent eclamptic seizures and in the prophylaxis of eclampsia [10]. Over the last decade there has been an increase in the use of magnesium sulphate for the prevention of seizures in women with severe pre-eclampsia or eclampsia [11].

In Ethiopia, magnesium sulphate is introduced as an anticonvulsant for treatment of severe pre-eclampsia and eclampsia. Diazepam is still in use as an alternative in the absence of magnesium sulphate. It is used as 30 IU/ 1000 ml of D/W, (D/S) 20 drops / min with an increase in the drops as needed depending on the patients' sedation status [4, 12].

Despite the use of different types of drugs, pre-eclampsia and eclampsia remain a massive cause of perinatal morbidity and mortality [3, 13].

Eclampsia is a common complication still associated with high level of perinatal mortality as well as morbidity in Ethioipia. The perinatal mortality rate of pre-eclampsia/eclampsia was 312.2/1000 deliveries in two teaching hospitals in Addis Ababa [14, 15]. In Jimma University Specialized hospital, severe pre-eclampsia was the most common hypertensive disorder of pregnancy followed by eclampsia contributing 51.9% and 23.4% of the cases respectively [16].

The Ethiopian Society of Obstetricians and Gynecologists has done a project from April 2009 to July 2011 to contribute towards the reduction of maternal mortality by introducing MgSO4 in all public hospitals in Ethiopia [17].

However, there are no studies done to assess the impact of the drug on maternal and perinatal outcomes and compare it with diazepam after its introduction in public hospitals in Ethiopia in general and in Jimma University Specialized Hospital in particular.

Magnesium sulphate has been included into the National Drug List of Ethiopia and is being used for prevention and treatment of severe pre-eclampsia and eclamptic seizures since January of 2011 in public hospitals though it's still not in the List of Essential Drugs for Ethiopia (EDL).

The study has brought findings to fill the information gap to what extent the drug affects perinatal outcomes as compared to diazepam since its introduction in our setting.

2. Materials and methods

This hospital based retrospective cross-sectional comparative study was conducted from mid-February to mid-April , 2012 in Jimma University Specialized Hospital (JUSH), which is found in Jimma town. The hospital is one of the oldest public hospitals in the country and provides almost all major types of medical services such as Clinical services including Delivery and maternal and child health Services for approximately 9000 inpatient and 80000 outpatient attendants a year from the catchment population of about 15 million in southwest Ethiopia [18]. JUSH is the only teaching and referral hospital in the southwestern part of the country and has a total of more than 750 staffs of both supportive and professional with a total bed capacity of 450 [18] of which 47 are found in the maternity ward. The labor and maternity wards are run by midwives, medical and health officer interns, resident physicians of obstetrics and gynecology, and senior physicians of obstetrics and gynecology. JUSH has an ICU of eight beds with two anesthesiologists and various groups of residents and nurses.

All newborns from mothers who admitted to JUSH maternity ward in the two years and three months period, from January 03, 2010 - April 02, 2012 were considered as source population and those whose mothers presented with the diagnosis of severe pre-eclampsia or eclampsia and took either magnesium sulphate or diazepam for prophylaxis or treatment of seizures were included in the study. Newborns whose mothers were diagnosed with severe pre-eclampsia or eclampsia but died before taking diazepam or magnesium sulphate and those perinates whose mothers were referred from other health institutions taking any anticonvulsant before reaching the hospital were excluded in the study.

Data was collected using a structured data collection format developed by the principal investigator after reviewing literatures and based on the objectives. The format consists of maternal details, diagnosis, type of anticonvulsants used, Apgar score of the baby at first and fifth minutes, admission status to the neonatal ward and other relevant information.

The data collection format was pre-tested on 19 patient records (5%) in order to check any inconsistencies and necessary adjustments were made before the actual period of the study.

The dependent variables were birth outcome (live birth, stillbirth), Apgar score at first and fifth minutes and admission to the neonatal ward.

Data was collected by a medical intern and a postgraduate clinical pharmacy student of Jimma University after orientation and training for three days. Data was obtained from the hospital delivery care register, Log Book and patient chart review. At the end of each day, the completeness and consistency of data collected was checked by the principal investigator. Then, the collected data was organized, cleaned, coded and analyzed by SPSS version 16.0 for windows.

Chi-square test was used to determine the presence of association between the type of anticonvulsant used and the outcome variables. A binary logistic regression was done to assess the degree of association between type of anticonvulsant used and some perinatal outcome variables using odds ratio with 95% confidence interval. Mann-whitney non-parametric test was employed to test the association of type of anticonvulsant used with Apgar score A P-value of <0.05 was considered statistically significant for all the tests.

Ethical clearance was granted from the college of Public Health and Medical sciences ethical review board (Ref. No RPGC/114/2012), Jimma University before data collection. Concerned bodies at all levels, including the hospital clinical director and department of obstetrics and gynecology, were communicated and approval was granted. Any personally identifiable information (e.g., name, address) was not recorded. Patient cards were returned to the card room after data collection.

3. Results

A total data of 343 births were included in this study. One hundred twenty six (35.3 %, n=357) and 231 (64.7%, n=357) mothers were diagnosed with eclampsia and severe pre-eclampsia respectively. Magnesium sulphate has been used as anticonvulsant for 217 (60.8%, n=357) mothers (table 1).

Table 1: Maternal details admitted with the diagnosis of eclampsia and severe pre-eclampsia, JUSH, January 2010 – April 2012 (n=357).

Maternal characteristics	Frequency	%
Gravidity		
Primigravida	204	57.1
Multigravida	153	42.9
Maternal Diagnosis		
Severe Preeclampsia	231	64.7
Eclampsia	126	35.3
Type of anticonvulsant used		
Magnesium sulphate	217	60.8
Diazepam	140	39.2

There were ninety eight still births, 52 (24.5%) (n=212) among magnesium sulphate and 46 (35.1%) (n=131) diazepam treated mothers. Birth outcome has a statistically significant association with the type of anticonvulsant used in severe pre-eclamptic mothers (P= 0.013) but not in eclamptic mothers (P= 0.952). Overall, birth outcome had a statistically significant association with the type of anticonvulsant used (P= 0.037) with (Table 2).

Table 2: Association of birth outcome with type of anticonvulsant used from severe pre-eclamptic and eclamptic mothers, JUSH, January 2010 - April 2012 (n=343).

Diagnosis	Birth outcome	Type of anticonvulsant used			p-value
		Magnesium sulphate (n=212) n (%)	Diazepam (n=131) n (%)	Total n (%)	
Severe pre-eclampsia	Still birth	31 (20.9)	27 (36.5)	58 (26.1)	
	Live birth	117 (79.1)	47 (63.5)	164 (73.9)	0.013
Eclampsia	Still birth	21 (32.8)	19 (33.3)	40 (33.1)	
	Live birth	43 (67.2)	38 (66.7)	81 (66.9)	0.952
Total	Still birth	52 (24.5)	46 (35.5)	98 (28.6)	
	Live birth	160 (75.5)	85 (64.9)	245 (71.4)	0.037

The number of newborns, with a first minute Apgar score of less than seven, was fewer in mothers who were treated with magnesium sulphate than diazepam (42.5% versus 63.5%). First minute Apgar score was statistically significant with the type of anticonvulsant used (P=0.002) (table 3). However, fifth minute Apgar score was not statistically significant with the type of anticonvulsant used (P=0.275) though there was still fewer number of children with Apgar score less than seven (table 3).

It was also recorded that there were 56 admissions to the neonatal ward. Twenty nine of perinates admitted to the neonatal ward were from mothers who had received magnesium sulphate as anticonvulsant. A higher proportion of babies from the mothers who received diazepam (18.1%, n=160) were admitted to the neonatal ward than from the magnesium sulphate received group (31.8%, n=85). A statistically significant association was found between perinatal admission to neonatal ward and type of anticonvulsant used (P=0.025) (table 5).

Table 3: Association of first minute Apgar score of perinates from severe pre-eclamptic and eclamptic mothers with type of anticonvulsant used, JUSH, January 2010 - April 2012.

Diagnosis	First minute Apgar score	Type of anticonvulsant used		Total n (%)	p-value
		Magnesium sulphate (n=160) n (%)	Diazepam (n=85) n (%)		
Severe pre-eclampsia	< seven	37 (33.9)	30 (60.0)	67 (42.1)	
	≥seven	72 (66.1)	20 (40.0)	92 (57.9)	0.002
Eclampsia	< seven	31 (60.8)	24 (68.6)	31 (64.0)	
	≥seven	20 (39.2)	11 (31.4)	55 (36.0)	0.460
Total	< seven	68 (42.5)	54 (63.5)	122 (49.8)	
	≥seven	92 (57.5)	31 (36.5)	123 (50.2)	0.002

Table 4: Association of fifth minute Apgar score of perinates from severe pre-eclamptic and eclamptic mothers with type of anticonvulsant used, JUSH, January 2010 - April 2012.

Type of anticonvulsant	Fifth minute Apgar score				P-valve
	< seven		≥ seven		
	Frequency	%	Frequency	%	
Magnesium sulphate	23	14.4	137	85.6	
Diazepam	16	18.2	69	81.8	0.275
Total	39	15.9	206	84.1	

Binary logistic regression analysis indicated that the likelihood of stillbirth birth outcome, perinates having an Apgar score of less than seven and admission of perinates to the neonatal ward in the magnesium sulphate treated mothers was 0.601, 0.424 and 0.484 times their counterparts in the diazepam treated group respectively (table 6).

Table 5: Association of perinatal admission to the neonatal ward with type of anticonvulsant used among newborns from severe pre-eclamptic and eclamptic mothers, JUSH, January 2010 - April 2012.

Diagnosis	Admission to the neonatal ward	Type of anticonvulsant used			p-value
		Magnesium sulphate (n=160) n (%)	Diazepam (n=85) n (%)	Total n (%)	
Severe pre-eclampsia	Yes	20 (18.3)	11 (26.2)	31 (20.5)	0.039
	No	89 (81.7)	31 (73.8)	120 (79.5)	
Eclampsia	Yes	9 (-)	16 (36.4)	25 (26.3)	0.025
	No	42 (82.4)	26 (63.6)	70 (73.7)	
Total	Yes	29 (18.1)	27 (31.8)	56 (22.9)	0.028
	No	131 (81.9)	58 (68.2)	189 (77.1)	

Table 6: Binary logistic regression of some outcome variables with type of anticonvulsant used, JUSH, January 2010 - April 2012.

Type of anticonvulsant	Outcome variable	p-value	OR	95% CI
Still Birth outcome				
Magnesium sulphate	52	0.036	0.601	0.373-0.967
Diazepam	46		1	Reference
First minute Apgar score<7				
Magnesium sulphate	68	0.002	0.424	0.247-0.729
Diazepam	54		1	Reference
Neonatal ward admission				
Magnesium sulphate	29	0.019	0.484	0.263-0.888
Diazepam	27		1	Reference

4. Discussion

The current study has attempted to compare the perinatal outcomes of magnesium sulphate use with diazepam in terms of birth outcome, first and fifth minute Apgar scores, and admission to the perinatal ward.

It has been revealed, in a typical systematic quantitative review and analysis, that magnesium sulphate was more effective than other interventions in preventing recurrent seizures in eclampsia and in preventing the first seizure in pre-eclampsia so that improves perinatal outcomes [5].

Eclampsia and pre-eclampsia are among the hypertensive disorders of pregnancy that result high rate of stillbirth. In this study, the stillbirth rate in magnesium sulphate treated mothers is lower than in diazepam treated mothers {(24.5% *versus* 35.1%) (OR 0.601, 95% CI 0.373 to 0.967)} yielding a total stillbirth rate of 285.7 per 1000 births. This finding is more or less consistent with other Literatures that support use of magnesium sulphate resulted in a lower stillbirth rate than diazepam [9, 19]. A study done in a teaching hospital in Nigeria (2010) showed a stillbirth rate of 368.4 per 1000 births among those treated with diazepam and 296.7 per 1000 births in the magnesium sulphate group [20]. According to a study done in Jimma University specialized hospital on hypertensive disorders of pregnancy the stillbirth rate was 27.5% [16]. The stillbirth rate in this study was found to be higher as eclampsia and severe pre-eclampsia are relatively more severe forms than other hypertensive disorders of pregnancy.

This study revealed that there were fewer newborns with low first minute Apgar score from magnesium sulphate treated mothers than from diazepam treated mothers (42.5% versus 63.5%). This could be explained by the fact that diazepam causes respiratory depression to the perinate. This finding is supported by other several studies such as the Ikramullah et al study in 2009 [21]. Crowther's study on Magnesium sulphate versus diazepam in the management of eclampsia showed that Significantly fewer infants born in the magnesium sulphate group had low Apgar scores (less than 7 at 1 min) compared with those in the diazepam group (RR 0.6; 95% CI 0.4 to 0.9) [19].This has also been observed that in the magnesium sulphate group, fewer live born babies had an Apgar score less than seven at one minute (two trials; 597 babies; RR 0.75, 95% CI 0.65 to 0.87) or at five minutes (RR 0.70, 95% CI 0.54 to 0.90) in the Cochrane study (2010) [22].

Regarding admission to the neonatal ward fewer babies from the magnesium sulphate treated mothers group were admitted to the neonatal ward than from the diazepam treated group {(18.1% versus 31.8%)(OR 0.484, 95% CI 0.263 to 0.888)}. The admission rate in this study is lower as compared to other studies such as a study done in America by *Greenberg MB et al* in 2011 where 21.1% of neonates whose mothers had been exposed to antenatal magnesium sulphate were admitted to the NICU [23]. Admission of newborns from magnesium sulphate treated mothers; to special care baby unit in the *Magpie Trial Collaborative Group* was 39% [24]. This could be due to limited space in the neonatal ward as JUSH is the only referral hospital in the area. But still the findings agree with other studies in terms of reducing perinatal admission to special care unit and there are some studies with a lower admission rate than this study in Nepal and Pakistan [21, 25].

5. Limitations of the study

The main limitation of this study was being retrospective and its dependence on patients' records. Because of this it was not possible to include the actual drug administration issues and outcomes of the infant after admission to the perinatal ward. Some patient cards did not contain all necessary information that affected the quality of the study. We

has also assumed that patients' management (dose, frequency of administration, etc) in either group was strictly in line with the hospital's protocol as we were unable to check it prospectively.

6. Conclusion

This study has shown a reduction in the number of newborns with low first minute Apgar scores from severe pre-eclamptic mothers who received magnesium sulphate as compared to those newborns from mothers who received diazepam as anticonvulsant. Admission of perinates to the neonatal ward from severe pre-eclamptic and eclamptic mothers was found to be higher in the diazepam treated group than magnesium sulphate treated group. There was also a reduction in still birth rate of newborns from mothers who received magnesium sulphate as compared to those newborns from mothers who received diazepam.

Acknowledgements

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