Original Article

Efficacy of intravenous paracetamol on pressor response in patients undergoing cesarean section under general anesthesia

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Abstract

Background and Aims: Profound hemodynamic alterations due to stress and pain during endotracheal intubation may cause deleterious effects. The purpose of this study was to evaluate the effect of intravenous (IV) paracetamol on hemodynamic changes due to endotracheal intubation during cesarean section under general anesthesia.

Material and Methods: Random allocation of one hundred and ten patients in two groups (Group A - placebo and Group B - paracetamol), was achieved as per computer generated table. The placebo (normal saline) and paracetamol solutions looked identical as both were available in 100 ml piggy bags and were labeled as study drug. Infusion of the drug was given 1 h before surgery. Two baseline readings of heart rate, systolic blood pressure (BP), diastolic BP and mean BP were recorded before induction, and these readings were repeated during intubation. Detrimental effect on neonate was evaluated by Apgar score measured at 1 and 5 min after birth.

Results: There were no significant demographic differences found between the two groups. Hemodyamic changes during intubation also did not differ between the two groups.

Conclusion: Administration of IV paracetamol 1 h before cesarean section has no significant effect in preventing hemodynamic changes at the time of endotracheal intubation.

Key words: Cesarean section, endotracheal intubation, hemodynamic changes

Introduction

During general anesthesia (GA), endotracheal intubation (ETI) results in stimulation of sympathetic nervous system and catecholamine release, and therefore, increase in BP and heart rate (HR).[1] The ETI-induced catecholamine release can result in fatal arrhythmia and intracranial hemorrhage.[2] Opioids have been used to minimize these responses to short-term stimuli such as ETI. However, opioid administration is not recommended in GA in parturients for cesarean section, because of its depressant effects on the newborn.

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Hemodynamic alterations due to stress and pain as a result of ETI may decrease uteroplacental blood flow and lead to adverse neonatal outcomes.[3] Many drugs have been employed to blunt the ETI response like lignocaine and opioid, nonnarcotic analgesics and gabapentin. Paracetamol has a well-established safety and analgesic profile[4] and is a safe drug during pregnancy. The main mechanism of action is inhibition of cyclo-oxygenase enzyme which is responsible for the production of prostaglandins, an important mediator of inflammation, pain and fever. Its maximum recommended dose in adults is 4000 mg/day. Onset of action is within 5-10 min of administration. The peak analgesic effect is obtained in 1 h and the duration of action is 4-6 h.[5,6] The purpose of the study was to observe the efficacy of intravenous paracetamol in preventing hemodynamic changes due to pain in cesarean sections at intubation, as well as its effect on neonatal Apgar score.[7,8]

Material and Methods

This study was conducted after obtaining the institutional ethical review committee approval and an informed patient consent. The study did not include American Society

of Anesthesiologists-III and above patients, emergency surgeries, patients allergic to paracetamol, anticipated difficult intubation with mallampatti Grade-III and above, preeclampsia and eclampsia. Patients with known hypertension, peripheral vascular disease, ischemic heart disease, cardiac arrhythmias or having cardiac pacemaker, patients taking any HR modifying drugs, monoamine-oxidase inhibitors, or any drug affecting autonomic nervous system were also excluded. Random allocation of patients in two groups was done by the hospital pharmacy as per computer generated table. Patients were allocated to one of the two study groups. The placebo group ($n = 55$) received normal saline and paracetamol group ($n = 55$) received 1 g intravenous paracetamol. The placebo or paracetamol solutions were given to the patient in a 100 ml piggy bag which was labeled as study drug. The drug was given 1 h before the surgery by a registered ward nurse who was not involved in the OR management of the patient. Every patient was given aspiration prophylaxis 1 h before going to the operating room. In the operating room, patient was placed in a supine position with 15° left tilt. Two intravenous lines were placed. Ringers lactate was given at the rate of 200 ml/h to all patients as soon as a patient entered the OR. Two baseline readings of HR, systolic BP (SBP), diastolic BP (DBP) and mean BP (MBP) were recorded before induction. General anesthesia was induced with rapid sequence induction by using the calculated dose of propofol (2 mg/kg) and succinylcholine (1.5 mg/kg). Macintosh laryngoscope blade size three with an endotracheal tube of size 7.0 mm internal diameter was inserted. O_2/N_2O 50% and 1% isoflurane were used. $EtCO_2$ was kept 30-35 mmHg throughout the procedure. Final HR, SBP, DBP and MAP readings were taken as soon as intubation started. Datex Ohmeda S/5 monitor was used to record HR and BP. Pethidine (1 mg/kg), atracurium (0.5 mg/kg) and syntocinon 40 units (10 units stat and 30 units in 500 ml fluid at 100 ml/h) were given after the cord was clamped. Hypotension (BP <20% of baseline) was treated by giving IV fluid boluses (3 × 2 ml/kg). Metoprolol 2 mg was available in case of hypertension. All variables (HR, SBP, DBP and MAP) and their management were noted in data collection sheets at baseline and the final outcome was measured at intubation. To see any detrimental effect on neonate, all neonates were assessed and Apgar score was measured at 1 and 5 min after the birth.

Statistical analysis

All statistical analysis was performed using Statistical Packages for Social Science version 19 (SPSS Inc., Chicago, IL, USA). Data were expressed as mean (standard deviation) for quantitative variables like age, weight, SBP, DBP, HR. Independent sample *t*-test and Mann-Whitney tests were applied to compare the mean/median difference between groups for age, weight. The paired *t*-test was used to compare within-subject effect for HR and BP. $P < 0.05$ was considered as significant.

Results

Mean age and weight were not significantly different between the groups [Table 1].

Comparison of mean HR, DBP, SBP and MAP at baseline and at intubation is presented in Table 2. Average HR, SBP, DBP and MAP were increased significantly from baseline in both groups, but significant differences were not observed in inter-group comparison as shown in Table 2.

Mean percent increase in HR, SBP, DBP and MAP from baseline were not significantly different in the two groups [Figure 1].

There was no significant difference between groups in altering hemodynamic during intubation when the age was divided into 30 or less and more than 30 years ($P = 0.57$).

Apgar score at 1 and 5 min remained above 7 in both the groups.

Table 1: Comparison of demographic variables between groups

Variables	Group A ($n = 55$)	Group B ($n = 55$)	*P*
Age (years)	27.67±5.17	27.33±3.88	0.69
Weight (kg)	73.18±11.06	71.22±10.31	0.34

Data are presented as mean±SD. Group A = Normal saline, Group B = Paracetamol. SD = Standard deviation

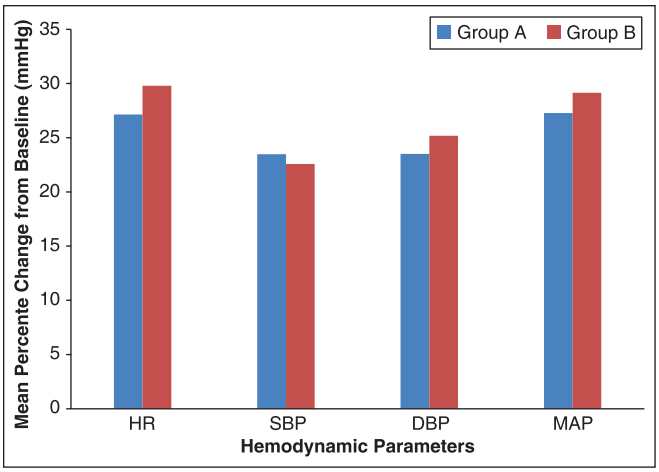

Figure 1: comparison of mean percent change of hemodynamic parameters between groups. Group A: Normal Saline; Group B: Paracetamol

Table 2: Comparison of mean hemodynamic parameters between groups

Hemodynamic parameters	Group A (n = 55)	Group B (n = 55)	Intergroup comparison P
HR (beat/min)			
Average baseline	89.00±10.64	86.96±10.14	0.31
At intubation	112.4±13.10*	112.45±12.95*	0.98
SBP (mmHg)			
Average baseline	126.93±9.69	126.59±8.69	0.84
At intubation	156.00±15.98*	154.93±15.92*	0.58
DBP (mmHg)			
Average baseline	80.52±7.79	81.12±7.73	0.68
At intubation	99.04±9.98*	100.91±7.56*	0.27
MAP (mmHg)			
Average baseline	94.17±8.46	92.75±8.05	0.36
At intubation	119.46±10.38*	119.16±9.87*	0.88

*Data expressed as mean ± SD. Pair wise analysis within group — Paired t-test followed. *Statistically significant change from base line. Inter group comparison — Independent sample t-test applied. Group A = Normal saline, Group B = Paracetamo, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, MAP = Mean arterial pressure, HR = Heart rate*

Discussion

Hemodynamic stability at intubation is important in all surgeries, under GA especially in cesarean sections where two lives are involved. Profound hemodynamic alterations due to stress and pain during intubation may cause deleterious effects. It may decrease uteroplacental blood flow and lead to adverse neonatal outcomes.[9] There are many published controlled trials for the pharmacological modifications of the sympathetic response to laryngoscopy, tracheal intubation, and surgical stimulation, including opioids, tenoxicam, ketorolac, lidocaine, and paracetamol.[10] However, opioids can readily cross the placenta and lead to adverse neonatal outcomes such as serious respiratory depression and bradycardia if given before clamping.[11] Nonsteroidal antiinflammatory drugs also cannot be used due to their effect on maternal and fetal hemorrhage and premature closure of fetal ductus arteriosus.[12,13]

Paracetamol is a safe drug during all stages of pregnancy and labor.[14] It belongs to aniline analgesic class of drugs and is an active metabolite of phenacetin. Its chemical name is para-acetylaminophenol. It has a well-established safety and analgesic profile. The main mechanism of action is inhibition of cyclo-oxygenase enzyme, which is responsible for the production of prostaglandins, an important mediator of inflammation and pain. Onset of action is within 5-10 min after the start of administration. Oral paracetamol is widely used as an over-the-counter nonopioid analgesic and antipyretic with few contraindications and lack significant drug interactions.[15]

Park *et al*. in his study compared the effects of remifentanil at 0.5 or 1.0 μg/kg on maternal hemodynamic responses to laryngoscopy and tracheal intubation in pregnant patients undergoing cesarean delivery under general anesthesia. SBP was increased by tracheal intubation in both groups. The peak systolic arterial pressure after intubation was greater in the R0.5 group than in the R1.0 group, whereas it did not exceed baseline values in either group. HR increased significantly above baseline in both groups with no significant differences between the groups. Neonatal Apgar scores and umbilical arterial and venous pH and blood gas values were comparable between the groups.[16] A double-blind randomized placebo-controlled study showed less mean HR change in the paracetamol group when compared to control group (76.1 ± 13.1 [95% confidence interval (CI): 69.9-82.23] vs. 80.6 ± 15 [95% CI: 73.6-87.62]).[17]

Another randomized controlled trial showed that intraoperative hemodynamics in cesarean sections were not statistically significant between clonidine versus control groups (9.1% vs. 12.7% respectively; $P > 0.05$).[18] The rationale of this study was to observe the efficacy of intravenous paracetamol in preventing hemodynamic changes due to pain in cesarean sections at intubation as well as its effect on neonatal Apgar score. As the literature shows that paracetamol has been used safely in labor as well as before induction to observe its analgesic effects postoperatively. Therefore, this study was designed to evaluate the efficacy of intravenous paracetamol in the prevention of hemodynamic changes due to pain on ETI. Significant difference was not observed between the groups. None of the patients in any intervention group had any untoward effects related to paracetamol.[19]

Although paracetamol proves to be a safe drug for both mother and neonate, but it probably has no role in preventing hemodynamic alterations due to intubation. Its combination with other nonnarcotic analgesics may be an area, which needs further research.

Conclusion

Administration of intravenous paracetamol 1 h before cesarean section has no significant effect in preventing hemodynamic changes at the time of ETI. There were no immediate side-effects of paracetamol on patient or neonate in both the groups.

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