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Effect of antenatal administration of magnesium sulphate and milking of umbilical cord during delivery on the incidence of intraventricular haemorrhage in preterm infants

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ABSTRACT

Background: Intraventricular hemorrhage (IVH) is commonly seen in preterm infants. The aim of this study was to look at the effect of antenatal magnesium sulphate administration and milking of umbilical cord during delivery in the incidence of IVH in preterm infants.

Methods: A randomized controlled study was conducted in the year 2015 on 80 preterm infants born less than 33 weeks of gestation during the study period. Magnesium sulphate was administrated to 25 pregnant women who were at imminent risk for delivery. Fourteen infants underwent milking of umbilical cord. The primary outcome was IVH detected in cranial ultrasound of day 28.

Results: The primary outcome showed only 1 infant who received magnesium sulphate developed IVH, whereas 3 infants with no intervention done developed IVH. None of the preterm infants who had undergone milking of umbilical cord developed IVH.

Conclusions: It was found that both antenatal administration of magnesium sulphate and milking of umbilical cord during delivery in preterm infants resulted in a significant reduction in the incidence of IVH. Further studies using more number of samples are required to understand the role of the interventions for long-term implications.

Keywords: Antenatal magnesium sulphate, Intraventricular hemorrhage, Preterm infants, Milking of the cord

INTRODUCTION

Intraventricular hemorrhage (IVH) is the most common type of neonatal intracranial hemorrhage and is associated with adverse neurological outcomes. It may result in cerebral palsy, epilepsy and future disabilities such as learning disability, visual and hearing impairments. Improvements in neonatal care have led to a persistent decline in the mortality associated with prematurity. Several observational studies show that administration of magnesium sulphate to mothers improves the neurodevelopmental outcome of fetuses that are delivered preterm. In humans, magnesium is

essential for key cellular processes. Magnesium has vasoactive properties, which increases cerebral blood flow due to cerebral vasodilatation.² The fetal and neonatal brain seems more susceptible to glutamate damage. Hence, blocking glutamate receptors through agents such as magnesium sulphate may reduce the risk of injury in perinatal period. Transplacental transfer of magnesium is rapid with magnesium concentration increased in fetal serum within one hour of maternal intravenous administration.³ Even though there are guidelines regarding use of magnesium sulphate in pregnant women at risk of preterm labour for

neuroprotection of fetus in several developed nations, none exist in India in this regard.⁴⁻¹²

Various studies in preterm neonates have shown that delayed cord clamping for atleast 30seconds results in increased circulating blood volume in first 24 hours of life and a lower incidence of IVH.^{8,9} After birth, the timing of cord clamping may have a substantial impact on the amount of blood transfused for newborn from placenta. In spite of the advantage, studies suggest that a delay in cord clamping may increase the risk of neonatal hyperbilirubinemia. Milking of cord is an alternative to the delayed cord clamping to achieve similar benefits with less interference with neonatal resuscitation. Milking the umbilical cord towards the baby before clamping takes less than 5 seconds and therefore does not interfere with neonatal resuscitation and maybe of comparable benefit to milking of the cord.

Present study aims to look at the effect of antenatal magnesium sulphate administration and milking of umbilical cord during delivery in the incidence of IVH in preterm infants.

METHODS

This was a randomized controlled trial conducted for one year from January to December 2015 in neonatal care centre at Jubilee Mission Medical College and Research Institute, Thrissur. The study included 80 pregnant women with single, twin and triplet fetus less than 33 weeks. Magnesium sulphate was administered to 25 women who were at imminent risk of early preterm birth. The dose of magnesium sulphate was 4 gm in 100 ml normal saline over 20-30 minutes followed by 4 gm in 100 ml over next 4 hours at 1 gm/hr.

Fourteen infants underwent milking of umbilical cord. About 20 cm length of the cord was held towards the placental side and cord was milked towards the baby at approximately 10 cm/sec speed. The process was repeated three times and the cord was clamped. Thus, milking of cord was done. Two antenatal mothers received magnesium sulphate administration and their infants underwent milking of the umbilical cord. Remaining 39 preterms did not receive any interventions. The data about the interventions were analyzed. The primary outcome was intraventricular haemorrhage detected in cranial ultrasound of 28th day. Data were analyzed using chi square test, student t-test, percentage analysis, odds ratio.

RESULTS

Among 80 patients enrolled, 25 women underwent antenatal administration of MgSO₄ and 14 infants underwent milking of cord. Two antenatal mothers received magnesium sulphate administration and their infants underwent milking of the umbilical cord. In this study, only 1 infant who received magnesium sulphate

developed intraventricular haemorrhage whereas 3 infants with no intervention done developed IVH (Figure 1).

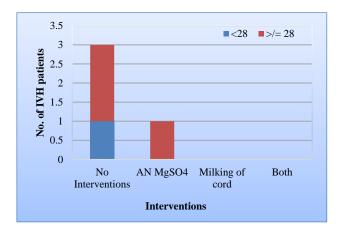


Figure 1: The incidence of IVH in day 28 cranial ultrasound.

None of the preterm infants who had undergone milking of umbilical cord and both of the interventions developed IVH.

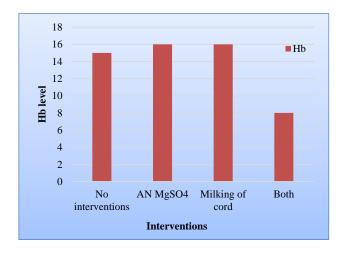


Figure 2: The hemoglobin levels in the study groups.

The hemoglobin levels were more than 14 gm/dl in most of the infants. The mean haemoglobin level was 16 gm/dl in both the intervention groups and 15 gm/dl in the group which did not undergo both the interventions (Figure 2).

Table 1: The PCV levels in the study groups.

Category	PCV (%)
No interventions	45
AN MgSO ₄	48
Milking of cord	50
Both	25

The PCV levels were less than 55% in most of the infants. The PCV level in the group undergone antenatal magnesium sulphate administration was 48% and 50% in the group undergone milking of cord (Table 1).

DISCUSSION

Preterm birth is a major contributor to perinatal mortality and morbidity including respiratory distress syndrome (RDS), chronic lung disease of prematurity, intraventricular haemorrhage (IVH), sepsis, cerebral palsy and other forms of neurodevelopmental impairment, blindness and deafness. Despite the improvements in the standards in obstetric and neonatal care over recent years, no progress has been made over the last two decades in reducing the incidence of preterm birth in part due to increasing obstetric interventions.

Antenatal magnesium sulphate administration and placental transfusion (either by delaying cord clamping or milking of umbilical cord) are two emerging interventions to improve the outcome in preterm neonates. Hence, we looked at the effect of these two interventions on the outcomes in these infants.

Even though use of antenatal magnesium sulphate for foetal neuroprotection is now recommended by the World Health Organization and many Pediatrics and Obstetrical societies, no such guidelines exist in India. In our study, we looked at only the short-term outcome of antenatal administration of magnesium sulphate. Due to its antiinflammatory action and its action as an N methyl-daspartate receptor blocker, magnesium sulphate has the potential to be neuroprotective in preterm infants. We found that the administration of magnesium sulphate to pregnant woman with fetus less than 33 weeks, reduces IVH rate significantly. This is similar to the findings of several studies that have shown that maternal administration of magnesium sulphate is associated with reduction in the risk of IVH, cerebral palsy and preterm mortality.⁵⁻⁷ Doyel et al, reported that antenatal magnesium sulphate administration to pregnant women relatively reduced the risk of death or cerebral palsy at two years of age in preterm infants.8

Delayed cord clamping and umbilical cord milking are two methods of placental transfusion. Various studies have shown reduced incidence of IVH in the imaging of babies with delayed cord clamping. 9-13 Delayed cord clamping, even though is the standard of care in term neonates, practical difficulties arise in the implementation of this practice in preterm infants due to the possible delay that it causes in the initiation of neonatal resuscitation. Milking of umbilical cord is proposed as an alternative method in such scenarios. Umbilical cord milking has now been shown to improve the neonatal hemodynamic stability and decreases major morbidity in preterm singletons. 14,15 Milking is a no cost intervention and we found no adverse effects in preterm infants who underwent this intervention. In our study, the neonates who underwent milking of the cord did not develop IVH. This is consistent with results of previous studies which showed less significance in developing IVH. 16-18 In the present study, none of the preterm infants who had undergone milking of the cord and antenatal administration of magnesium sulphate developed IVH.

Limitations of the study is the small sample size and the study needs to be validated by conducting large multicentre trials in resource limited setting with long term follow up.

CONCLUSION

We report that antenatal magnesium sulphate and milking of umbilical cord resulted in a significant reduction in the incidence of IVH. These low-cost interventions may be of immense importance in the improvement of neurologic outcome of preterm infants in resource limited countries and hence may be considered for the primary prevention of IVH in preterm infants born below 33 weeks of age.

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Institutional Ethics Committee

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