

Alfentanil in Elective Caesarean Sections under General Anaesthesia: Maternal Haemodynamic Changes Due to Intubation

Srinivas Rapolu*, K. Anil Kumar**, Syed Ali Aasim***

Abstract

Background: Opioids administered before caesarean section under general anaesthesia reduce maternal stress response related to intubation and surgery but may decrease the Apgar score after delivery and when opioids are used. **Aim:** effect of low dose of short-acting opioid alfentanil on haemodynamic changes due to tracheal intubation during general anaesthesia for caesarean sections. **Materials and Methods:** Patients were taken for a period of 2 years in 60 pregnant patients between the ages of 18 and 40 years, scheduled for elective caesarean section, were assigned to two equal groups. Group-A:(N=30) Received alfentanil 10 mg/kg, diluted in normal saline (total volume of 10 ml), Group-P:(N=30) Received 10 ml normal saline as placebo for premedication. **Results:** There were no significant statistical differences among the two groups regarding age, weight, BIS and maternal pre-operative haemodynamic parameters. Following alfentanil administration, systolic blood pressure decreased at 1, 5 and 10 min after endotracheal intubation. Diastolic blood pressure decreased only 1 min after intubation and heart rate decreased 1 and 5 min after intubation. There were

significant statistical differences between the two groups in regard to mean heart rate 1 min after induction of anaesthesia ($P = 0.01$), 1 min after endotracheal intubation ($P = 0.000$) and 5 min after endotracheal intubation ($P = 0.04$). Mean BIS values were not significantly different between the two groups ($P = 0.3$). Mean of neonatal Apgar scores at 1 and 5 min and neonatal SpO_2 were not significantly different between the two groups. **Conclusion:** Alfentanil as premedication decreased maternal systolic, diastolic blood pressure and heart rate in the 1st min of general anaesthesia for caesarean sections.

Keywords: Alfentanil; Haemodynamic changes; Caesarean sections; Intubation.

Introduction

Opioid are justified for management in conditions such as maternal haemorrhage, overt coagulopathy, life-threatening foetal compromise, maternal heart diseases, patient refusal for regional anaesthesia, etc [1]. Regional anaesthesia may be an alternative to general anaesthesia in selected patients with dilated or restrictive cardiomyopathy. Usually it is

omitted at induction of general anaesthesia for cesarean delivery because of the concern that they may cause neonatal respiratory depression. use of available opioids may be ideally suited for use in obstetrics because of its rapid metabolism by nonspecific blood and tissue esterases in both mother and neonate.

In general anaesthesia endotracheal intubation can produce severe maternal haemodynamic changes during caesarean sections under general anaesthesia. However, administration of narcotics before endotracheal intubation to prevent these changes may affect the Apgar score in neonates [2]. This study was designed to evaluate the effect of intravenous alfentanil on haemodynamic changes due to endotracheal intubation in elective caesarean sections performed under general anaesthesia.

Author's Affiliation:

*Associate Professor **Assistant Professor ***Professor and Head, Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana

Corresponding Author:

Srinivas Rapolu, Associate Professor, Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar - 505001, Telangana, India.

E-mail:

drapolukmc@rediffmail.com

Received on 18.01.2017

Accepted on 07.02.2017

Materials and Methods

It is a randomised controlled clinical study, Patients were taken for a period of 2 years from January 2014 to 2016 in Chalmeda Anand Rao Institute of Medical Sciences. 60 pregnant patients between the ages of 18 and 40 years, scheduled for elective caesarean section, were assigned to two equal groups.

Inclusion Criteria

Age 18-40 years, Gravida 1 and 2,

Exclusion Criteria

Age > 40 years, multiparous women, Patients with a positive history of cardiovascular disease, Difficult intubation, uterine incision-delivery time more than 90 s and induction-delivery time more than 5 min drug like antihypertensive, sedative, analgesic, antihistaminic and psychoactive drugs.

After approval by the institutional ethical committee. Pre anesthetic check-up was carried out pre operatively with a detailed history, general physical examination and systemic examination.

The following laboratory examinations were done in all the subjects in study - Hemoglobin, Urine analysis, Blood sugar, Blood urea, Serum creatinine, Coagulation profile, Blood grouping and Rh typing, ECG-for patients and Chest X-ray. All patients were assessed clinically preoperatively and investigated

to rule out any systemic disease.

One minute before induction of anaesthesia patients divided into following groups.

Group-A:(N=30) Received alfentanil 10 µg/kg, diluted in normal saline (total volume of 10 ml) for premedication.

Group-P:(N=30) Received 10 ml normal saline as placebo

For induction of anaesthesia, all patients received sodium thiopentone 5 mg/kg and succinylcholine 1.5 mg/kg. During maintenance of anaesthesia, atracurium 0.5 mg/kg, isoflurane 1 minimum alveolar concentration and O₂ -N₂O (50-50%) were used. Haemodynamic parameters in this study were measured at different time periods from the time of injection of premedication until 50 min after endotracheal intubation. Bispectral index system was used to assess depth of anaesthesia and awareness. Oxygen saturation (SpO₂) and Apgar score were determined in neonates.

After neonatal delivery, patients in two groups received the same dose of oxytocin, midazolam and fentanyl. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) for windows version 16.0 SPSS software. P < 0.05 was considered statistically significant.

Results

It is a randomised controlled clinical study for a 2

Table 1: Comparison of mean of Blood pressure in two groups

| Variable | Group -A Alfentanil | Group -P Placebo | P-Value |
|--------------------------|---------------------|------------------|---------|
| Systolic blood pressure | 126±9.1 | 116±7.8 | 0.08 |
| Diastolic blood pressure | 77±9.6 | 75±7.8 | 0.321 |
| Heart rate(beats/min) | 99.1±10.23 | 92.5±9.98 | 0.05 |
| BIS | 96±8.72 | 91±7.12 | 0.04 |

Table 2: Comparison of neonatal Apgar score and SpO₂ in both groups

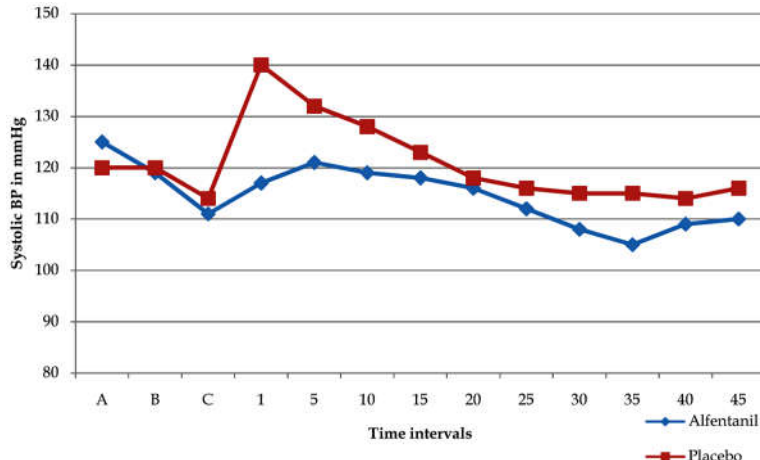
| Variable | Alfentanil | Placebo | P-Value |
|----------------------|------------|------------|---------|
| Apgar score at 1 min | 8.81±0.31 | 8.78±0.37 | 0.67 |
| Apgar score at 5 min | 10 ±0.00 | 9.88±0.33 | 0.51 |
| SpO ₂ | 88.83±3.45 | 88.71±4.87 | 0.49 |

years period in 60 pregnant patients scheduled for elective caesarean section.

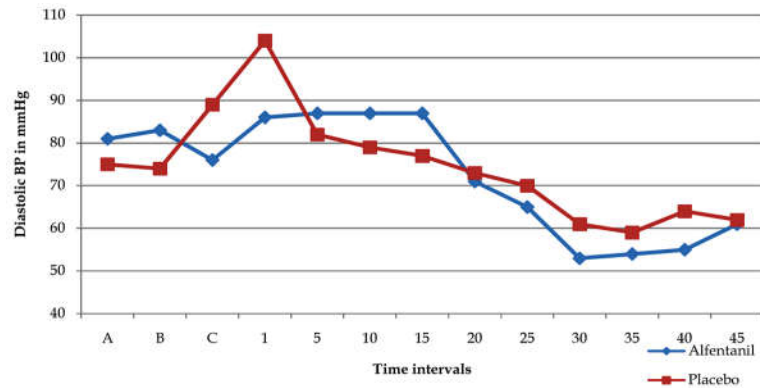
Mean of age (years) of patients was 31.4 ± 6.1 in alfentanil group and 31.8 ± 6.4 in placebo group. Average weight (kg) of patients was 78.7 ± 9.8 in alfentanil group and 79.8±7.5 in placebo group. The two groups were comparable with

respect to pre-operative haemodynamic parameters and BIS Comparison of mean of Blood pressure in two groups (A) 1 min before drug administration, (B) 1 min after drug administration, (C) 1 min after induction of anaesthesia, 1-45 Min after endotracheal intubation

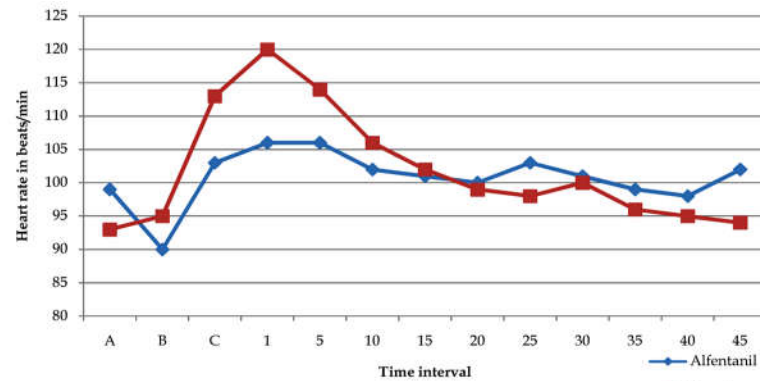
The mean systolic blood pressure changed



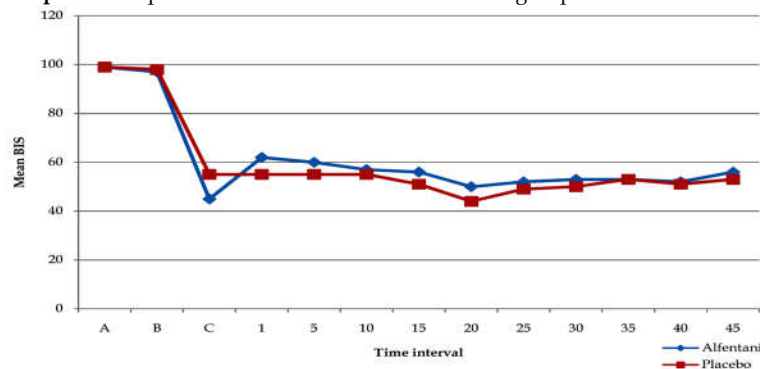
Graph 1: Comparison of mean of Systolic blood pressure in two groups



Graph 2: Comparison of mean of diastolic blood pressure in two groups



Graph 3: Comparison of mean of heart rate in two groups



Graph 4: Mean BIS values were not significantly different between the two groups ($P = 0.3$)

minimally in alfentanil group as compared to placebo group at 1 min ($P = 0.0001$), 5 min ($P = 0.000$) and 10 min ($P = 0.01$) after endotracheal intubation.

Diastolic blood pressure decreased only 1 min after intubation and heart rate decreased 1 and 5 min after intubation.

There were significant statistical differences between the two groups in regard to mean heart rate 1 min after induction of anaesthesia ($P = 0.01$), 1 min after endotracheal intubation ($P = 0.000$) and 5 min after endotracheal intubation ($P = 0.04$)

Mean of neonatal Apgar scores at 1 and 5 min and neonatal SpO₂ were not significantly different between the two groups.

Discussion

Alfentanil is a potent but short-acting synthetic opioid analgesic drug, used for anaesthesia in surgery. It is an analogue of fentanyl with around 1/4 to 1/10 the potency of fentanyl and around 1/3 of the duration of action, but with an onset of effects 4x faster than fentanyl.³ This unique characteristic is responsible for its rapid onset. It is an agonist at mu opioid receptors. While alfentanil tends to cause fewer cardiovascular complications than other similar drugs such as fentanyl and remifentanyl, it tends to give stronger respiratory depression and so requires careful monitoring of breathing and vital signs. Almost exclusively used by anesthesia providers during portions of a case where quick, fast acting pain control is needed.

There were no significant statistical differences among the two groups Demographic details, BIS and maternal pre-operative haemodynamic parameters. Following alfentanil administration, systolic blood pressure decreased at 1, 5 and 10 min after endotracheal intubation. Diastolic blood pressure decreased only 1 min

after intubation and heart rate decreased 1 and 5 min after intubation. So, we can say that alfentanil prevented exaggerated haemodynamic responses to endotracheal intubation in our patients. With respect to maternal BIS, neonatal Apgar score and SpO_2 , similar changes were seen in the both groups.

In general, we use opioids as premedication for general anaesthesia. The opioid usage might be associated with reduced maternal anxiety, making stable haemodynamic conditions during laryngoscopy and endotracheal intubation and decreasing anaesthetic requirement for maintenance of anaesthesia. Administration of opioids before induction of general anaesthesia is a matter of challenge in obstetric anaesthesia.

Safavi et al [4]. showed that some drugs such as nitroglycerin are effective in attenuating the pressor response to tracheal intubation in severe pre-eclampsia and could be used instead of opioids to control haemodynamic responses. Maghsoudloo et al [5]. demonstrated that administration of $1 \mu\text{g}/\text{kg}$ fentanyl intravenously 3 min before induction of anaesthesia leads to stable haemodynamic situation in mothers.

Hosseini et al [6]. studied the effect of remifentanyl on haemodynamic parameters of parturients and Apgar score of the neonate in elective caesarean section under general anaesthesia. They concluded that remifentanyl ($0.7 \mu\text{g}/\text{kg}$) controls haemodynamic change in parturients without producing adverse effects on Apgar scores of neonates.

Kan et al [7]. who described the use of a remifentanyl infusion during epidural anesthesia for caesarean delivery. The reason for this is unclear he explained it by their observation of a slightly increased MA PCO_2 , which was consistent with a maternal respiratory depressant effect of remifentanyl. Kan et al. infused remifentanyl at $0.1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ after establishing an epidural block and deliberately delayed skin incision for at least 15 min to establish a steady state concentration of remifentanyl at delivery. Remifentanyl has been shown to attenuate cardiovascular responses to tracheal intubation during general anaesthesia for Caesarean delivery. However, its optimal dosage to attenuate the response remains to be established. Ngan Kee and colleagues [8] demonstrated that remifentanyl $1 \mu\text{g} \cdot \text{kg}^{-1}$ as a single bolus in healthy patients undergoing Caesarean delivery was effective in controlling maternal haemodynamics after tracheal intubation. However, Draisci and colleagues [9] found that a bolus dose of remifentanyl $0.5 \mu\text{g} \cdot \text{kg}^{-1}$ followed by an infusion of $0.15 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ until peritoneal incision

was ineffective.

Pournajafian et al [10]. compared the effect of remifentanyl versus fentanyl regarding haemodynamic changes due to endotracheal intubation in pre-eclamptic parturients for caesarean delivery. They found that remifentanyl ($0.05 \mu\text{g}/\text{kg}/\text{min}$ for 3 min before induction and continued until intubation time) can be used in parturients for delivery under general anaesthesia to prevent severe increase in blood pressure and heart rate during tracheal intubation without adverse effects on newborn. Remifentanyl has unique pharmacokinetics properties. Its effects are altered negligibly by liver or kidney disorders and age variations, and is associated with rapid recovery [11,12].

In our study mean BIS values were not significantly different between the two groups ($P = 0.3$). In previous studies [13], where anaesthesia was induced with thiopentone 4 mg kg^{-1} and maintained with 1% end-tidal sevoflurane with 50% N_2O mean BIS values during the period between tracheal intubation and delivery were above 60, which is considered at risk of awareness [14]. Since opioids reduce the BIS response to a painful stimulus, we postulated that alfentanil given before induction may reduce BIS changes and hence the risk of maternal awareness during induction of general anaesthesia. However, BIS values after tracheal intubation did not differ between the groups. This finding suggests that a small dose of alfentanil may not affect BIS responses and the maternal awareness. Nevertheless, it has been shown that clinical sedation significantly increases even with the addition of a small to moderate dose of alfentanil to a sevoflurane anaesthetic [15] even though the BIS does not reflect an increased hypnotic effect. Thus, alfentanil may have the potential to enhance hypnosis and thereby to reduce the occurrence of maternal awareness regardless of the changes in BIS values.

Mean of neonatal Apgar scores at 1 and 5 min and neonatal SpO_2 were not significantly different between the two groups. As the magnitude of the difference was small and neonates in the alfentanil group had lower Apgar scores, for uncomplicated elective cases, the routine use of alfentanil was not recommended. In comparison, in the current study, we found no significant differences in indices of fetal oxygenation and thus no evidence for a fetal benefit of giving remifentanyl. Nonetheless, because there was no difference in Apgar scores between groups, this suggests that if a rapid-acting opioid is required in an obstetric patient, at the doses studied, remifentanyl may be a better choice than alfentanil.

The use of alfentanil was, however, associated with maternal hypotension and neonatal respiratory depression requiring ventilatory support. Although alfentanil is a useful adjunct to improve maternal haemodynamic stability, it should be used with adequate facilities for neonatal respiratory resuscitation. Further studies involving a larger number of high-risk patients such as those with severe pre-eclampsia and different doses of alfentanil with or without infusion are needed.

References

1. Amini S, Yaghmaei M. The use of remifentanil in general anesthesia for cesarean section in a parturient with severe mitral stenosis and pulmonary edema. *Middle East J Anaesthesiol.* 2010; 20:585-8.
2. Amin SM, Amr YM, Fathy SM, Alzeftawy AE. Maternal and neonatal effects of nalbuphine given immediately before induction of general anesthesia for elective cesarean section. *Saudi J Anaesth.* 2011; 5:371-5.
3. Jacob Mathew, J. Kendall Killgore. Methods for the synthesis of alfentanil, sufentanil, and remifentanil. US Patent 7,208,604.
4. Safavi M, Honarmand A, Azari N. Attenuation of the pressor response to tracheal intubation in severe preeclampsia: Relative efficacies of nitroglycerine infusion, sublingual nifedipine, and intravenous hydralazine. *Anesth Pain Med.* 2011; 1:81-9.
5. Maghsoudloo M, Eftekhar N, Ashraf MA, Khan ZH, Sereshkeh HP. Does intravenous fentanyl affect Apgar scores and umbilical vessel blood gas parameters in cesarean section under general anesthesia? *Acta Med Iran.* 2011; 49:517-22.
6. Hosseini F, Khalili M, Kamali A, Elyasi H, Fathi M, Ahmadi F. Effect of remifentanil on hemodynamic parameters of parturients and Apgar of the neonate in elective cesarean section under general anesthesia. *Pajoohandeh J.* 2012; 17:57-61.
7. Kan RE, Hughes SC, Rosen MA, Kessin C, Preston PG, Lobo EP: Intravenous remifentanil: Placental transfer, maternal and neonatal effects. *Anesthesiology,* 1998; 88:1467-74.
8. Ngan Kee WD et.al. Maternal and neonatal effects of remifentanil at induction of general anesthesia for cesarean delivery: a randomized, double-blind, controlled trial. *Anesthesiology,* 2006; 104:14-20.
9. Draisci G, Valente A, Suppa E, et al. Remifentanil for cesarean section under general anesthesia: effects on maternal stress hormone secretion and neonatal well-being: a randomized trial. *Int J Obstet Anesth,* 2008; 17:130-6.
10. Pournajafian A, Rokhtabnak F, Kholdbarin A, Ghodrati M, Ghavam S. Comparison of remifentanil and fentanyl regarding hemodynamic changes due to endotracheal intubation in preeclamptic parturient candidate for cesarean delivery. *Anesth Pain Med.* 2012; 2:90-3.
11. Richardson SP, Egan TD. The safety of remifentanil by bolus injection. *Expert Opin Drug Saf.* 2005; 4: 643-51.
12. Servin FS, Billard V. Remifentanil and other opioids. *Handb Exp Pharmacol.* 2008; 182:283-311.
13. Yoo KY, Jeong CW, Kang MW, et al. Bispectral index values during sevoflurane-nitrous oxide general anesthesia in women undergoing cesarean delivery: A comparison between women with and without prior labor. *Anesth Analg,* 2008; 106:1827-32.
14. Glass PS. et al. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. *Anesthesiology,* 1997; 86:836-47.
15. Manyam SC, Gupta DK, Johnson KB, et al. When is a bispectral index of 60 too low?: Rational processed electroencephalographic targets are dependent on the sedative-opioid ratio. *Anesthesiology* 2007; 106:472-83.