Pregnancy Hypertension 17 (2019) 100–103

Contents lists available at ScienceDirect

Pregnancy Hypertension

journal homepage: www.elsevier.com/locate/preghy

Significance of pre-hospital care to reduce the morbidity of eclampsia in rural Zambia

Yasuhiro Miyoshi[a], Keiichi Matsubara[b], Norimi Takata[c], Yasunori Oka[b,*]

[a] Zimba Mission Hospital, Zimba, Zambia
[b] Ehime University, Ehime, Japan
[c] Shikoku University, Tokushima, Japan

ARTICLE INFO

Keywords:
Eclampsia
Magnesium sulfate
Preeclampsia
Zambia

ABSTRACT

Objectives: Preeclampsia (PE) is the 2nd leading cause of maternal mortality in developing countries. Maternal deaths caused by PE mainly result from eclampsia. The aim of this study was to survey the current status of PE at a local hospital in Zambia and identify preventive measures against eclampsia.
Study design: The obstetric data of normal pregnant women and patients complicated with gestational hypertension (GH), PE, and eclampsia in 2017 at Zimba Mission Hospital, Zambia were collected from admission and delivery registries and analyzed.
Main outcome measures: The mode of delivery, maternal and perinatal mortality.
Results: Among 1704 deliveries, 42 women (2.5%) were complicated with hypertensive disorders of pregnancy (HDP) (GH: 17, PE: 25). There were 2 stillbirths and 1 neonatal death in PE. Magnesium sulfate ($MgSO_4$) was administered to severe PE patients (11 cases) based on the Pritchard regimen for a resource poor setting. No eclampsia happened after starting $MgSO_4$. All eclampsia (8 cases) happened out of hospital at the gestational age of 35–40 weeks. All the eclamptic patients were primigravidae aged 15–23 years old. $MgSO_4$ injection was started on admission. Cesarean section was performed in 7 cases. All the patients of PE including eclampsia were discharged without any sequelae.
Conclusion: The Pritchard regimen is considered to be suitable in the setting. However, the morbidity of eclampsia was high out of hospital. We have to educate pregnant women about the risks of PE and encourage the measurement of blood pressure at health facilities.

1. Introduction

Preeclampsia (PE) is a hypertensive disorder of pregnancy (HDP) that is associated with proteinuria or some organ failure. PE is a major underlying disease of late fetal and early neonatal death, accounting for between 1 in 10 and 1 in 4 perinatal deaths respectively [1]. Maternal death from PE is mainly caused by eclampsia [2]. While eclampsia is really rare in developed countries, it is still occurring in developing countries. In most of Western Europe and North America, the incidence is 2–3 per 10,000 deliveries [3,4] compared to 13 per 1000 deliveries in developing countries [5]. Its mortality in developing countries is up to 15% [6]. According to WHO, massive hemorrhage is the first leading cause of maternal mortality while HDP is the 2nd cause in developing countries, accounting for 14.0% of all maternal deaths [7]. In sub-Saharan Africa, 1 of every 1500 pregnancies ends in a maternal death attributable to eclampsia/PE [1].

It is important to understand why the incidence and case fatality rates associated with eclampsia/PE are high in developing countries to find the measures to reduce them. Usually, pregnant women have poorer access to adequate medical care in rural areas than in urban areas in developing countries. However, hospital-based data in rural areas is scarce. So, it is necessary to know the current status of PE in rural areas of Africa.

The aims of this study were to survey the current status of PE at a local hospital in Zambia and identify preventive measures against eclampsia.

2. Materials and methods

This retrospective cross-sectional study was conducted at Zimba

Abbreviations: PE, preeclampsia; GH, gestational hypertension; HDP, hypertensive disorders of pregnancy

* Corresponding author at: Shitsukawa, Toon, Ehime 791-0295, Japan.
E-mail address: oka.yasunori.mm@ehime-u.ac.jp (Y. Oka).

https://doi.org/10.1016/j.preghy.2019.05.008
Received 22 October 2018; Received in revised form 27 February 2019; Accepted 8 May 2019
Available online 09 May 2019

Mission Hospital in Southern Province of Zambia. This district hospital is located 400 km south of Lusaka, the capital city of Zambia. It accepts patients referred from many health centers in the catchment area, in which the population is 98,000. In Zambia, pregnant women and their families are responsible for their transport from home to the health center in their catchment area. Physicians are not affiliated with the health centers and there is no ultrasonography to assess the fetal condition in any institute. Registered nurses or midwives provide medical care to the patients in such institutes. The nurses/midwives transfer patients with a potential maternal or fetal complication to the district hospital by ambulance or transport arranged by the patient's family. However, it usually takes several hours for the patient to reach the hospital. It takes much longer at nighttime or on a rainy day because of poor road condition. Pregnant women living far from the hospital can stay in the Mother's shelter beside the hospital free of charge while waiting for the onset of labor. High-risk women such as those with breech presentation, multiple pregnancy, or HDP are supposed to be admitted at the antenatal ward in the hospital. There was an obstetrician at this hospital but no pediatrician. Therefore, the obstetrician served both mothers and neonates.

We extracted data from admission and delivery registries which collected information of all women who delivered and neonates born at Zimba Mission Hospital. The obstetric data of the patients complicated with HDP including PE and eclampsia from January 1st through December 31th in 2017 were all extracted and analyzed. The patients were categorized into gestational hypertension (GH) and PE. PE was subcategorized into PE with or without eclampsia. The information on maternal characteristics such as maternal age, parity and gestational age of delivery was collected in each category. Perinatal and maternal outcomes were analyzed in each category. The information on the mode of delivery, birthweight, number of stillbirth, Apgar score and number of neonatal death was collected as perinatal outcome. The information on treatment (e.g. the use of magnesium sulfate ($MgSO_4$)), occurrence of eclampsia, maternal sequelae and mortality was collected as maternal outcome. $MgSO_4$ was given in the Pritchard regimen for resource poor settings. 14 g of $MgSO_4$ was given as a loading dose (4 g was given intravenously over 5–20 min and 5 g was given intramuscularly on each buttock). Afterwards, 5 g was given intramuscularly every 4 h as a maintenance dose. $MgSO_4$ administration was continued for 24 h after delivery.

Descriptive statistics were presented as means (± SD) and percentages. Unpaired *t*-test was used to compare data in the groups and χ square test for qualitative variables. Statistical analysis was performed using GraphPad Prism, version 6 (GraphPad Software, La Jolla, CA).

Research ethics committee approval was obtained at Zimba Mission Hospital, Zambia. No ethical issues arose during this study and no consent was necessary as the study was a retrospective one and all the data were anonymous.

3. Results

Maternal characteristics are shown in Table 1.

Among the 1704 deliveries at the hospital, 42 women (2.5%) were complicated with HDP. These 42 cases consist of 17 cases of GH and 25 cases of PE including 8 cases of eclampsia. Among the 17 cases of PE without eclampsia, 11 were severe and 6 were mild.

Incidence of PE was 1.5% (25/1704): 2.5% (14/567) for primigravidae and 1.0% (11/1124) for multigravidae ($p < 0.05$). Incidence of eclampsia was 0.46% (8/1704): 1.4% (8/567) for primigravidae and 0% (0/1,1124) for multigravidae ($p < 0.0005$).

Eclamptic patients were all primigravidae and 75% (6/8) of them were teenagers. Mean age of eclamptic patients was much younger than normotensive women ($p < 0.05$).

Rate of preterm birth was 19.7% (302/1,532), 28.6% (4/14) and 34.8% (8/23) in normotensive, GH and PE group respectively.

Cesarean section rate was 17.3%, 17.7%, 35.3% and 87.5% in normotensive, GH, PE w/o eclampsia and eclampsia group respectively ($p < 0.0001$: normotensive vs. eclampsia).

Perinatal outcomes are shown in Table 2. There were 2 stillbirths (8%) and 1 neonatal death (4%) due to severe birth asphyxia in PE group. Low birth weight (< 2500 g) accounted for 12.5% (302/1697), 35.2% (6/17 cases) and 28.0% (7/25 cases) in normotensive, GH and PE group respectively.

$MgSO_4$ was administered to severe PE patients (11 cases) to prevent the occurrence of eclampsia. No eclampsia had happened after we began $MgSO_4$ injection. However, all eclampsia happened out of our hospital. $MgSO_4$ was injected to all the patients. All the mothers with PE including eclampsia were discharged from our hospital without any sequelae.

4. Discussion

The incidence of eclampsia at the hospital was 8 out of 1704 deliveries (0.47%). This rate might be relatively low in Sub-Saharan African countries [5]; however, it is higher compared to the standard of developed countries [3,4]. In Zimba, eclampsia accounted for very high 32% of PE, whereas only 0.8% of preeclamptic cases progress to eclampsia in developed countries [8]. Moreover, all the patients were primigravidae. Our finding is in keeping with similar studies that found eclampsia to occur more in the primigravidae [9,10].

The problem we have found is that all the eclampsia happened out of hospital. Antenatal visits in Zambia are performed no more than 4 times: the first visit by 16 weeks, the second visit at 24–28 weeks, the third visit at 32 weeks, and the fourth visit at 36 weeks. Antenatal visit should be more frequent after 8 months of pregnancy for early identification of HDP, especially for high-risk cases such as primigravidae. Blood pressure is supposed to be measured even at rural health centers on every antenatal visit; however, sometimes this procedure is not done due to the malfunction or absence of the blood pressure measurement apparatus, or simply due to lack of batteries. Poor assessment of high blood pressure at rural health centers is also a challenge. Even if patients are asked to visit the hospital due to hypertension, etc., some of them don't visit because they cannot understand the risks well or they do not have enough money for the transportation. Those eclamptic cases might have been prevented if blood pressure was regularly measured, correctly assessed and referred to the hospital earlier. Furthermore, it is deemed that education to pregnant women is essential because they tend to visit the health facilities only after the condition gets really serious. We need to encourage them to go to the antenatal clinic for blood pressure check and go to health facilities as soon as possible when they have some danger signs such as headache, blurred vision and epigastralgia, etc. It is also important to educate the staff at health centers. They need to detect the problems and refer the patients to the hospital with proper timing.

$MgSO_4$ is an affordable and effective treatment for PE and eclampsia. When properly administered, $MgSO_4$ reduces the onset of eclamptic seizures by 58% for preeclamptic patients and eclamptic patients treated with $MgSO_4$ have a 52% and 67% lower recurrence of convulsions than those treated with diazepam and phenytoin respectively [8]. In developed countries, intravenous $MgSO_4$ therapy is typically administered following the Zuspan regimen: an initial loading dose of 4 g $MgSO_4$ over 15–20 min followed by a 1–2 g/h maintenance dose. Use of an infusion pump is recommended to provide accurate delivery of $MgSO_4$ [11]. However, infusion pump is not available in developing countries like Zambia due to the cost [12]. Thus, the protocol recommended by University Teaching Hospital, Zambia is being followed at Zimba Mission Hospital. It is based on the Pritchard regimen [11]. Clinical practice patterns on the use of $MgSO_4$ are different depending on the regions. The Pritchard regimen and its modifications are more common in Africa, whereas the Zuspan regimen and its modifications are more common in Latin America and Asia [13]. The former regimen prevented the occurrence of eclampsia in all severe PE

Table 1
Maternal characteristics.

Variables	Normotensive		GH		PE w/o Eclampsia		Eclampsia		
	n = 1,662		n = 17		n = 17		n = 8		
Age (n)									p < 0.01
Mean ± SD (y.o.)	26.3 ± 8.1		29.8 ± 7.6		30.1 ± 9.8*		18.0 ± 2.6*		
< = 19	458	27.6%	3	17.6%	4	23.5%	6	75.0%	
20–34	850	51.1%	9	52.9%	5	29.4%	2	25.0%	
> = 35	346	20.8%	5	29.4%	8	47.1%	0		
Missing data	8	0.5%	0		0		0		
Parity (n)									p < 0.01
Mean ± SD	3 ± 3		3 ± 3		3 ± 3		0 ± 0*		
0	548	33.0%	5	29.4%	6	35.3%	8	100%	
1–3	568	34.2%	6	35.3%	4	24.5%	0		
> = 4	533	32.1%	5	29.4%	7	41.2%	0		
Missing data	13	0.8%	0		0		0		
Gestational weeks of delivery (n)									p < 0.01
Mean ± SD (weeks)	38.7 ± 2.7		37.6 ± 2.8		37.9 ± 2.3		38.6 ± 2.0		
< = 33	88	5.3%	2	11.8%	2	11.8%	0		
34–36	214	12.8%	2	11.8%	4	24.5%	2	25.0%	
37–41	1092	65.7%	9	52.9%	9	52.9%	6	75.0%	
> = 42	138	8.3%	1	5.9%	0		0		
Missing data	130	7.8%	3	17.6%	2	11.80%	0		
Mode of delivery									p < 0.0001
Vaginal delivery	1374	82.7%	14	82.4%	11	64.7%	1	12.5%	
Cesarean section	288	17.3%	3	17.7%	6	35.3%	7	87.5%*	

*: p < 0.05, vs. normotensive.

Table 2
Perinatal outcomes.

Variables	Normotensive		GH		PE w/o Eclampsia		Eclampsia		
	n = 1710		n = 18		n = 18		n = 8		
Birth weight (n)									p < 0.01
Mean ± SD (kg)	3.0 ± 0.6		2.9 ± 0.7		2.9 ± 0.8		3.2 ± 0.4		
< 1.5	26	1.5%	0		0		0		
1.5–2.5	186	10.9%	6	33.3%	7	38.9%	1	12.5%	
2.5–4.0	1440	84.2%	11	61.1%	10	55.6%	7	87.5%	
> 4.0	45	2.6%	1	5.6%	1	5.6%	0		
Missing data	13	0.7%	0		0		0		
Stillbirth (n)									
	34	2.0%	0		2	11.1%	0		
Apgar score at 5 min (n)									n.s.
Mean ± SD	9 ± 2		9 ± 1		8 ± 3*		8 ± 2		
< =6	62	3.6%	1	5.6%	2	11.1%	1	12.5%	
7–10	1,613	94.3%	17	94.4%	16	88.9%	7	87.5%	
Missing data	35	2.0%	0		0		0		
Neonatal death (n)									
	31	1.8%	0		0		1	12.5%	

*: p < 0.05, vs. normotensive.

cases without any serious complication of $MgSO_4$ in our facility. All the patients of PE including eclampsia were discharged without any sequelae. So, the protocol is considered to be suitable in a resource poor setting. Both the groups are comparable in terms of control and prevention of recurrence of convulsions, maternal and perinatal morbidity and mortality [14]. All health professionals not only at hospitals but also at health centers need to be appropriately trained in the use of $MgSO_4$.

High-income countries have been able to reduce both the incidence and case fatality rates associated with eclampsia by about 90% using a combination of early detection with blood pressure and urine protein measurement during perinatal care and increasing access to hospital care for timely induction of labor or cesarean delivery for women who developed severe PE [15]. So, eclampsia/PE related mortality in developing countries could also be improved by those effective interventions even if resources are poor. Those interventions are considered to reduce not only maternal mortality but also perinatal mortality.

This is an important study at a resource poor district hospital in sub-Saharan Africa as it documents the incidence and the problems of the 2nd most contributory cause of maternal death. This helps in decision-making and prioritization of health policies, programs, and funding to reduce maternal deaths.

There are some limitations of the study. The gestational age of the mothers on delivery might not be correct because the ultrasound in early pregnancy is not available at health centers and it is usually computed from last menstrual period they remember. It is difficult to distinguish if low birth weight is due to preterm labor or intrauterine growth retardation for the same reason. The population was too small to conclude that the protocol for the use of $MgSO_4$ based on the

Pritchard regimen was useful in this study. The rate of PE in the study might not reflect the rate in the whole district because some people deliver at home without any antenatal visit and others deliver at health centers without blood pressure properly measured.

5. Conclusion

We surveyed and evaluated the obstetric profile and morbidity of PE patients. The Pritchard regimen for MgSO4 use is considered to be suitable at a local health center and a hospital in Zambia. However, the morbidity of eclampsia is high out of hospital, especially for primigravidae. We have to educate pregnant women about the risks of PE and encourage the measurement of blood pressure at local health centers and hospitals so that early interventions can be done. Early interventions lead to the reduction of maternal and perinatal mortality due to PE.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Contribution to authorship

YM and KM conceived the idea and wrote the manuscript. KM performed statistical analysis. NT and YO reviewed the manuscript.

Declaration of Competing Interest

All authors report no conflict of interests in relation to this work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2019.05.008.

References

[1] S. Hodginsa, Pre-eclampsia as underlying cause for perinatal deaths: time for action, Global Health: Sci. Practice 3 (2015) 525–527.
[2] A.K. Lal, W. Gao, J.U. Hibbard, Eclampsia: maternal and neonatal outcomes, Pregnancy Hypertens. 3 (2013) 186–190.
[3] M. Knight, UKOSS, Eclampsia in the United Kingdom 2005, BJOG 114 (2007) 1072–1078.
[4] ACOG Committee on Obstetric Practice, ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists, Int J Gynaecol Obstet 77 (2002) 67–75.
[5] E.T. Agida, B.I. Adeka, K.A. Jibril, Pregnancy outcome in eclamptics at the University of Abuja Teaching Hospital, Gwagwalada, Abuja: A 3 year review, Niger J. Clin. Pract. 13 (2010) 394–398.
[6] L. Ghulmiyyah, B. Sibai, Maternal mortality from preeclampsia/eclampsia, Semin. Perinatol. 36 (2012) 56–59.
[7] L. Say, D. Chou, A. Gemmill, et al., Global causes of maternal death: a WHO systematic analysis, Lancet Glob. Health 2 (2014) e323–e333.
[8] EngenderHealth. Balancing the Scales: Expanding Treatment for Pregnant Women with Life-Threatening Hypertensive Conditions in Developing Countries, 2007. https://www.engenderhealth.org/files/pubs/maternal-health/engenderhealth-eclampsia-report.pdf/ (accessed 1.10.2018).
[9] C.O.U. Esike, U.I. Chukwuemeka, Q.B. Anozie, et al., Eclampsia in Rural Nigeria: the unmitigating catastrophe, Ann. Afr. Med. 16 (2017) 175–180.
[10] A.O. Fabamwo, O.I. Akinola, A.O. Tayo, et al., Socio-demographic characteristics of eclamptic patients at a tertiary institution in Lagos, Nigeria, Niger Med. Pract. 52 (2007) 91–93.
[11] E. Skerrett, E. Kommwa, K. Maynard, et al., Evaluation of a low-cost, low-power syringe pump to deliver magnesium sulfate intravenously to pre-eclamptic women in a Malawian referral hospital, BMC Pregnancy Childbirth 17 (2017) 191.
[12] E. Skryabina, T. Dunn, Disposable infusion pumps, Am. J. Health-Syst. Pharm. 63 (2006) 1260–1268.
[13] Q. Long, O.T. Oladapo, S. Leathersich, et al., Clinical practice patterns on the use of magnesium sulphate for treatment of pre-eclampsia and eclampsia: a multi-country survey, BJOG 124 (2017) 1883–1890.
[14] V. Kanti, A. Gupta, S. Seth, et al., Comparison between intramuscular and intravenous regimen of magnesium sulfate in management of severe preeclampsia and eclampsia, Int. J. Reprod. Contracept Obstet. Gynecol. 4 (2015) 195–201.
[15] R.L. Goldenberg, E.M. McClure, E.R. Macguire, et al., Lessons for low-income regions following the reduction in hypertension-related maternal mortality in high-income countries, Int. J. Gynaecol. Obstet. 113 (2011) 91–95.