Short Communication

Progesterone versus magnesium sulfate in the management of preterm labour

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Preterm labour is the leading cause of prenatal and neonatal mortality morbidity and long term neurodevelopmental problems. Diverse treatments have been employed in past to suppress preterm labour. Magnesium sulfate is often used as first line in suppression of preterm labour. Side effect of this includes thirst, hyperthermia, headache, diplopia, respiratory depression and rare cases respiratory paralysis and arrest. We take a decision that compares the ability of magnesium sulfate with progesterone in suppression of preterm labour. In this randomized clinical trial, 132 cases were chosen from pregnant women between the 26 to 34 weeks of pregnancy who were suffering from preterm contractions of uterus with intact amniotic sac and cervical dilatation of less than 4 cm. These women had been referred to obstetric ward of Ali – Ebne – Abitalib hospital, Zahedan, during the year of 2008 to 2009 and randomly were divided into two equal groups (66 cases in each group). The results were analyzed by Chi-square and T-test with SPSS software. In first group, primarily 4 g of magnesium sulfate was infused. And then 10 g (2 g/h) was continued. In second group, progesterone used 200 mg vaginal suppository as single dose. Sixty six women in magnesium sulfate group in 58 cases (89%) suppressed delivery at least for 48 h. In second group, from 66 women 52 case (79%) suppressed delivery at least for 48 h. In this study, differentiation was not significant (p value = 0.161) in two group. 95% women in first group (magnesium sulfate) had side effects and 5% women progesterone group had involved with side effects. This finding shows that the ability of progesterone in suppression of preterm labour is similar to magnesium sulfate; however, maternal side effect of magnesium sulfate was 95% while it was not for progesterone.

Key words: Progesterone, magnesium sulfate, preterm labour, tocolytic.

INTRODUCTION

Labour happens when some mechanisms drive the uterus to delivery of the gestation product. If it happens between the 20 and 37 of pregnancy weeks, it is called premature labour. Theoretically, this happens as a consequent of pathologic activation of the labour process (Scott et al., 2008).

Premature labour, which occurs in 7.23% of deliveries (Dodd et al., 2006), is associated with prenatal morbidity and mortality (Dodd et al., 2006; Farine et al., 2008). American Academy of Pediatrics and American College of Obstetricians and Gynecologists have suggested criteria for diagnosis of preterm labour as follows:

1) Presence of 4 uterine contractions in 20 min or 8 contractions in 1 h accompanied by progressive cervical
Prevention of delivery is still a great challenge when dealing with preterm labour. Currently, there is no evidence based on proven treatment for this struggle. Different tocolytic regimens (for example, beta blockers, magnesium sulfate, anti-prostaglandins and calcium channel blockers) have been used to suppress uterine activity in order to improve neonatal outcome (Scott et al., 2008).

Magnesium ion in high concentrations is able to alter the contractility of the myometrium through antagonizing calcium ion. Clinical evidences show that magnesium in pharmacologic doses is able to suppress the labour, but Cuningham et al. (2010) showed that magnesium sulfate is ineffective as a tocolytic.

Progestrone is a steroidal hormone which plays important roles throughout pregnancy. Early in pregnancy, it is secreted by corpus luteum until the placenta takes over in weeks 7 to 9 and its main role is to maintain the product of gestation. In the second half of the pregnancy, the role of progesterone is less clear. It is possible that it plays a role in suppressing the myometrial contraction by inhibiting the stimulatory prostaglandins and related protein genes (Sfakianaki and Norwitz, 2006). In a meta-analysis of three randomized controlled trials, effectiveness of progesterone in treating preterm labour was shown (Mackenzie et al., 2006). Systematic review of 9 clinical trials also showed the efficacy of these products (Coomarasamy et al., 2006).

Many studies have shown that tocolytic agents are effective for 2 to 7 days, a golden time to administer corticosteroids to mature the fetal lungs. Tocolytic agents are contraindicated in placenta abruption, intrauterine infecetion, fetal anomalies and placenta previa (Resnik, 2005).

When plasma level of magnesium reaches 10 mEq/L, patellar reflex disappears and respiration depression happens. This is a sign of imminent magnesium toxicity (Cuningham et al., 2010). Medroxyprogesterone has been effective in suppressing preterm labour and anti-inflammatory effects in animal models. Defonseca et al. (2007) reported the effect of vaginal progesterone in decreasing premature delivery in high risk groups.

Looking at the side effects of magnesium sulfate in one hand (maternal respiratory depression, diplopia, muscle paralysis and rarely cardiac arrest) and progesterone which is relative safe in the other hand (Farine et al., 2008), this study was designed to compare the efficacy and safety of these two drugs in management of premature labour.

Table 1. Efficacy of progesterone versus magnesium sulfate in managing preterm labour.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Suppress labour</th>
<th>Unsuppressed labour</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number Percent</td>
<td>Number Percent</td>
<td></td>
</tr>
<tr>
<td>Progesterone</td>
<td>52 79</td>
<td>14 21</td>
<td>0.16</td>
</tr>
<tr>
<td>Magnesium sulfate</td>
<td>58 89</td>
<td>8 12</td>
<td></td>
</tr>
<tr>
<td>Sum</td>
<td>110 83</td>
<td>22 17</td>
<td></td>
</tr>
</tbody>
</table>

changes,
2) Cervical dilatation greater than 1 cm,
3) Cervical effacement equal or greater than 80% (Cunningham et al., 2010).

RESULTS

Of 132 patients, 110 were considered eligible. Paper case report files were transcribed to SPSS version 17 and analyzed by Chi-square test. Out of 132 participants, tocolysis was successful in 110 (83%) for 48 h. 52 of these patients were from the progesterone group and 57 from the magnesium sulfate group (Table 1). There was no significant difference between the groups (p = 0.16).

In the progesterone group, side effects were observed in 5% of patients (headache, nausea and restlessness, each in one patient); however, tocolysis was effective in these patients and completely disappeared after 48 h. None of the 63 patients showed treatment adverse effects. In magnesium sulfate, 95% of patients experienced side effects (most common was thirst in 32% followed by hyperthermia 24%) (Table 2).
Table 2. Prevalence and types of side effects observed in the study.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Hyperthermia (%)</th>
<th>Vomiting (%)</th>
<th>Nausea (%)</th>
<th>Thirst (%)</th>
<th>Vertigo (%)</th>
<th>Restlessness (%)</th>
<th>Headache (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>30</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Magnesium sulfate</td>
<td>24</td>
<td>1</td>
<td>12</td>
<td>30</td>
<td>18</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

Figure 1. Cases of suppression of preterm labour using magnesium sulphate and progesterone.

DISCUSSION

Findings of this study show that the efficacy of magnesium sulfate and progesterone in management of preterm labour are similar; however, maternal side effects of magnesium sulfate in 95% patients, and in the progesterone group 3% were observed (Figure 1).

To suppress the premature labour, vaginal progesterone was effective in 79%, comparing to 89% of patients in magnesium sulfate group.

Defonseca et al. (2007) administrated vaginal progesterone (200 mg/day) between 24 and 34 weeks in patients with short cervix. As a result, risk of premature labour was decreased from 34 to 19%.

In this study, severity of the side effects observed in the progesterone group were mild to moderate and were completely resolved after 48 h. On the other hand, despite the frequent control of the vital signs, severity of side effects of magnesium sulfate was more severe and irksome.

Different studies have not shown any maternal or fetal side effects related to progesterone (Coomarasamy et al., 2006). The most common adverse effect of magnesium sulfate is thirst (30%) and hyperthermia (24%) which occurs simultaneously in 87% of cases which results in irritability and restlessness.

Sakhavar et al. (2008) performed a study to compare the efficacy of magnesium sulfate and human chorionic gonadotropin (HCG) in management of preterm labour. In that study, the most common side effect of magnesium sulfate was hyperthermia and thirst (observed in 53 and 48% of patients, respectively). All patients in the magnesium sulfate group experienced some kind of adverse effects (Sakhavar et al., 2008).

Despite the advantages of progesterone, it should be noted that the final purpose for tocolysis is improving fetal outcome. Therefore, it is suggested for future studies, to use the data of this research along with other information to evaluate the efficacy of progesterone in decreasing mortality, morbidity, and the need for neonatal intensive care. We hope that future studies will introduce safer and more effective tocolytic regimens.

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REFERENCES


