ORIGINAL ARTICLE

ROLE OF ALFENTANIL IN MAINTAINING CARDIO-CIRCULATORY STABILITY IN PEDIATRIC AGE GROUP ANAESTHESIA: A PHASE II COMPARATIVE STUDY

Tabish Hussain[1,2], Tumenjavkhlan Sosorburam[1], Jawad Zahir[2], Qudsia Anjum[2]
Li YuShu[1], Cheng Xiang[1], Mumtaz Hussain Shah[2]

ABSTRACT

OBJECTIVE: The aim of our study was to evaluate the efficacy of fentanyl and alfentanil in relation to hemodynamic stability of pediatric patients during routine general anesthesia.
PLACE AND DURATION OF STUDY: A prospective double staged clinical trial was conducted at Anesthesia department of the Hospital over a period of 1 year from June 2010 till May 2011.
METHODS: Total of 102 children, aged 7.3±2.1years, scoring ASA I-II, undergoing general anesthesia were recruited and randomly divided in two groups. Group A received fentanyl bolus injection while group B received alfentanil. High flow oxygen was followed by inflow of fentanyl and alfentanil administered in the respective groups. The dose was adjusted to 1.5µg/kg for both fentanyl and alfentanyl. Induction was done by 2mg/kg propofol and rocuronium was administered via automatic infusion pump system. Lungs were mechanically ventilated with a mixture of 60 % (NO) nitrous oxide and (O2) oxygen along with 1% isoflurane. Hemodynamic parameters in terms of blood pressure and pulse were recorded before and after intubations
RESULTS: Time for the systolic Blood Pressure to reach its peak value and then to normal i.e.: (51 ± 16sec vs.71 ± 34 sec, 95% CI 1.243-2.458, P 0.01) and (119 ± 33 sec vs. 74 ± 31, 95% CI 2.589-4.821, P 0.01) was statistically significant among the two groups. In addition to this, the time for the pulse to reach maximal value and then back to normal i.e., (54 ± 27sec vs.103 ± 39, 95% CI 3.035-4.786, P 0.01) and (123 ± 28sec vs. 59 ± 18, 95% CI 3.212-4.789, P 0.01) was also clinically and statistically significant among the two study groups. It shows that fentanyl group patients achieved maximal values of blood pressures and pulse quickly, but retained their peak and returned to baseline levels after a prolonged interval in comparison to the group of patients who received alfentanil.
CONCLUSIONS: Alfentanil 1.5-2µg/kg bolus injection dose in children provides a safe circulatory and hemodynamic balance with minimal cardiovascular response and a stable anesthetic state.
KEY WORDS: Fentanyl, Alfentanil, Opioids, Surgical Analgesia

INTRODUCTION

Tracheal intubation in children is usually linked with a temporary hemodynamic cardiovascular response[1]. The fentanyl groups of opioids usually attenuate the cardiovascular intubation response, when they are used in small doses[2, 3]. This potential response is directly related to drug dosage and can completely obviate the cardiovascular intubation response if high doses are used in pediatric anesthesia[4].

Intravenous bolus injections are usually a safe and efficient way of administering fentanyl and alfentanil in the routine anesthetic situations[5,6].

Intravenous fentanyl is a good option for pain management for various surgical procedures among children[7]. It is a potent synthetic narcotic analgesic with a rapid onset and short duration of action. It is a strong agonist at the μ-opioid receptors[8].

Although fentanyl has been administered by subcutaneous or intramuscular routes, it is recommended that fentanyl should be given by direct intravenous route only as it has a short half-life and multiple doses may be required. Respiratory rate should be monitored prior to and following every dose and naloxone should be close at hand for emergency administration. Onset of action after IV administration

1. Department of Anesthesia, Intensive and Cardiac Care, Union Hospital,Tongji Medical College, Huazhong University of Science and Technology,Wuhan,430030,P.R.China.
2. Department of Anesthesia and Intensive Care, Holy Family Hospital,Rawalpindi Medical College,Rawalpindi

Correspondence to:
Dr.Tabish Hussain
Department of Anaesthesia,
Intensive care and pain Medicine
Holy Family Hospital, Rawalpindi Medical College
Rawalpindi, 46000, Pakistan
E-mail: drtabish@hotmail.com

of Fentanyl is 3-5 minutes; duration of action is 30-60 minutes.

Many other fentanyl analogues have also been developed and are currently in medical practice, including sufentanil, alfentanil and remifentanil. Alfentanil is an analogue of fentanyl with around 1/10 the potency of fentanyl and around 1/3 of the duration of action, but with an onset of effects four times faster than fentanyl [7, 9]. It is an OP3 mu-agonist. While alfentanil tends to cause less cardiovascular complications than other similar drugs such as fentanyl and remifentanil it tends to give stronger respiratory depression and so requires careful monitoring of breathing and vital signs [10].

Opioids like alfentanil and remifentanil are usually associated with attenuation of the cardiovascular intubation response, when used in small doses .In large doses, these drugs seem to be strongly related with significant bradycardia and hypotension with cardiovascular hemodynamic depression which may be life threatening depending upon drug dose [11], thus needs critical monitoring of the vital signs. Contrary to this, fentanyl gives very stable results. It is usually not involved in producing bradycardia and keeps the patient in a state of well hemodynamic stability .[12]

The basic aim of this study was to evaluate the efficacy of fentanyl and alfentanil in relation to hemodynamic stability of pediatric patients during routine general anesthesia and mutually compare while assessing the cardiovascular intubation response.

MATERIAL AND METHODS

It was a double staged prospective clinical trial conducted at the Anesthesia department, of Union Hospital, Tongji Medical College, Huazhong University Teaching Hospital over a period of 1 year from June 2010 till May 2011.The first segment of study was conducted for the first six months where a total of 48 patients were recruited. Overall, we recruited 102 patients in a year.

Children undergoing general anesthesia for routine surgeries were recruited. All fell in grade I-II of the American Society of Anesthesia (ASA) scale.

Blood pressures, Pulse, Oxygen saturation and electrocardiographic recordings were obtained from the beginning in the operating room by non invasive methods of digital monitors. An IV catheter of 22G was introduced for drug administration and it was assured that all the study participants were stable and hemodynamically fit for the procedure.

The participants were then randomly divided in to two groups depending upon the drug given. Group A included participants who received fentanyl bolus injection while group B received alfentanil. Each group recruited 51(50%) patients.

High flow oxygen was followed by inflow of fentanyl and alfentanyl in the respective groups. The dose was adjusted to 1.5 μg/kg for both fentanyl and alfentanil. After about 45 seconds, induction was done by 2mg/kg propofol slowly.100% pure oxygen was provided for adequate initial ventilation and rocuronium with minimal cardiac side effects was administered via automatic infusion pump system to achieve adequate muscle relaxation and tracheal intubation with laryngoscope.

Propofol bolus dose was used as an induction agent. Since the time required to reach peak concentration and maximal effects is 1-2 minutes for alfentanyl, 4-5 minutes for fentanyl and 2-3 minutes for propofol, efforts were maximized to achieve peak effects at the same time so as to effectively attenuate the cardiovascular intubation response. Fentanyl, propofol and alfentanyl were started 4, 2 and 1 minutes before intubation, respectively. Side effects of opioids were minimized by slow infusion of the drugs as well as their small dosages.

Intubation was performed 3-4 minutes after administration of all concerned drugs with a pediatric laryngoscope. The (ETT) endotracheal tube was inserted into the glottis until the cuff was 1 cm below the vocal cords under direct vision. Following successful tracheal intubation the lungs were mechanically ventilated with a mixture of 60 % (NO) nitrous oxide and (O2) oxygen along with 1% isoflurane. The gas flow was maintained around 3 L/min.

Hemodynamic parameters in terms of blood pressure and pulse were recorded before and after intubation. These parameters were also noted during the whole procedure after every 10 minutes to get an average value. A heart rate of less than 60/minute was considered significant for bradycardia and was managed according to the individual case.

Participants with known allergy to medications, severe respiratory infections, airway obstructive complaints, gastric reflux syndrome, failed or complicated intubations were excluded from the study.

All the statistical analyses were performed using SPSS version 15 and SAS (Statistical Analysis System) version 8.2 .Standard descriptive statistics were used to characterize sample mean and standard deviation. Student's t-test was used to test for possible significant differences in ordinal and continuous variables. Range was calculated for continuous variables and frequencies and percent for categorical variables. The chi-square test was carried out to compare proportions. A p-value <0.05

was considered statistically significant.

RESULTS

The basic study parameters of the patients recruited have been mentioned in Table 1.It clearly reflects that all of these parameters have no clinical significance in relation to the two study groups of our trial (All p>0.05).

TABLE 1: Parameters of Participants

Sr No.	Parameters	Group A (Fentanyl)	Group B (Alfentanil)	95%CI	P Value
1	Sex/Total	51	51	NS	NS
	Male	31(%)	29(%)		
	Female	20(%)	22(%)		
2	Age(Years)	7.3±2.1	7.5±1.4	0.01	0.19
3	Weight(Kg)	36.1±1.8	33.6±3.2	0.01	0.21
4	Height(cm)	135.1±2.1	134.5±1.1	0.01	0.13
5	BMI(Kg/m2)	22.4±2.4	23.1±1.2	0.01	0.11

Time for the systolic Blood Pressure to reach its peak value and then to normal i.e.: (51 ± 16sec vs.71 ± 34 sec, 95% CI 1.243-2.458, P 0.01) and (119 ± 33 sec vs. 74 ± 31, 95% CI 2.589-4.821, P 0.01) was statistically significant among the two groups.

In addition to this, the time for the pulse to reach maximal value and then back to normal i.e., (54 ± 27sec vs.103 ± 39, 95% CI 3.035-4.786, P 0.01) and (123 ± 28sec vs. 59 ± 18, 95% CI 3.212-4.789, P 0.01) was also clinically and statistically significant among the two study groups. It shows that fentanyl group patients achieved maximal values of blood pressures and pulse quickly, but retained their peak and returned to baseline levels after a prolonged interval in comparison to the group of patients who received alfentanil. These results are in the same directions as were obtained for the first phase of clinical trial.

Both of these findings have been summarized in Table 2.

TABLE 2: Hemodynamic parameters of Participants

Sr No.	Variable	Group A (Fentanyl)	Group B (Alfentanil)	95%CI	P Value
1	Pre-Op Pulse	91±15	98±5	0.152-0.195	0.1
2	Pre-Op Syst.BP	108±11	110±7	0.041-0.039	0.2
3	Pre-Op Diast.BP	61±13	66±07	0.051-0.061	0.1
4	Time to reach Max.Syst.BP(Sec)	51±16	71±34	1.243-2.458	0.01*
5	Time to reach Max Pulse(Sec)	54±27	103±39	3.035-4.786	0.01*
6	Time for Syst.BP to reach Normal	119±33	74±31	2.589-4.821	0.01*
7	Time for Pulse to reach Normal	123±28	59±18	3.212-4.789	0.01*

?P-value: ≤0.05 is considered significant* ?Pulse: n/minute ?BP: mmHg ?Time: Seconds

The values of hemodynamic parameters like pulse, systolic and diastolic blood pressures before intubation, after intubation, during the operative procedure with average values, all were statistically significant among the two groups. It shows that alfentanil keeps the undergoing subjects more hemodynamically stable with markedly reduced fluctuations in circulatory parameters. These findings suggest the significance of the current study and possible stable maintenance of hemodynamics during routine general anaesthesia among pediatric age group.

All these characters have been summarized in Table 3.

TABLE 3: Hemodynamic parameters of Study Participants

Sr No.	Parameters	Pre Intubation	Post Intubation	Average (Intraoperative)	Maximal (Peak Value)
1	**Pulse**				
	Group A	94±11*	104±13*	93±05*	117±22*
	Group B	81±06*	81±12*	84±07*	91±14*
2	**Systolic. BP**				
	Group A	94±03*	102±11*	100±13*	126±14*
	Group B	82±08*	87±16*	90±03*	101±13*
3	**Diastolic. BP**				
	Group A	45±11*	59±16*	41±09*	81±16*
	Group B	33±06*	41±14*	35±08*	56±11*

? P-value: ≤0.05 is considered significant*

DISCUSSION

Fentanyl is used as an analgesic drug especially for maintaining the cardio-circulatory stability among patients on extremes of ages like children and older aged group .It can effectively maintain the hemodynamics of the patients while controlling the operative pain adequately. Among children, a dose of 0.5 to 2ug/kg is usually adequate for an excellent pain control and can be tapered about 30-40 minutes prior to the end of surgery so as to provide adequate ventilation and avoiding cardiac inhibition[13].

Intrathecal as well as intravenous routes, both can provide better hemodynamic stability and a less pronounced stress response after a single dose injection of fentanyl for the control of intra-operative pain control in child age group[14,15].

Alfentanil is an advanced narcotic pain medication used before or during surgery given slowly by intravenous route. Oxygen saturation, blood pressure, and heart rate should be monitored while this drug is being used and throughout the recovery period. Pain at the injection site, dizziness, drowsiness, nausea, vomiting, and itching has been reported as side effects of alfentanil[16].

Alfentanil allows a better pain control while assuring a good analgesic cover for all short surgical procedures without risk of early respiratory depression in postoperative period. It also provides an early postoperative recovery with cardio-circulatory stability[17].

CONCLUSIONS

Alfentanil 1.5-2µg/kg bolus injection dose in children provides a safe circulatory and hemodynamic balance with smooth cardiovascular response and more stable anesthetic state. It can keep pulse and blood pressures changes more streamlined with minimal fluctuations, thus providing a safe way to provide analgesia for surgical procedures.

ACKNOWLEDGEMENTS

I am really thankful to Mrs.Roshan Ara, Muhammad Ismail Anwar, Seid Adji, Janak Lal Pathak, Pankaj Deo, Altansukh Samadan and Qudsia Anjum for their unremarkable attention, guidance and motivation in completing this research project.

CONFLICT OF INTERESTS

There are no conflicts of interests and there is nothing to declare.

REFERENCES

1. Anila D. Malde and Vineet Sarode. Attenuation of The Hemodynamic Response To Endotracheal Intubation: Fentanyl Versus Lignocaine. The Internet Journal of Anesthesiology. 2007 , Vol 12 (1):24-26.
2. Xue FS, Liu KP, Liu Y, Xu YC, Liao X, Zhang GH et al. Assessment of small-dose fentanyl and sufentanil blunting the cardiovascular responses to laryngoscopy and intubation in children. Paediatr Anaesth. 2007 Jun; 17(6):568-74.
3. Ko SH, Kim DC, Han YJ, Song HS. Small-dose fentanyl: optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg. 1998 Mar; 86(3):658-61.
4. Xue FS, Xu YC, Liu Y, Yang QY, LiaoX, Liu HP, Zhang YM, Liu JH, Luo MP. Different small-dose sufentanil blunting cardiovascular responses to laryngoscopy and intubation in children: a

randomized, double-blind comparison. Br J of Anaesth 2008 May; 100 (5): 717–23.
5. Paech M. Newer techniques of labor analgesia. Anesthesiol Clin North America, 2003 Mar; 21(1):1 – 17.
6. Rawal N. Analgesia for day-case surgery. Br J Anaesth, 2001 Jul; 87(1): 73–87.
7. Mencía SB, López-Herce JC, Freddi N. Analgesia and sedation in children: practical approach for the most frequent situations. J Pediatr (Rio J) 2007 May; 83 (2 Suppl): S71–82.
8. Stanley TH. The history and development of the fentanyl series. J Pain Symptom Manage. 1992 Apr; 7 (3 Suppl): S3–7.
9. Gurbet A, Goren S, Sahin S, Uckunkaya N, Korfali G. Comparison of analgesic effects of morphine, fentanyl, and remifentanil with intravenous patient-controlled analgesia after cardiac surgery. J Cardiothorac Vasc Anesth. 2004 Dec; 18(6): 755-8.
10. Kim JJ, Ha MH, Jung SH, Song NW. The efficiency of IV PCA with remifentanil and ketorolac after laparoscopic-assisted vaginal hysterectomy. Korean J Anesthesiol. 2011 July; 61(1): 42–49.
11. Philbin DM, Rosow CE, Schiender RC, Koski G, D'Ambra MN. Fentanyl and sufentanil anaesthesia revisited: how much is enough? Anesthesiology, 1990 Jul; 73(1):5-11.
12. Smydo J. Delayed respiratory depression with fentanyl. Anesth Prog, 1979 Mar-Apr; 26 (2): 47–8.
13. Peterson KL, DeCampli WM, Pike NA, et al. A report of two hundred twenty cases of regional anesthesia in pediatric cardiac surgery. Anesth Analg 2000; 90:1014–9.
14. Pirat A, Akpek E, Arslan G. Intrathecal versus IV fentanyl in pediatric cardiac anesthesia. Anesth Analg. 2002 Nov; 95(5):1207-14.
15. Ambuel B, Hamlett KW, Marx CM, Blumer JL. Assessing distress in pediatric intensive care environments: the COMFORT scale. J Pediatr Psychol 1992; 17:95–109.
16. Willens JS, Myslinski NR. Pharmacodynamics, pharmacokinetics, and clinical uses of fentanyl, sufentanil, and alfentanil. Heart Lung 1993; 22:239–51.
17. Orfei P, Bigetti E, Patrizio A, Pinto G. The use of alfentanil for short duration surgery in pediatric anesthesia. Minerva Anestesiol. 2000 Mar; 66(3):123-9.