Clinical Management and Outcome of Eclampsia at Rajavithi Hospital

PRATHARN CHINAYON, M.D.*

Abstract

The purpose of this clinical study was to review experience in the management, and outcome of eclamptic patients at Rajavithi Hospital. Standardized treatment for all cases of eclampsia has consisted of magnesium sulfate intravenously and intramuscularly to control convulsions by means of Chesley and Tepper's regimen, intravenous hydralazine intermittently to lower diastolic blood pressure when it exceeds 110 mmHg, and initiation of delivery as soon as the patient has regained consciousness and is stable. During a ten - year period there were 167,200 deliveries and 90 eclamptic patients, yielding an incidence of eclampsia of 1 in 1,857 deliveries. There were three maternal deaths (3.3%) due to intracerebral hemorrhage. Serious adverse maternal outcomes were more frequent in women whose convulsions occurred before delivery. Excluding postpartum cases, perinatal mortality of fetuses weighing 1,000 g or more was 11.7 per cent.

Magnesium sulfate is the drug of choice for treatment of eclamptic convulsions. In most situations, clinical assessment of deep tendon reflexes, respirations, and urine output is adequate to monitor maternal magnesium toxicity without the need to determine actual maternal serum magnesium levels.

Eclampsia remains one of the leading causes of maternal and perinatal mortality in many parts of the world. Although it is becoming a rare complication in the Western world, it is still a major health problem in developing countries. Prompt treatment of convulsions, control of severe hypertension, stabilizing the mother and delivery are the basic principles of management of eclampsia[1]. Although several drugs have been used for the management of eclampsia throughout the world, the three most widely used today are magnesium sulfate[2-6], diazepam[7,8] and phenytoin[9,10]. The widespread use of magnesium sulfate in the United States is based primarily on empiric data. In Thailand, there was a report of 298 cases of eclampsia treated from 1967 to 1974

* Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok 10400, Thailand.

at Siriraj Hospital, Medical School, Bangkok. For the first 3 years of the study period, convulsions were controlled by injection of paraldehyde and chlorpromazine; diazepam was used thereafter[11]. There were also reports from two other medical schools, using magnesium sulfate for treatment of eclampsia, published in local Thai journals[12,13]. The evaluation of a drug used in the treatment of eclampsia has usually been difficult because other agents have been used as well. There is now compelling evidence in favour of magnesium sulfate, rather than diazepam or phenytoin, for the treatment of eclampsia[14].

Rajavithi Hospital (former Women's Hospital), Bangkok, Thailand is a tertiary care referral center. In the past, the treatment of eclampsia varied greatly. Since 1977 treatment of all cases of eclampsia at Rajavithi Hospital has been standardized by using Chesley and Tepper's regimen[3]. From 1977 to 1986, there were 206 eclamptic patients with a maternal mortality of 3.4 per cent and perinatal mortality of fetuses weighing 1,000 g or more of 12.35 per cent. Treatment guidelines have been used to the present time. The objectives of this study were to evaluate the magnesium sulfate regimen and maternal and perinatal outcomes in eclamptic patients during the period 1987 to 1996.

MATERIAL AND METHOD

This is a retrospective review of 90 eclamptic patients treated between 1987 and 1996, at Rajavithi Hospital. Pregnant women presenting to the hospital with eclampsia were considered for entry into the study regardless of any previous anticonvulsant therapy received. The regimen for management of eclamptic patients was as follows: Magnesium sulfate 3 g (30 ml of a 10 per cent solution) was given intravenously slowly over 3-5 minutes to stop the convulsion. This was immediately followed by 10 g of magnesium sulfate given intramuscularly (10 ml of a 50 per cent magnesium sulfate solution into the upper outer quadrant of each buttock), to prevent recurrence of convulsions. Subsequent doses of 5 g were given at intervals of four hours, into alternating buttocks, provided that, on assessment, the patellar reflexes were present, the respirations were not depressed, and urine output was at least 100 ml during the previous 4 hours. This dose of magnesium sulfate was continued for 24 hours after delivery.

Intermittent intravenous bolus Nepresol® (dihydralazine methane sulfonate) 5 mg was given to control hypertension when the diastolic blood pressure was 110 mmHg or greater. The blood pressure was monitored every 5 minutes. If the diastolic blood pressure was not lowered to about 100 mmHg in 20 minutes, a 10 mg dose was administered and its effects monitored.

In case of eclampsia before delivery, as soon as the patient was fully conscious and oriented, she was evaluated for delivery. The state of the cervix and station of the fetal presenting part were ascertained. The delivery was by vaginal or cesarean birth, depending on fetal and maternal conditions.

RESULTS

In the 10 years between 1987 and 1996, there were 167,200 deliveries and 90 eclamptic patients at Rajavithi Hospital, giving an incidence of eclampsia of 1 per 1,857 deliveries. Because this is a tertiary care center, 18 of the 90 eclamptic patients were referred cases.

The mean age of the patients was 24.50 ± 5.94 years (range 14 - 39 years) (Table 1). The range of gravidity was 1 - 6 (Table 2). There were 50 antepartum eclampsias (55.5%), 25 intrapartum eclampsias (27.8%) and 15 postpartum eclampsias (16.7%). Of 15 cases of postpartum eclampsia, 7 cases occurred following cesarean section, 3 cases following normal vaginal delivery, 2 cases following vacuum extraction, and 1 case each following forceps extraction, breech assisted and twin delivery (spontaneous *vs* breech assisted). The onset of convulsion in postpartum eclampsia most commonly occurred within 2 hours (46.7%) (Table 3).

Table 1. Age of 90 eclamptic patients Rajavithi Hospital, 1987-1996.

Age (yrs)	Cases	%
14	1	1.1
15 - 19	19	21.1
20 - 24	33	36.7
25 - 29	19	21.1
30 - 34	9	10
35 - 39	9	10

Mean age ± SD = 24.50 ± 5.94 years (range 14 - 39)
SD = standard deviation

Table 2. Gravidity of 90 eclamptic patients Rajavithi Hospital, 1987-1996.

Gravida	Cases	%
1	60	66.7
2	15	16.7
3	9	10
4	4	4.4
5	1	1.1
6	1	1.1

Table 3. Onset of convulsion in 15 cases postpartum eclampsia Rajavithi Hospital, 1987-1996.

Onset	Cases	%
within 2 h	7	46.7
between 4-8 h	3	20
after 8 h - 12 h	2	13.3
after 12 h	3	20

Table 4. Method of delivery in 75 cases of antenatal eclampsia Rajavithi Hospital, 1987-1996.

Methods	Cases	%
Cesarean section	57	76
Forceps extraction	9	12
Vacuum extraction	5	6.7
Spontaneous delivery	1	1.3
Hysterotomy	2	2.7
Induced abortion	1	1.3

Table 5. Indication of cesarean section in 57 eclamptic cases Rajavithi Hospital, 1987-1996.

Cephalopelvic disproportion	7	
Twins	5	
Failed induction	4	
Fetal distress	3	
Breech presentation	3	(54.4%)
Abruptio placentae	2	
Previous cesarean section	2	
Failed vacuum extraction	1	
Other medical complications	4	
Unfavorable cervix	26	(45.6%)

The most distant convulsion was 18 hours after delivery. Ten of these patients had mild preeclampsia before delivery, one patient was normotensive but became hypertension after delivery. None of the patients received magnesium sulfate therapy prior to the onset of convulsion. There were four severe preeclamptic patients who received magnesium sulfate therapy before cesarean delivery but this was not continued postoperatively.

Out of a total of 75 cases of antepartum and intrapartum eclampsia, 57 cases (76%) were delivered by cesarean section. In 9 cases, delivery was completed using forceps extraction and in 5 other cases, with vacuum extraction. Only 1 patient delivered spontaneously (Table 4). The indications for cesarean section are shown in Table 5.

Maternal Outcome

The following maternal complications in antepartum eclampsia were recorded:

Abruptio placentae	2 cases
HELLP syndrome	1 case
Pulmonary edema	1 case
Retinal detachment	1 case
Postpartum psychosis	1 case
Cerebral hemorrhage	3 cases

There were three maternal deaths and the maternal mortality was 3.3 per cent (3/90).

Case Mortality

Case 1.

A 32 - year - old primigravida woman with antepartum eclampsia was transferred from a regional hospital in a comatose condition, pupils dilated and not responding to light. Reflexes were negative. Neuromedical consultation confirmed brain death. The patient underwent cesarean section and a 1,400 g stillborn female baby was delivered. The patient had 25 per cent placental abruption. Following the cesarean section, she was maintained for three days on a continuous infusion of pressor agents and a respirator until she expired.

Case 2.

A 23 - year - old primigravida woman with antepartum eclampsia was transferred from a private clinic. On admission, she was rigid with unequal response of the pupils noted. A magnesium sulfate regimen was given and CT scan performed, showing intracerebral hemorrhage. A cesarean section was carried out under general anesthesia and

a live, female, 2,450 g infant delivered. Following the procedure, the neurosurgeon performed a craniotomy to remove the clot. The patient was maintained for three days on continuous infusion of pressor agents and a respirator until her death.

Case 3.

A 23 - year - old patient, gravida 3, para 1-0-1-1, antepartum eclampsia, was transferred from a regional hospital. Before her transfer, she had developed the symptoms of headache and epigastric distress, which her physician attributed to gastritis. By the time of her admission, she was unconscious, had flaccid right extremities and somewhat dilated pupils. Laboratory tests confirmed a diagnosis of HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome. A neurosurgeon was consulted and a subsequent CT scan showed basal ganglion hemorrhage with intraventricular hemorrhage. Labor was induced and the patient delivered a live, female infant weighing 1,570 g with an Apgar score of 2 at 1 min, 6 at 5 min. The baby died in the early neonatal period. The patient underwent ventriculostomy and lapsed into deep coma, from which she never emerged. She was maintained for two days on a continuous infusion of pressor agents and respirator until she expired.

Perinatal Outcome

Table 6 gives the fetal results according to the birthweights of infants of eclamptic mothers. Among antepartum and intrapartum eclampsias, there were 9 perinatal deaths out of 77 cases (11.7%). The most common causes of fetal death were prematurity and fetal asphyxia.

DISCUSSION

The clinical management of patients with eclampsia is definitive. Definitive therapy consists of treating and preventing convulsions, controlling blood pressure, and instituting delivery. Treatment and prevention of convulsions is based on the parenteral use of magnesium sulfate. Magnesium sulfate is highly effective in preventing convulsions in women with preeclampsia and in stopping them in eclamptic patients. Pritchard[2] as well as Chesley and Tepper[3] observed that the concentration of magnesium in plasma rose rather slowly after intramuscular injection, requiring from 90 to 120 minutes to attain maximal levels. Accordingly, they combined an intravenous injection with the initial intramuscular dose of 10 g; Pritchard used 4 g and Chesley and Tepper 3 g as the priming intravenous dose. They also increased the frequency of the subsequent intramuscular doses of 5 g to every four hours. In view of Thai patients having smaller frames than Western patients, Rajavithi Hospital adopted Chesley and Tepper's regimen. Intramuscular rather than intravenous administration of magnesium sulfate is preferred at Rajavithi Hospital, in the belief that it is just as efficacious, is safer from the viewpoint of sudden respiratory depression, and, in restless patients, is easier to administer. Any of the initial doses described is safe, but subsequent doses may not be unless certain precautions are observed. The second or any later dose of magnesium sulfate is withheld if the knee jerk is absent, and not given until the reflex returns. In view of clinical practice, precautionary criterion for using magnesium sulfate are very important, and monitoring serum levels of

Table 6. Fate of fetus in 75 cases of eclampsia before delivery Rajavithi Hospital, 1987-1996.

Weight (g)	Total fetus	Stillbirth	Neonatal death	Perinatal death	Living
1,000 - 1,499	20	2	2	4	16
1,500 - 1,999	10	1	2	3	7
2,000 - 2,499	14	0	0	0	14
2,500 - 2,999	17	0	1	1	16
3,000 - 3,499	13	1	0	1	12
3,500 - 3,999	3	0	0	0	3
Total	77*	4	5	9	68

* Excluding 3 nonsurvivors weighing less than 1,000 g
* Including 5 sets of twins

magnesium sulfate should not replace regular careful clinical assessment of the patient[4]. There have been concerns about the effect of magnesium sulfate on neonates. Although Lipsitz and English[15] suggested that hypermagnesemia in newborn infants of mothers treated with magnesium sulfate might have an adverse depressive effect, the findings of Stone and Pritchard[16] dispel this implied threat. They did not observe neonatal compromise after intramuscular therapy with magnesium sulfate. No deleterious effect upon either fetus or newborn was noted.

A major concern with pregnancy - induced hypertension is maternal intracranial hemorrhage. Magnesium sulfate, while an effective anticonvulsant agent, does not substantially affect blood pressure; therefore, if blood pressure control is necessary, additional agents are mandatory[17]. The objective of antihypertensive treatment is to prevent intracranial bleeding and left ventricular failure[18]. If the diastolic blood pressure exceeded 110 mmHg, hydralazine was administered. A 5 mg test dose of hydralazine was injected as bolus intravenously and the blood pressure monitored every 5 minutes. If the diastolic pressure was not lowered to about 100 mmHg in 20 minutes, a 10 mg dose was similarly administered, and its effects were monitored as described[5]. Assali[19] regards the slow infusion of hydralazine as ineffective and prefers the use of single injections, as does Chesley[20] and Pritchard[5]. According to Sibai[21], the administration of hydralazine by a continuous infusion method is no longer used because of the high incidence of fetal distress associated with that therapy.

Even though prompt and proper treatment of convulsions and hypertension have priority in the sequence of treating eclampsia, the stabilization of the eclamptic patient before delivery is another important process. The immediate induction of labor and delivery of the infant by cesarean section may induce a catastrophic insult on the already hypoxemic and acidotic mother and fetus. For this reason, before delivering the baby, it is essential to allow time for both the mother and the fetus to recover from the metabolic insult that follows major motor seizures[22]. In general, once the mother becomes responsive and oriented, one can presume that sufficient recovery has taken place and efforts to deliver the infant can be started safely. The ideal period for stabilization after arresting the convulsions has been variously defined. Usually, this degree of improvement will occur within three to six hours[23] or four to eight hours[22] from the last convulsion.

The most common method of delivery for eclampsia before delivery in this study was cesarean section (76%). Twenty six cases (45.6%) (Table 5) underwent cesarean section due to unfavorable cervices. Cesarean section has certain advantages over induction of labor in women with eclampsia. Fetuses with gross placental insufficiency will not withstand the stress and strain of labor and, unless delivery is imminent, they are better delivered by section. The arguments against induction of labor and for delivery by cesarean section in women with cervices unfavorable for the induction of labor are: (1) Labor often precipitates convulsions, perhaps because of the rise in blood pressure. (2) Induction of labor is more likely to be successful if the fetal membranes are ruptured. If the cervix is long, firm, and posterior, the membranes are not so accessible for artificial rupture. Moreover, if the fetal presenting part is not engaged and if labor does ensue, prolapse of the umbilical cord becomes a theoretical hazard. (3) Time would be lost in unsuccessful attempts at induction of labor. (4) If the induction succeeded, the labor might be protracted, which would (a) increase the possibility of more convulsions and (b) necessitate prolonged sedation of the patient and her fetus. (5) The sooner the fetus is removed from the hostile uterine environment, the better its chance of survival, especially because (6) uterine hypertonus is characteristic of eclampsia and the superimposition of labor might well impair the placental blood flow and further jeopardize the fetus[20].

Ten out of fifteen women with postpartum eclampsia had clinically mild preeclampsia and one was normotensive when convulsions occurred. None received magnesium sulfate therapy prior to convulsions. Of course, the risk of convulsions is greater in clinically severe than in clinically mild preeclampsia, but reliance on the level of blood pressure for grading severity can be disastrous. Chesley[20] almost routinely administers parenteral magnesium sulfate during spontaneous or induced labor in women with preeclampsia, even of apparently mild degree. In his experience, no preeclamptic patient treated with magnesium sulfate has had a convulsion.

Pregnancies complicated by eclampsia are associated with poor maternal and perinatal outcomes depending on the experience and facilities of the reporting center, as well as on the condition of the patient on admission to the center. There were three maternal deaths (3.3%) among 90 cases of eclampsia managed at Rajavithi Hospital. However, it is important to note that these patients were referred and admitted in a moribund state with intracerebral hemorrhage.

The perinatal death rates are based upon all cases of antepartum and intrapartum eclampsia; by exclusion of fetuses weighing less than 1,000 g, the perinatal loss was 11.7 per cent (Table 6). The inclusion of postpartum cases is not logical because the mothers had preeclampsia rather than eclampsia when the infants were born[20]. Pritchard's perinatal loss in antenatal eclampsia was 9.9 per cent by exclusion of fetuses weighing less than 1,000 g, and Chesley's was 15.9 per cent[5,20].

In conclusion, magnesium sulfate is the drug of choice for the prevention or treatment of eclamptic convulsions. Therapy with magnesium sulfate should be initiated intravenously with a loading dose followed by an intramuscular injections regimen. Severe hypertension with a diastolic blood pressure of 110 mmHg or greater increases the maternal risk of cerebrovascular accidents and congestive heart failure. Reducing diastolic blood pressure by hydralazine is used for the treatment of acute hypertension, has almost complete efficacy, and is safe. Although the most effective treatment is delivery, other considerations also affect management.

ACKNOWLEDGEMENT

The author wishes to thank Stephen Hamann for assistance in editing this article.

(Received for publication on April 17, 1998)

REFERENCES

1. Leveno KJ, Whalley PJ. Acute hypertension in pregnancy. In : Quilligan EJ, editor. Current therapy in obstetrics and gynecology 2. Philadelphia : WB Saunders, 1983 : 3-4.
2. Pritchard JA. The use of the magnesium ion in the management of eclamptogenic toxemias. Surg Gynecol Obstet 1955 ; 100 : 131-40.
3. Chesley LC, Tepper I. Plasma levels of magnesium attained in magnesium sulfate therapy for preeclampsia and eclampsia. Surg Clin North Am 1957 ; 37 : 353-67.
4. Zuspan FP. Treatment of severe preeclampsia and eclampsia. Clin Obstet Gynecol 1966 ; 9 : 954-72.
5. Pritchard JA, Pritchard SA. Standardized treatment of 154 consecutive cases of eclampsia. Am J Obstet Gynecol 1975 ; 123 : 543-52.
6. Pritchard JA, Cunningham FG, Pritchard SA. The Parkland Memorial Hospital protocol for treatment of eclampsia : evaluation of 245 cases. Am J Obstet Gynecol 1984 ; 148 : 951-63.
7. Lean TH, Ratnam SS, Sivasamboo R. Use of benzodiazepines in the management of eclampsia. J Obstet Gynaecol Br Commonw 1968 ; 75 : 856-62.
8. Crowther C. Magnesium sulfate versus diazepam in the management of eclampsia : a randomized controlled trial. Br J Obstet Gynaecol 1990 ; 97 : 110-7.
9. Domisse J. Phenytoin sodium and magnesium sulfate in the management of eclampsia. Br J Obstet Gynaecol 1990 ; 97 : 104-9.
10. Coyaji KJ, Otiv SR. Single high dose of intravenous phenytoin sodium for the treatment of eclampsia. Acta Obstet Gynecol Scand 1990 ; 69 : 115-8.
11. Porapakkham S. An epidemiologic study of eclampsia. Obstet Gynecol 1979 ; 54 : 26-30.
12. Tannirandorn Y, Witoopanit P. Eclampsia at Chulalongkorn Hospital : eight - year experience. Chulalongkorn Hosp Gaz 1987 ; 31 : 871-82.
13. Tongsong T, Simarak S. Seven - year experience of eclampsia at Maharaj Nakorn Chiangmai Hospital. Siriraj Hosp Gaz 1991 ; 43 : 545-52.
14. The Eclamptic Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. Lancet 1995 ; 345 : 1455-63.
15. Lipsitz PJ, English IC. Hypermagnesemia in the newborn infant. Pediatrics 1967 ; 40 : 856-62.
16. Stone SR, Pritchard JA. Effect of maternally administered magnesium sulfate on the neonate. Obstet Gynecol 1970 ; 35 : 574-7.
17. Cotton DB, Gonik B, Dorman KF. Cardiovascular alterations in severe pregnancy - induced hyper-

tension : acute effects of intravenous magnesium sulfate. Am J Obstet Gynecol 1984 ; 148 : 162-5.
18. Arias F. Practical guide to high - risk pregnancy and delivery. 2nd ed. St. Louis : Mosby Year Book, 1993 : 183-210.
19. Assali NS. Hemodynamic effects of hypotensive drugs used in obstetrics. Obstet Gynecol Surv 1954 ; 9 : 776-94.
20. Chesley LC. Hypertensive disorders in pregnancy. New York : Appleton - Century - Crofts, 1978 : 341-57.
21. Sibai BM. Eclampsia : VI. Maternal - perinatal outcome in 254 consecutive cases. Am J Obstet Gynecol 1990 ; 163 : 1049-55.
22. Gant NF Jr, Worley RJ. Hypertension in pregnancy. New York : Appleton - Century - Crofts, 1980 : 107-65.
23. Scott JR. Hypertensive disorders of pregnancy. In : Scott JR, DiSaia PJ, Hammond CB, Spellacy WN, editors. Danforth's obstetrics and gynecology. 7th ed. Philadelphia : J.B. Lippincott, 1994 : 351-65.

การดูแลรักษาทางคลินิกและผลของการรักษาผู้ป่วยโรคชักแห่งครรภ์ที่โรงพยาบาลราชวิถี

*ประธาน จินายน, พ.บ.**

วัตถุประสงค์ในการศึกษาเพื่อทบทวนประสบการณ์ในการดูแลรักษาทางคลินิก และผลของการรักษาผู้ป่วยโรคชักแห่งครรภ์ที่โรงพยาบาลราชวิถี มาตรฐานการรักษาผู้ป่วยโรคชักแห่งครรภ์ทุกรายประกอบด้วย การฉีดแมกนีเซียมซัลเฟตเพื่อควบคุมการชักทางหลอดเลือดดำและทางกล้ามเนื้อโดยวิธีการของ Chesley และ Tepper ฉีด hydralazine ทางหลอดเลือดดำเป็นครั้งคราว เพื่อลดความดันโลหิตไดแอสโทลิกที่สูงกว่า 110 มิลลิเมตรปรอท และพิจารณาให้คลอดเมื่อผู้ป่วยรู้สึกตัวดีแล้ว ผลการศึกษาพบว่าในช่วงระยะ 10 ปี มีการคลอด 167,200 ราย มีผู้ป่วยโรคชักแห่งครรภ์ 90 ราย คิดเป็นอุบัติการของโรคนี้ 1 ต่อการคลอด 1,857 ราย มีมารดาตายจากเลือดออกในสมอง 3 ราย (ร้อยละ 3.3) และภาวะแทรกซ้อนที่รุนแรงพบบ่อยในผู้ป่วยที่เกิดชักก่อนการคลอด อัตราตายปริกำเนิดของทารกที่มีน้ำหนัก 1,000 กรัมหรือมากกว่า เฉพาะในผู้ป่วยที่เกิดชักก่อนการคลอดเท่ากับร้อยละ 11.7

แมกนีเซียมซัลเฟตเป็นยาที่เลือกสรรใช้รักษาการชักในผู้ป่วยโรคชักแห่งครรภ์ การประเมินทางคลินิกโดยอาศัยการตรวจรีเฟลกซ์หัวเข่า การหายใจ และปริมาณการขับถ่ายปัสสาวะ สามารถใช้เฝ้าระวังการเกิดพิษของแมกนีเซียมซัลเฟตได้โดยไม่จำเป็นต้องหาระดับแมกนีเซียมในซีรัม

* กลุ่มงานสูติ-นรีเวชกรรม, โรงพยาบาลราชวิถี, กรุงเทพฯ 10400