

The Effect of Premedication by Remifentanil and Magnesium Sulfate in Hemodynamic Responses to Tracheal Intubation in Cesarean Section Delivery: A Randomized Double-Blinded Controlled Study

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Abstract

Background: The preventing effects of remifentanil and magnesium sulfate on hemodynamic responses to tracheal intubation were evaluated in a double-blinded controlled trial on pregnant women undergoing cesarean section delivery.

Methods: A total of 54 American Society of Anesthesiologists Class I-II women candidate for cesarean section delivery were randomly assigned to one of three groups (n = 18) to receive one of the following premedication: Intravenous (IV) remifentanil 0.75 µg/kg, IV magnesium sulfate 30 mg/kg, or IV normal saline 10 cc as placebo. All hemodynamic profiles were recorded immediately before and after intubation, and 2, 3, 5 minutes after tracheal intubation.

Results: Heart rate and systolic and diastolic blood pressures were significantly lower in the remifentanil group than in other groups both before and immediately after intubation. The trend of the changes in hemodynamic responses within 5 minutes following intubation in the magnesium sulfate and placebo group was similar, but this trend in the remifentanil group was significant difference. In the same time, 1st and 5th minute Apgar scores were slightly lower in the remifentanil group than others. The measured parameters of umbilical cord blood pH and PO₂ had no significant differences between the groups.

Conclusions: Remifentanil can attenuate hemodynamic response to tracheal intubation more effectively than magnesium sulfate, and thus it can be considered safe for a pregnant candidate for cesarean section.

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Keywords: Cesarean section, Hemodynamic response, Intubation, Intratracheal, Magnesium sulphate, Pregnant women, Remifentanil

Introduction

Hemodynamic responses to rapid sequence induction of anesthesia and tracheal intubation, commonly appears as hypertension and tachycardia, which are potentially harmful. These serious adverse effect can be attenuated by premedication by different medication protocols such as administration of vasodilators, beta-receptors blockers, and particularly opioids that have a central role for preventing hemodynamic instability (1,2). However, most of these medications pass placenta and affect fetus in various ways. In this regard, remifentanil is now commonly used to provide instance analgesia of rapid onset and short duration and possibly less adverse effects on the fetus (3).

Remifentanil is a potent ultra short-acting synthetic opioid analgesic, which is given to patients during different surgical procedures to relieve pain and as an adjunct to an anesthetic (4). It has been suggested that administration of this drug can lead often to more hemodynamic stability during surgery and a quicker post-operative recovery time (5-7).

The preventive effect of magnesium sulfate on anesthesia-induced hemodynamic instabilities has been evaluated. This drug, not only can inhibit catecholamine releasing, but also can limit the pressor response to tracheal intubation (8,9). In some studies, intravenous magnesium sulfate administration was associated with increased cardiac index, a minimal increase in heart rate (HR) and a significant decrease in

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mean arterial pressure (MAP) and systemic vascular resistance and thus it could be a useful adjuvant to attenuate endotracheal intubation (10). Magnesium sulfate has been used in preterm pregnant women with preeclampsia without serious effect on the fetus.

In the present study, it was hypothesized, premedication by remifentanyl or magnesium sulfate hemodynamic changes related to tracheal intubation. Changes observed in MAP recorded after intubation was considered as the primary outcome. Systolic and diastolic blood pressure (SBP and DBP) and HR were evaluated as secondary outcomes.

Materials and Methods

After obtaining approval from the ethics committees of Tehran University of Medical Sciences and obtaining written informed consent of all mothers, 54 American society physical status classification [American Society of Anesthesiologists (ASA)] class I-II women aged 18-40 years and gestational age 38-42 weeks which were candidate for cesarean section delivery under general anesthesia were randomly enrolled in this study. Parturient with intrauterine growth retardation, mothers with history of any kind of cardiovascular disorders, diabetes mellitus and renal dysfunction who had preeclampsia, morbid obese mothers and those with cigarette or substance abuse, those who had Mallampati class 3 or 4, and thyroid-mandible distance less than 6 cm were not enrolled in the study. Cormack laryngoscopy grade 3 or 4, more than one intubation attempt or unsuccessful intubation and intubation with guided styles, prolonged laryngoscopy (more than 15 seconds) and uterine incision to umbilical cord clamping time of more than 90 seconds were considered as exclusion criteria.

Patients were randomly enrolled in three groups to receive the following medication: Remifentanyl 0.75 µg/kg bolus given over 30 seconds; magnesium sulfate 30 mg/kg bolus; or normal saline 10 cc as placebo. All regimens were given immediately before induction of anesthesia. Anesthesia was induced with a bolus dose of thiopental sodium (5 mg/kg), followed by administration of succinylcholine (1.5 mg/kg), and atracurium (0.3 mg/kg). Hemodynamic profiles were recorded immediately before intubation, immediately after intubation, and 2, 3, and 5 minutes after tracheal intubation. Arterial SBP and DBP were non-invasively measured using an automatic oscillometric device and HR was recorded from the electrocardiogram trace.

Considering a 20 mmHg of the expectable minimum difference of MAP between the groups and the alpha value of 0.05, and the power of 0.80, as well as considering 10% probable exclusion of the samples within trial, the calculated sample size for each group was finally 18 patients in each group.

Results were presented as mean ± standard deviation for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with Kruskal-Wallis H-test. The trend of the changes in hemodynamic parameters across the groups was assessed using the repeated measure ANOVA test. Statistical significance was determined as a $P \geq 0.05$. All statistical analysis was performed using SPSS for windows (version 20; IBM Corp., Armonk, NY, USA).

Results

The mean age of the patients in three groups was 28.67 ± 4.17 years in the Remifentanyl group, 27.61 ± 5.20 years in the magnesium sulphate group, and 28.67 ± 5.40 years in the placebo group. Furthermore, mean body weight was 77.33 ± 9.37 kg, 76.17 ± 15.60 kg, and 77.72 ± 10.80 kg, respectively.

There were no significant differences in hemodynamic indices before induction of anesthesia in between the three groups. However, HR, SBP, and DBP were significantly lower in the remifentanyl group than in the other two non-remifentanyl groups both before and immediately after intubation. Although MAP was increased immediately after intubation in all groups, but this change was not statistically significant between the three groups. As shown in figures 1-3, trend of the changes in hemodynamic responses within 5 minutes after intubation in the two Magnesium sulfate and placebo group was slightly similar, but this trend in the remifentanyl group was significantly different compared with other groups. On the other hand, those in the remifentanyl group experienced a slight change in the trend of clinical signs in comparison with other groups.

Discussion

This study illustrated that pre-treatment by remifentanyl lead to better hemodynamic profile the following tracheal intubation in comparison with magnesium sulfate or placebo.

Earlier studies have shown that remifentanyl mitigated or even abolished post-tracheal intubation hemodynamic changes (2,11). High doses of remifentanyl were frequently associated with bradycardia and/or hypotension (2,11). In our observation, arterial pressures had a crescendo-decrescendo pattern during 5 minutes after intubation, both SBP and DBP were decreased after induction, then increased until 3 minutes after intubation and finally were decreased.

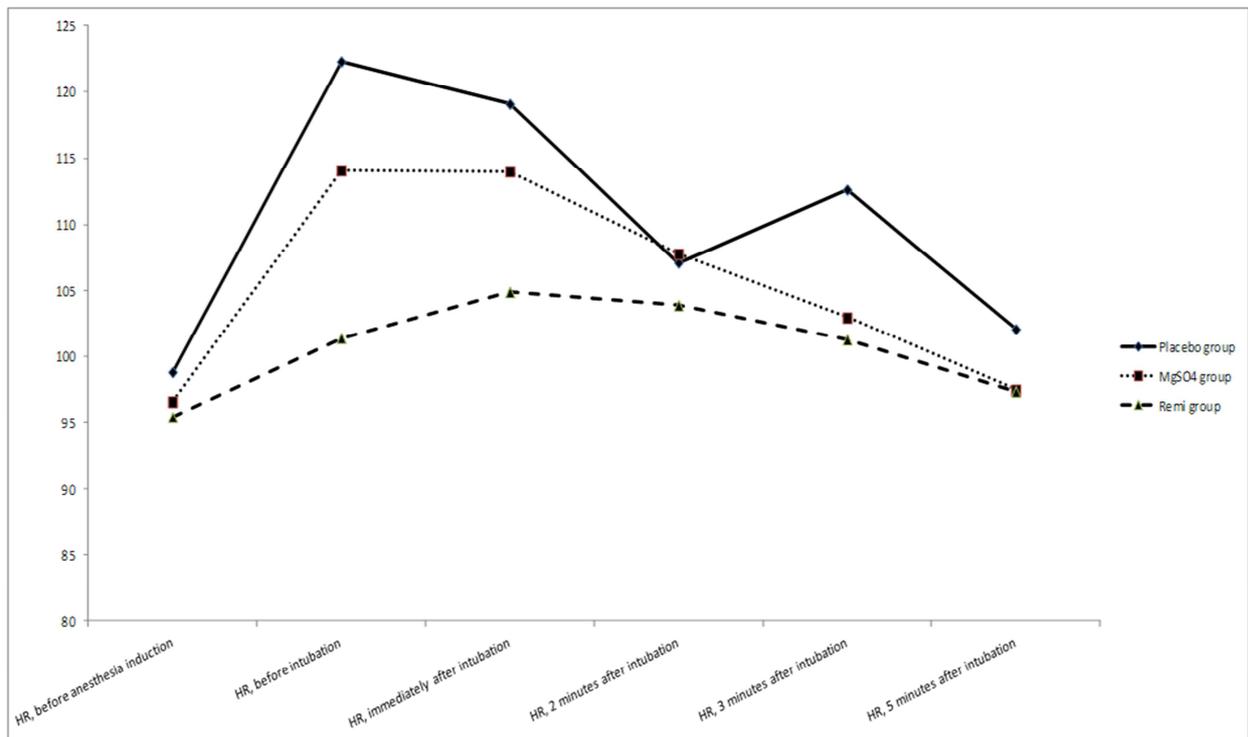


Figure 1. Trend of the changes in heart rate at the three intervention groups

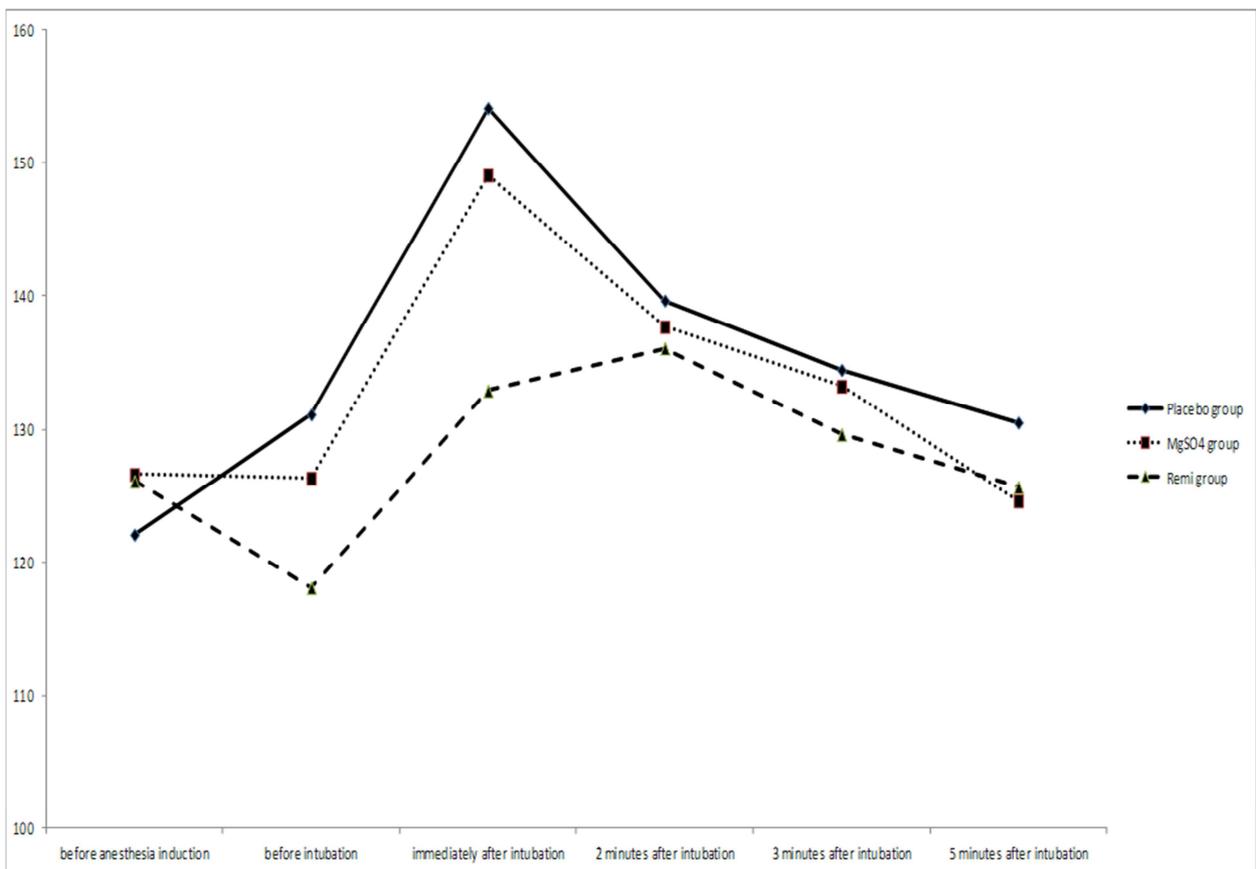


Figure 2. Trend of the changes in systolic blood pressure at the three intervention groups

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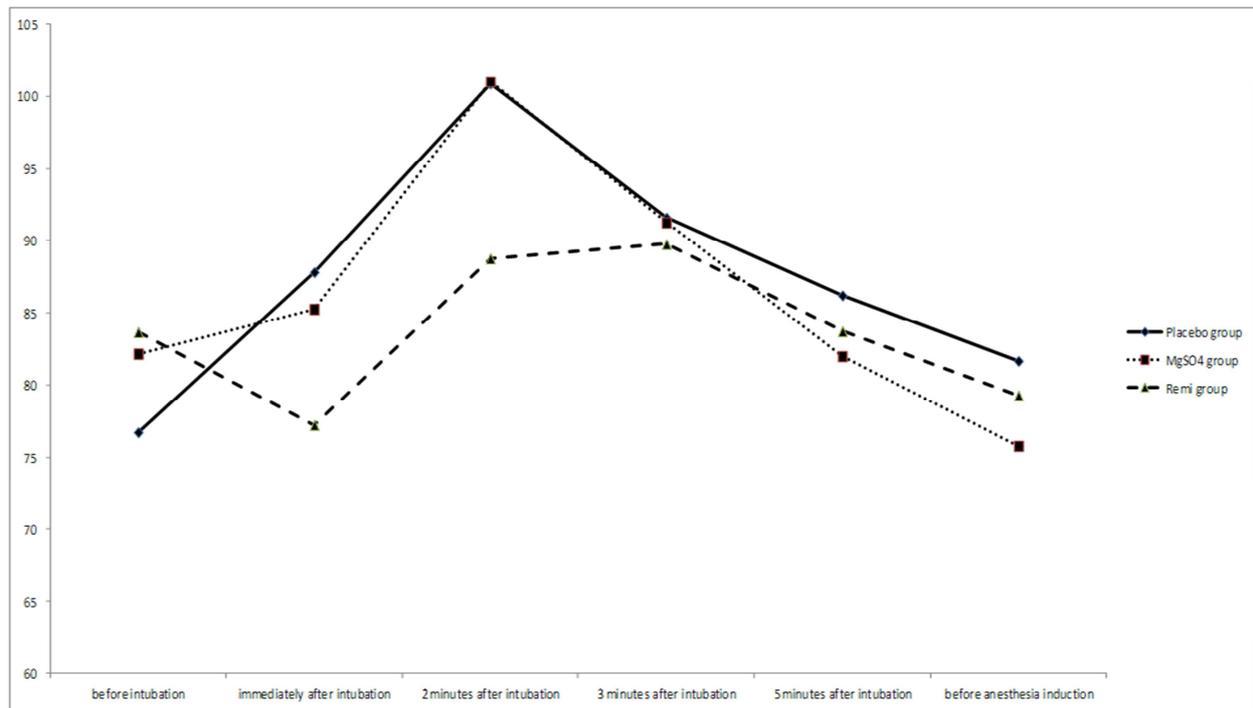


Figure 3. Trend of the changes in diastolic blood pressure at the three intervention groups

In some studies, the low-dose regimen of remifentanyl produced a partially similar pattern of hemodynamic responses to tracheal intubation: arterial pressures decreased after induction of anesthesia, then increased with tracheal intubation without exceeding baseline values (12-15). In the investigations done in Koreans, however, greater sensitivity to remifentanyl, given either by bolus or infusion, was demonstrated with no further increases in hemodynamic responses even after intubation (16,17). These trends of hemodynamic changes were similarly seen in the sulfate magnesium group. However, HR and blood pressures remained lower in the remifentanyl group and therefore hemodynamic stability was more expectable following administration of remifentanyl than magnesium sulfate.

A few studies have assessed the effect of remifentanyl on hemodynamic profile in women presenting for cesarean delivery. In present study, remifentanyl caused a slight decrease in 1th and 5th minute Apgar scores compared with the magnesium and placebo, it did not induce any change in parameters such as umbilical cord pH and PO₂. Although remifentanyl has been proposed as the most suitable systemic opioid for use in the first stage of labor (18), but there are some important concerns. First, attention to infant's respiratory condition should be paid because remifentanyl can cross the placenta and lead to mild neonatal depression (19,20). Furthermore, because of given the risk of neonatal depression, this resource should be used selectively and the means for neonatal resuscitation should be available (21).

Furthermore, administration of remifentanyl seems to be safe for cesarean section candidates considering neonatal respiratory supportive care and continuous monitoring of respiratory function.

Although magnesium administration has beneficial maintaining effects on hemodynamic status, its trend seems to be different compared with remifentanyl. The present study shows that magnesium administered before endotracheal intubation can attenuate this response but not better than remifentanyl. The ability of magnesium ions to inhibit the release of catecholamines has been known for many years (22). More recent studies have shown that magnesium may exert a vasodilator effect on human coronary arteries (23-25). Magnesium has also direct vasodilation properties on coronary arteries and inhibits catecholamine release, thus attenuating the hemodynamic effects during endotracheal intubation. In comparison with placebo group in our study, the trend of hemodynamic changes were the same, this result may be caused by the role of magnesium in decreasing of epinephrine level that has been observed in previous studies (8,9). However for more clearing superiority of remifentanyl on magnesium and other routine medications, other clinical trials on greater sample size and considering efficacy and tolerability of these agents is recommended.

Conclusion

In summary, in cesarean delivery section candidates, pre-treatment by remifentanyl lead to better

hemodynamic profile following tracheal intubation in comparison with magnesium sulfate or placebo.

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The authors declare no conflict of interest.

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