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Comparison of 0.5 or 1µg/kg fentanyl for prevention of haemodynamic changes during intubation in parturients undergoing caesarian section under general anaesthesia

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Introduction: Present study was designed to find low, safe and efficacious dose of fentanyl to avoid its foetal side effects by comparing two doses of fentanyl to prevent haemodynamic hazards at induction and intubation in patients undergoing caesarean section (CS) under general anaesthesia (GA).

Method: Forty five full term parturients posted for emergency/elective caesarean section under GA of ASA Grade I or II, age group between 18 to 35 years were randomly distributed into three groups. Intravenous fentanyl 0.5µg/kg or1µg/kg diluted to 5 ml or normal saline 5 ml was administered three minutes before induction in Group F 0.5, Group F1or Group C respectively. Maternal haemodynamic parameters and foetal parameters were recorded at different time intervals.

Results: Group F and Group F1 showed significant reduction and stability in maternal haemodynamics when compared with the control group, but no statistical difference was observed amongst them. No difference was observed in foetal Apgar score and cord blood pH in all three groups.

Conclusion: Fentanyl in doses as low as 0.5µg/kg can be used safely in parturients to prevent haemodynamic hazards at intubation in patients undergoing CS under GA.

Keywords: Fentanyl; caesarean section; general anaesthesia

Introduction

General anaesthesia for caesarean section is very challenging for the anaesthesiologist as safety of both mother and foetus needs to be ensured. Minimizing haemodynamic changes in the mother during induction, intubation, maintenance and recovery from anaesthesia is the responsibility of the anaesthesiologist. Awareness during anaesthesia also needs to be prevented. Safety of foetus is ensured by maintaining adequate oxygenation and by preventing unwanted effects of anaesthetic drugs. Sudden changes in maternal haemodynamics (pulse and blood pressure) at laryngoscopy and intubation (stress response) are alarming and need to be prevented without affecting foetal physiology.[1] Previous studies have used fentanyl[2], tramadol[3,] remifentanil[4],fentanyl and midazolam in low doses[5] andlignocaine[6] i.v.in premedication and halothane or sevoflurane[7]during preoxygenation to minimize these effects. Researchers are continuously working on this. Present study has been designed to find low, safe and efficacious dose of fentanyl to avoid its foetal side effects by comparing two different doses of fentanyl. Primary outcome measure compared was Mean Arterial Pressure (MAP at 1 min after intubation. Other parameters compared were demographic characteristics, duration of pregnancy, parity, incision delivery time, systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR), oxygen saturation (SpO_2), End tidal carbon dioxide ($EtCO_2$) at different time intervals and foetal parameters

(umbilical artery pH, APGAR score at 1, 5 and 10 minutes after birth).

Method

A prospective randomized double blind controlled study was carried out in a medical college hospital during the period from April to December 2012, after approval from institutional ethics committee and research cell. Forty five full term parturients posted for emergency/elective CS under GA of ASA Grade I or II, age group between 18 to 35 years and willing to participate in the study were randomly divided into three equal parallel groups after obtaining informed written consent. Parturients with complicated pregnancy including pregnancy-induced hypertension, placenta praevia, abruptio placenta, maternal bleeding; with indication for CS being foetal distress, foetal anomaly or congenital syndromes, prolonged labour, past history of complicated GA were excluded. Patients having hypertension, heart disease, diabetes mellitus, history of opioid and/or alcohol misuse, allergy to fentanyl, who have received sedatives, benzodiazepines and opioids, alpha and/or beta agonists, beta antagonists in last 24 hours were also excluded from the study.

Group F 0.5 [n=15]: i.v. fentanyl 0.5µg/kg diluted to 5ml 3minutes before induction
Group F 1 [n=15]: i.v. fentanyl1µg/kg diluted to 5ml 3 minutes before induction
Group C [n=15]: i.v. normal saline 5ml 3 minutes before induction

Method of randomization was blocked randomization. Total blocks 15, block size 3 and treatment allocation of 1:1:1 for group F 0.5, group F1 and group C. Both patient and anaesthesiologist providing the anaesthesia and recording the observations were blinded regarding the group allocation.

After allocation into three groups, patients were placed supine with 15 ^{0} left lateral tilt by placing wedge under right hip. Intravenous line was secured. All the parameters such as HR, SBP, DBP,MAP and FHS were recorded at base line, before induction during preoxygenation, 1 minute after intubation, 1 minute and 5 mins after delivery of foetus, and at recovery.

All parturients were pre-oxygenated for 5 minutes before induction. Two minutes after starting the preoxygenation and three minutes before induction all parturients were injected intravenously 5ml of normal saline (group C), 0.5µg/kg of fentanyl (group F) or 1µg /kg of fentanyl (group F1). Injection syringes were prepared by a person knowing the coding and the anaesthesia provider was blinded. Rapid sequence induction was done in all patients using i.v. thiopental sodium5mg/kg and succinylcholine1.5mg/kg and applying cricoid pressure. Intubation was done with appropriate size of cuffed endotracheal tube and airway was secured. Anaesthesia was maintained initially with 0.5MAC isoflurane (end tidal concentration) and 50% nitrous oxide / oxygen (N_2O/O_2) till the delivery of foetus. After delivery and clamping of umbilical cord further doses of i.v. fentanyl were administered up to 2µg/kg. Intravenous vecuronium was given for muscle relaxation in a dose of 0.1mg/kg. Anaesthesia was maintained with 35% to 40% O_2 with N_2O, and isoflurane. Mechanical ventilation settings were adjusted to maintain $ETCO_2$ at 32-36mmHg and end-tidal isoflurane1.0 -1.5 vol%. At the end of surgery all patients were extubated after reversal of neuromuscular block with neostigmine 0.04 mg/kg and glycopyrrolate 0.008 mg/kg i.v. and routine post-operative care was provided. The Apgar score at 1 minute, 5 minutes and 10 minutes was assessed by a paediatrician blinded to the groups. Immediately after clamping the cord blood sample was collected from umbilical artery and arterial pH was measured and recorded.Statistical analysis was carried out using software Stata 10. ANOVA tests of significance were applied for the 3 groups and unpaired students 't' test for the 2 groups. $P < 0.05$ was considered significant. Sample size had been decided after a pilot study of 30 patients; 10 in each group which gave a result for primary outcome measure MEP 1 showed that it was 113.9±7.51, 104.8±7.0 and 101.8±9.90 respectively in group C, group F and group F1 respectively.Estimated sample size for two-sample comparison of means Test with Assumptions: alpha = 0.05 (two-sided), power =0.90 for group C and group F turned out to be 28, 14 in each group, while for group C and group F1 it turned out to be 24, 12 in each group.

Results

There is no significant difference between the demographic parameters in all these groups as shown in Table 1.

Table 1: Demographic characteristics

Parameter	**Group C** (n=15) Mean ±SD	**Group F**(n=15) Mean ±SD	**Group F1**(n=15) Mean ±SD
Age (years)	22.8 ± 1.86	23.6 ± 1.80	22.87 ± 1.88 *
Height (cms)	152.2 ± 5.82	154.27 ± 6.16	151.0± 6.13 *
Weight (Kgs)	53.93 ± 6.88	53.13 ± 6.93	53.47 ± 6.20*
Pregnancy (Weeks)	38.33 ± 1.76	37.33 ±1.63	38.53 ±1.64 *

*** p-value> 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table 2 and Table 3 show that haemodynamic parameters HR, MAP, SBP and DBP were reduced significantly in parturients premedicated with fentanyl in both groups when compared with the Control Group. There was no significant difference between Group F and Group F1. Foetal parameters measured are shown in Table 4. There is no significant change in foetal Apgar score or cord blood pH in all three groups.

Table 2: Maternal haemodynamic parameters

Parameter measured at time interval	Heart Rate per minute			Mean Arterial Pressure (MAP) mm of Hg		
	Group C (n=15) Mean ± SD	**Group F**(n=15) Mean ± SD	**Group F1**(n=15) Mean ± SD	**Group C**(n=15) Mean ± SD	**Group F**(n=15) Mean ± SD	**Group F1**(n=15) Mean ± SD
Baseline	86.53± 11.40	87.33 ± 7.39 *	88.4±14.02*	87.8 ± 5.23	86.2 ± 5.02*	87.33± 6.83*
Before Induction	94.8 ± 11.18	90.93 ± 9.96 *	87.67± 13.24*	90.93 ± 5.26	87.67± 5.81 *	87.4 ± 7.07*
One min after intubation	117.33 ± 14.31	105.8± 11.75**	101.6± 12.66**	112.73± 6.42	106.2± 6.24 ***	103.33 ±8.57**
One min after delivery	99.27± 10.59	95.87± 13.32 *	99±17.51 *	98.2 ± 5.70	91.93 ± 8.05 **	92.27± 6.72 **
Five min after delivery	86.27± 10.92	86.6 ± 9.44 *	90.07± 14.27*	86.47 ± 5.46	84.13 ± 6.21 *	85.53± 5.85*
Recovery	83.13 ± 7.52	82.2 ± 6.62 *	84.73± 8.84*	86.93 ± 3.77	84.8 ± 4.95 *	85.33± 6.69*

*** p-value> 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table 3: Maternal haemodynamic parameters

Parameter Measured at time interval	Systolic Blood Pressure mm of Hg			Diastolic Blood Pressure mm of Hg		
	Group C (n=15) Mean ± SD	**Group F**(n=15) Mean ± SD	**Group F1**(n=15) Mean ± SD	**Group C**(n=15) Mean ± SD	**Group F**(n=15) Mean ± SD	**Group F1**(n=15) Mean ± SD
Baseline	118.4 ± 6.94	116.2 ± 6.81*	117.87 ± 6.39*	75.13 ± 7.20	71.07± 6.35 *	73.73 ± 5.90*
Before Induction	120.47 ± 7.31	117 ± 6.60 *	117.67 ± 8.26*	77.47 ± 9.63	71.8 ± 6.75 *	73 ± 7.38*
1 min after intubation	147.13 ± 11.47	132 ± 11.28 ***	126.93±12.70 ***	94.13 ± 6.76	83.2±7.75***	81.27± 7.29***
1 min after delivery	129.33 ± 11.27	118.47 ± 9.81***	120.13± 9.05***	82.8 ± 7.65	72.87± 9.31***	75.13 ± 7.75 ***
5 min after delivery	115 ± 9.47	110.33 ± 6.98*	112.8 ± 7.03*	73.87 ± 8.29	69.53 ± 9.49*	73.07 ± 7.11*
Recovery	117.27 ± 5.95	114 ± 5.29 *	116.27 ± 6.05 *	71.73 ± 7.69	69.47 ± 5.63 *	72.13 ± 5.96 *

*** p-value> 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Table 4: Foetal parameters

Parameter	**Group C**(n=15) Mean ±SD	**Group F**(n=15) Mean ±SD	**Group F1**(n=15) Mean ±SD
Induction delivery interval (mins)	7.47 ± 1.36	6.67 ± 2.32 *	6.2 ± 1.90 *
Umbilical artery pH	7.24 ± 0.021	7.25 ± 0.024 *	7.23 ± 0.030 *
APGAR at 1min	7.47 ± 0.64	7.27 ± 0.46 *	7.07 ± 0.26 *
APGAR at 5min	8.47 ± 0.52	8.27 ± 0.46 *	8.33 ± 0.49 *
APGAR at 10min	9.47 ±0.52	9.40± 0.51 *	9.47 ± 0.52*

*** p-value> 0.05 ** p-value significant at 0.05; *** p-value significant at 0.01**

Discussion

Although fentanyl has been used as premedication by different workers, many anaesthesiologists are reluctant due to its potential detrimental effects on foetus. Frolith[5]used1µ/kg and Baraka[3] used 2µ/kg of fentanyl, while Mieyer-Breting[2] showed minimal detrimental effects on foetus even up to 5µg/kg. They showed significant correlation between umbilical-venous fentanyl concentration and the induction-delivery time: the longer the induction-delivery time the lower the fentanyl concentration in the umbilical vein. Fentanyl

premedication in doses of 1µg/kg has been studied by MaziarMaghsoudloo[8] with no adverse effects on fetus. Levy[9]in his review article on "Emergency caesarean section: best practice" states that the dose-dependent respiratory depression effect on foetus, is predictable and easily treatable. Our observations showed that at doses as low as 0.5µg/kg fentanyl helps in controlling haemodynamic changes in the mother due to the stress response and there is no significant advantage in increasing the dose of fentanyl from 0.5µg/kg to 1µg/kg. Our results are consistent with those of Maghsoudloo[8]who administered i.v. fentanyl 1µg/kg 3 minutes before induction. Their conclusion was in favour of administering 1µg/kg fentanyl intravenously, 3 minutes before induction of anaesthesia. We observed similar results with fentanyl as low as 0.5 µg/kg. Hence we conclude that use of fentanyl as premedication in doses as low as 0.5 µg/kg is safe in parturients to prevent haemodynamic hazards at laryngoscopy and intubation in patients undergoing CS under GA and is safe for foetus as well.

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