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Use of Magnesium Sulphate in the Management of Severe Preeclampsia at the Centre University Hospital of Mother and Child (CHU-MEL) Cotonou Benin

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Abstract

Objectives: To evaluate professionals practices and the contribution of magnesium sulphate in a better medical care for persons with severe preeclampsia at CHU-MEL.

Materials and Method: We conducted a retrospective and cross-sectional study with the aim come up with a descriptive and analytical paper. Our study was conducted from January 15th, 2015 to July 15th, 2016, i.e. during eighteen (18) months. The sampling was exhaustive. The population was made of all patients admitted for severe preeclampsia with or without complications. Confidentiality requirements were met and informed consent obtained from all subjects. For the analytical study, the chi-square test was used and the difference was statistically significant with a p-value inferior than 0.05.

Results: The prevalence of preeclampsia during the study period was 7.70% (447/5805 deliveries). Out of the 312 files that we were able to find and exploit, 272 revealed that patients were administrated a dose of magnesium sulphate, at a frequency estimated at 87.18%. Irregularities were noted in the protocol implementation: the maintenance dose was administered in 30% of cases, as a slow infusion (66.33%), for less than 24 hours in 37.24% of cases, and under supervision only in 22.62% of cases. Primary and secondary prevention of eclampsia was achieved in 98.5% and 80% of cases, respectively. Respecting the duration of treatment significantly reduces the onset and recurrence of seizures (p=0.003 and p=0.004). Decreased reflexes and respiratory distress were noted in 34.78% and in 8.7% of cases respectively. The maternal lethality rate was 1.34% and the stillbirth rate was 11.40%.

Conclusion: Magnesium sulphate intake is undeniable in dealing with severe preeclampsia, but this solution/drug is misused at the CHU-MEL. Appropriate solutions must therefore be taken in the execution and monitoring of the protocol.

Keywords: Severe preeclampsia; Magnesium sulphate

Introduction

3 to 5% of pregnant subjects suffer from high blood pressure which is one of the main causes of maternal and neonatal morbidity and mortality, particularly in developing countries [1-3].

Introduced in the medical field since 1905, magnesium sulphate ($MgSO_4$) was used for the first time in 1925 to treat convulsions. It was recommended by the WHO as the most effective, safe and cheapest drug to treat Severe preeclampsia and eclampsia [1,4]. Several studies show that it is the best cure to prevent patients from re-suffering from eclampsia crisis, as it is more effective than Phenytoin [(5.7%) vs. (17.1%)] or Diazepam [(13.2%) vs. (27.9%)] [2].

The exact mode of action of magnesium sulphate in pre-eclampsia remains to be elucidated, but it has been proved that it prevent calcium from entering into the cell [4,5].

In Benin, particularly at the CHU-MEL, it is the first-line molecule used when it comes to curing severe preeclampsia. However its use is subject to certain shortcomings.

To evaluate how health professionals use the magnesium sulphateand how it helps in the cure of severe preeclampsia in CHU-MEL.

Materials and Method

We conducted a retrospective, cross-sectional, descriptive and analytical study from January 15th, 2015 to July 15th, 2016, i.e. eighteen (18) months. The sampling was exhaustive. The patients were pregnant, parturient, or childbirth admitted for pre-eclampsia associated with at least one severity criterion, and treated with magnesium sulfate according to the ZUSPAN protocol. It was:

- Severe hypertension with PAS ≥ 160 mm Hg (systolic blood pressure) and / or PAD ≥ 110 mm Hg (Diastolic blood pressure);

- Renal injury with oliguria (<500 ml / 24h) or serum creatinine greater than 135 µmol / L or proteinuria greater than 5 g/L;

- Acute Lung Edema (OAP) or persistent epigastric bar or HELLP Syndrome;

- Eclampsia or rebellious neurological disorders;

- Thrombocytopenia <100G/L and

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- A Retro Placental Hematoma (HRP) or fetal repercussion

The Zuspan protocol was conducted as it follows: Administration of a loading dose of 4 g in IVL of magnesium sulfate for 15 to 20 minutes, then a maintenance dose of 1g per hour administrated with an electric syringe. In the event of recurrence of seizures, a bolus of 2 g is injected within 5 minutes. The duration of the treatment is 24 hours following the delivery or the last crisis depending on the case were not included, patients with mild or moderate preeclampsia without severity criteria or severe preeclampsia, who did not benefit from the magnesium sulfate protocol or who refused to participate in the study.

The variables studied were: sociodemographic, Clinic, paraclinical, therapeutic related to the protocol by the magnesium sulfate (protocol monitoring, progression of severe pre-eclampsia under the protocol, side effects developed, maternal complications occurring under this protocol); Prognosis (maternal and fetal).

The analysis and statistical tests were carried out on the "Epi Info" software by comparing the mean and standard deviations, the qualitative variables by the Student test, the dichotomous variables by the Pearson chi square, accepting a significant probability $p \leq 0.05$. Confidentiality was respected. The patients were informed and their consent obtained through signature. Confidentiality was also kept during data collection.

Results

The prevalence of preeclampsia during the study period was 7.7% (447/5805 deliveries).

Frequency of use of magnesium sulphate

Of the 312 files examined, 272 patients had benefited from the administration of magnesium sulphate, i.e. a frequency of use of 87.18%.

Socio-demographic aspects

The average age was 23.6 years old. The patients were in primigravida (41.5%), nulliparous (48.2%) and mostly merchants (34.2%). Pregnancy was poorly monitored with less than 4 prenatal consultations (68.0%). The reference was the mode of admission in 76.1% of the cases by non-medical transport (61%). Previous history of vasculo-renal syndrome was found in previous pregnancies in 13.6% (37/272); 12 cases of diabetes (4.4%); 06 cases of HIV infection (2.2%) and 5 cases of hemoglobinopathy (1.8%).

Clinical aspects and explorations

Our sample included: 162 pregnant women (59.6%); 89 parturient (32.7%); 21 delivered (7.7%). Pregnancy was at term in 43.0% (108/251) of the cases. There were 222 singleton birth pregnancies; 28 twin pregnancies and 01 trimellular pregnancies. The most severe signs of severity were severe hypertension with SAD ≥ 160 mm Hg and TAD ≥ 110 mm Hg in 73.90% and 63.6% of cases respectively, followed by eclampsia in a proportion of 29.4% (Table 1).

Treatment

Process of $MgSO_4$ protocol: The Zuspan protocol was the one applied with a loading dose of 4G to IVL in 15 to 20 minutes administered to all patients. The maintenance dose of 1 g/h was given to 196 patients (72.1%), slow infusion to 130 patients (66.3%).

Duration of the treatment: The 24-hour maintenance dose was performed on 55.6% of the patients (Figure 1).

Monitoring of the magnesium sulphate protocol: A surveillance record file was opened on 221 patients with irregular surveillance in more than ¾ of the cases. Diuresis was the most monitored element in 80.2% (Table 2).

Side effects observed with magnesium sulphate: 23 patients (08.5%) suffered from side effects. These were oliguria (60.9%), decreased osteotendinous reflexes (34.8%), respiratory distress (8.7%) and altered consciousness (4.4%).

Results of treatment with magnesium sulphate: We observed in our study, after the administration of magnesium sulphate to the patients:

- 03 cases of convulsive seizures, i.e. 1.6% of patients who had not presented seizures before initiating treatment.

- 16 cases of recurrence of seizures on the 80 eclampsia, i.e. a frequency of 20%.

	Count	Frequency in %
Functional signs		
Epigastric pain in bar	11	04.0
Visual Disorders	26	09.6
Headache	74	27.2
Physicalsigns		
PAS ≥ 160 mm Hg	201	73.9
PAD ≥ 110 mm Hg	173	63.6
Syndrom HELLP	11	04.0
HRP	14	05.2
Eclampsia	80	29.4
OAP		0.7
Biologiccalsigns		
Renalfailure	13	04.4
Severethrombocytopenia	15	05.5
Hyperuricemia	39	14,3
Cytolysis	30	11.0
IUGR	16	06.4
Severeoligoamnios	19	07.6
Fetaldeath	10	10.5

Table 1: Distribution of patients according to the severity of the pre-eclampsia at admission.

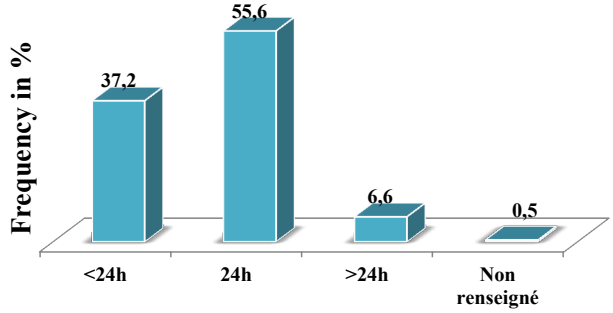

Figure 1: Distribution of patients according to the duration of the treatment with magnesium sulfate

	Number	Frequency in %
HourlyDiuresis (ml/h)	218	80.2
RR (cycle/min)	59	21.7
OTR	75	27.6

Note: Caption: RR=Respiratory Rate; OTR=Osteotendinous reflexe

Table 2: Distribution of patients according to surveillance elements.

A correlation was found between the duration of treatment and the occurrence of seizures as well as their recurrence under treatment (p=0.003 and p=0.004).

The state of consciousness had normalized in 93.0% of cases in patients with altered consciousness at admission.

A combination with antihypertensive was instituted and Nicardipine (Loxen) was the molecule used in 59.6% of the cases with a relay by Methyl-dopa (Aldomet) in 73.2% of the cases. Normalization of blood pressure was observed in 144 patients (52.9%). The average time spent before a return to normal BP was 44.4 h and varied between 3 to 72 h.

Obstetrical treatment

Out of the 251 pregnant and parturient, a uterine evacuation was performed in 98.4% of the cases. The delivery route was caesarean section in 83% of cases.

Maternal and fetal prognosis

At the maternal level, the evolution was marked by the occurrence of 3 eclampsia, 2 HRP, 1 disseminated intravenous coagulation and 1 stroke. The mean hospital stay was 6.4 days with extremes of 1 and 27 days. Six maternal deaths were recorded. The maternal lethality rate was 1.34% for all severe pre-eclampsia cases collected during the period.

At the perinatal level, 245 newborns were born alive; 29 stillborn or 10.5% and 2 newborns resuscitated in vain or 0.7%. They were premature in 52.2% of cases with a low birth weight in 67.4%.

Discussion

Epidemiological aspects

The prevalence of severe preeclampsia stood at 7.7%. This result is not far from those reported in the literature, which was between 2 and 8% [6]. In France, the prevalence would be lower, estimated to be between 1 and 2% [7].

Our study confirmed the classic epidemiological data characterizing severe preeclampsia, namely a young primiparous carrier of a pregnancy near the term and poorly followed.

Clinical aspects

The diagnosis of hypertension was made in 3 out of 10 cases during an eclampsia, reflecting the inadequacy of the screening and the poor management of the hypertensive states associated with the pregnancy. It should be noted that the accurate assessment of the severity of the disease was hampered by poor completion of complementary examinations such as complete blood count, coagulation assessment, liver and renal function assessment.

Significant efforts will have to be made at the periphery to better organize the screening, management of pre-eclampsia and their transfer to the reference maternities before the complications occur.

Therapeutic aspects

The frequency of use of magnesium sulphate was 87.18%. This result is close to that of Millochau and col in France which was 91.5% [8]. Some authors have reported lower frequencies of use. This is the case for Monia (52%) and Van (37.5%) [9,10].

The Zuspan protocol was the one used in all cases. It is the same in the studies of Omu in Kuwait, Bourretin France and Maia in Brazil [11-13]. On the other hand, the Pritchard protocol was the one prescribed in Nigeria [14].

Rozenberg points out that there is no clear consensus in the randomized trials published on the route of administration (intramuscular or intravenous). However, it can be considered that the intravenous route should be preferred to the intramuscular route, which has significantly more side effects [15].

One out of four patients did not receive the maintenance dose and the duration of the treatment was not respected in 43.87% of the cases. Apart from those that had developed a toxicity effect justifying the discontinuation of treatment, the protocol was interrupted due to the availability of the molecule. A significant statistical relationship was found between the duration of treatment and the onset of seizures (p= 0.003) and recurrence of seizures (p=0.004).

$MgSO_4$ was administered in 2/3 of the cases as a slow infusion because of the limited number of electrical syringes which posed the problem of the distribution of the dose administered over 24 hours. According to the literature, t is better to administrate it by using an electric syringe [8,16,17].

The use of magnesium sulfate requires rigorous, repeated monitoring of the consciousness (Glasgow=15), respiratory rate (>12 c/ min), diuresis (>30 ml /h) and osteotendinous reflexes. Indeed its use is associated with a high rate of minor side effects (15 to 67%), such as heat sensation, flushing, nausea, vomiting, muscle weakness, dizziness and irritation at the site of 'injection. Major side effects include respiratory distress (1%) and hemorrhage from the delivery (1.4% increase in risk). Fatal toxicity has been reported in the United States [18] and South Africa [19].

Surveillance in our series was only effective in 22.62% of cases. Side effects were observed in 23 patients, ie 8.45% of the patients treated with magnesium sulphate. This result is lower than those reported in France by Millochau (18.9%) and Naeimi (31.4%) [8,20]. This discrepancy is probably due to the irregular surveillance of patients who do not allow the diagnosis of side effects in most of our patients.

Beucher, in his article, emphasizes that the undeniable existence of side effects requires that magnesium sulphate be used only within the framework of a well-established therapeutic protocol with strict adherence to the conditions of use (dosage, surveillance) [17]. The French recommendations stipulate that patients must be in the intensive care unit, with multi-day clinical control and multiparametric monitoring (ECG, SpO_2, blood pressure).

Magnesium sulphate administration correlates with 98.44% efficacy in primary prevention and 80% in secondary prevention of eclampsia.

Thus, Maia and col in their series had noted a 100% efficacy rate in the prevention of eclampsia [13]. As for Bourret et al., efficacy was 95% in the secondary prevention of eclampsia [12].

Although its efficacy is demonstrated by several studies, some authors [21] are opposed to the broad prescription of magnesium sulphate in primary prevention, as this molecule can be dangerous or even fatal to the mother-child couple. Indeed, this molecule has a therapeutic serum level close to the toxic serum level with potential consequences during an overdose (respiratory distress and cardiac arrest). Doses of magnesium sulphate greater than 50 g would be responsible for brain lesions in the newborn with involvement of the thalamus and basal ganglion [22].

As regards antihypertensive agents, the combination of MgSO4 and calcium channel blockers is likely to exert synergistic depression on cardiac function, hence the need for rigorous monitoring during their use [23]. Nicardipine was used in 6 out of 10 cases in our study.

Obstetrically, $MgSO_4$ is not the etiological treatment of severe toxemia, the severe forms of which require the termination of pregnancy, often by Caesarean section. In our study, uterine evacuation was performed in 98.41% and by Caesarean section in 83% of cases.

Prognosis

The incidence of maternal complications (44.1%) was very high in our patients at the time of diagnosis. The maternal mortality rate was 1.3%. In the work of Aabidha in South India and Ugwu in Nigeria, no cases of death were recorded under Magnesium sulphate [3,14]. In contrast, in Gabon and France, the authors reported 3% and 2.5% respectively of deaths despite treatment [24,12]. Chhabra and Kakani [25] refer to HELLP syndrome, OAP and eclampsia as the three leading causes of death in hypertensive disorders of pregnancy.

For Rozenberg, magnesium sulfate is associated with a non-significant decrease in maternal mortality [15].

The incidence of fetal complications was also very high in our population with a preterm birth rate of 52.23% and / or IUGR of 6.37% and stillbirths of 11.40%.

The reduction of materno-fetal morbidity and mortality associated with severe pre-eclampsia is at first implied by earlier diagnosis and active management of the disease.

Conclusion

Magnesium sulphate is the first-line molecule in the management of severe preeclampsia at the CHU-MEL in Cotonou. Its effectiveness is demonstrated but its use has several irregularities, hence the need to establish a protocol of use and strict monitoring.

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