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A COMPARATIVE STUDY OF DEXMEDETOMIDINE VS FENTANYL AS AN ANAESTHETIC ADJUVANT IN ANAESTHESIA FOR COCHLEAR IMPLANTATION IN PEDIATRIC PATIENTS: DOUBLE BLIND CONTROL STUDY

Anaesthesiology

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ABSTRACT

Cochlear implant surgery is a great advancement in ear surgery for patients with irreversible hearing loss. It mandates deliberate hypotension to provide a better surgical field. Dexmedetomidine is an alpha-2 adrenoceptor agonist that provides adequate sedation with high cardiovascular stability. This randomized double blind study was aimed to compare Dexmedetomidine with Fentanyl, an opioid, as an anaesthetic adjuvant in forty pediatric patients undergoing cochlear implantation. They were divided into two groups by using intravenous bolus and infusion doses of Dexmedetomidine and Fentanyl intraoperatively following intravenous induction. Use of muscle relaxant was limited to a single dose to facilitate monitoring of the facial nerve using a peripheral nerve stimulator. Both groups were also compared with regards to the quality of the surgical field, intraoperative hemodynamics, recovery from anaesthesia, discharge time, postoperative pain using objective pain score and the need for rescue analgesics and anti-emetics in the post anaesthesia care unit (PACU). Our study found that patients in the Dexmedetomidine (D) group had quicker recovery and discharge time, significantly better surgical field and less pain compared to Fentanyl (F) group ($p<0.05$). Statistical Analysis was done using the Chi-squared test and Fisher's exact test.

KEYWORDS

INTRODUCTION :

Cochlear implant surgeries in children are performed to improve hearing in patients with congenital or acquired deafness of age ranging from 2 to 8 years. It is a great advancement in otology for patients with irreversible hearing loss and deaf-mutism and poses a big challenge to the pediatric anaesthesiologist.(1) Management of anaesthesia is aimed at ensuring a bloodless surgical field to facilitate microscopic surgery by providing stable hemodynamics such as controlled hypotension, securing an efficient airway, positioning the head carefully to avoid venous obstruction and congestion, limiting the usage of muscle relaxants to facilitate monitoring the facial nerve, achieving a smooth recovery and minimizing postoperative complications such as sedation, emergence delirium, pain and nausea and vomiting. (2)

Controlled hypotension can be achieved using a range of pharmacological agents such as inhalational agents, opioids, vasodilators, beta blockers, magnesium sulphate and alpha-2 adrenergic agonists. (3,4)

Dexmedetomidine is a potent an agonist alpha-2 agonist that causes sedation without respiratory adrenoceptor leading to its increasing use in critical care for sedation and in minor surgical procedures as a sole anesthetic agent. (5) It has many uses as an adjuvant in anesthesia in adults though there are few studies to substantiate its role in pediatric age group. One review concludes that dexmedetomidine provides perioperative analgesia thus decreasing opioid requirement, reduced pain scores and postoperative nausea and vomiting (PONV). Dexmedetomidine is also used to decrease stress response to laryngoscopy, intubation and extubation, by suppressing the sympathetic activity. (6) In a large number of studies dexmede tomidine has been used successfully to prevent emergence delirium and postoperative shivering in children. A 2013 meta-analysis of various trials done proved that pharmacokinetics and dose effects of dexmedetomidine are similar in pediatric age group as seen in adults.

On the other hand, Fentanyl is a potent lipophilic synthetic opioid and a mu receptor agonist with a short onset time and moderate duration of action. It has little effects on the circulation but produces vagally mediated bradycardia and a slight fall in systemic vascular resistance. Adverse effects of fentanyl include nausea, vomiting, pruritus, increased intracranial pressure in severe head injury patients and respiratory depression. In view of these undesirable effects various studies have recommended the use of Dexmedetomidine instead of Fentanyl to enhance the effects of anaesthesia.(7,8)

This study was designed to evaluate the postoperative recovery time by modified Aldrete recovery score, to assess postoperative pain by FLACC behavioural pain assessment scale, to assess intraoperative hemodynamics, to assess the quality of the surgical field and to assess the need for rescue analgesia and antiemesis in the PACU by using infusion doses of Dexmedetomidine 0.4mcg/kg/hr and Fentanyl 1mcg/kg/hr in two groups of patients undergoing cochlear implantation surgery.

METHODS:

This was a randomized, prospective, double blind placebo controlled study conducted in a tertiary care hospital after prior approval from the Institute's Ethics Committee. Written and informed consent was obtained from parents/guardians of all the patients after explaining about the objective of the study, the drug that was used for the study and its related complications.

Forty patients under ASA I and II category and below the age of 8 years and belonging to either sex, scheduled for elective cochlear implantation were enrolled in this study. All these forty patients were selected from the study population using computer generated random table [https://www.randomizer.org/]. The patients were randomly allocated into one of the two study groups using sealed envelope technique.

Patients with known history of allergy to dexmedetomidine or fentanyl were excluded from the study. Moreover patients with fever, upper respiratory tract infection, history of coagulopathy, congenital abnormalities, prolonged QT interval and cardiac arrhythmias were also excluded from this study.

Patients were randomized into two groups and each group comprised twenty patients. Group I received an initial IV Dexmedetomidine bolus (Dextomid injection – 100mcg/ml – 1 ml ampoule – Neon Labs) followed by infusion whereas Group II was administered an initial IV Fentanyl

bolus (Fenstud injection – 50mcg/ml – 2ml ampoule – Rusan Healthcare Pvt.Ltd.) followed by an infusion.

All the patients were assessed preoperatively through history taking, clinical examination and conducting routine laboratory investigations such as CBC, PT, PTT, INR, Liver function tests including liver enzymes, serum albumin, bilirubin, renal function tests such as blood urea and serum creatinine and serum electrolytes. A screening echocardiogram along with cardiological consultation was also done. Careful search for endocrine abnormalities such as hypothyroidism, adrenal involvement and IDDM was also made. All the patients were

kept NPO as per standard ASA guidelines for children. The drugs were diluted in a 50 ml syringe with 48 ml of 0.9% NaCl to get a concentration of 4mcg/ml of Dexmedetomidine and 2mcg/ml of Fentanyl for Groups I and II respectively. Demographic data were recorded including age, sex and weight.

After the patients were wheeled into the operating room, an intravenous catheter was inserted. Monitors including electrocardiography, noninvasive blood pressure, pulse oximetry were applied as per ASA standards. All patients were premedicated with Injection Glycopyrolate 0.01mg/kg IV and Injection Dexamethasone 0.15mg/kg IV to prevent postoperative nausea and vomiting. Peripheral nerve stimulator was used to assess recovery from muscle relaxant as well as to monitor facial nerve intraoperatively. After preoxygenation for 3 minutes with 100% oxygen, patients were induced with IV Propofol 2mg/kg followed by IV Atracurium 0.5mg/kg to facilitate intubation. Study drugs were prepared in similar syringes keeping the drug volume

constant by an anaesthesiologist, who then handed over the syringes to another anaesthesiologist who was unaware of the contents of the syringes and administered the bolus and the infusion doses and also monitored all the patient variables. Dexmedetomidine group received a bolus of 0.4mcg/kg, which was given over a period of 10 minutes followed by an infusion at the rate of 0.4mcg/kg/hr until the end of surgery. Fentanyl group was given a bolus dose of 1mcg/kg over 10 minutes followed by an infusion of 1mcg/kg/hr till the end of surgery.

Anaesthesia was maintained using a mixture of oxygen and air in a ratio of 1:1 with 2% sevoflurane. Controlled ventilation with a tidal volume of 8ml/kg was used and normocapnia was maintained by utilizing the other ventilator parameters. Mean arterial pressure was aimed at a range of 50 to 60 mmHg. Bradycardia was managed with injection atropine 0.02mg/kg IV if heart rate dropped 20% below the baseline value. IV fluids were administered at 10ml/kg/hr with Lactated Ringer's solution. At the end of surgery, patients were extubated in a deeper plane to prevent coughing and dislodgement of the electrode array of the cochlear implant before shifting to the recovery room.

Intraoperative data such as heart rate (HR), systolic and diastolic blood pressure, mean arterial pressure (MAP) and SpO2 were recorded. These data were recorded before induction (baseline value), one minute after induction,

one minute after intubation and then every 15 minutes till the end of surgical procedure. The above vital signs at the completion of surgery were noted. Hypotension was defined as a fall in systolic BP of >30% from baseline or MAP <60mm of Hg. This was managed with increments of Inj.Ephedrine 6mg. Bradycardia was defined as a heart rate <50/min and this was managed with Inj.Atropine 0.01mg/kg IV. Blood loss more than the allowable loss was replaced with packed RBCs.

To assess the quality of the surgical field according to the quality scale proposed by Fromme and colleagues, the surgeon who was blinded of the selective hypotensive agent was asked to do it on a scale of 0 to 5, starting from no bleeding to severe bleeding in an ascending manner.(9)

Recovery time and discharge time were recorded for all patients postoperatively. Recovery time was defined as the period of time from discontinuation of Sevoflurane till the patients achieved a modified Aldrete recovery score of at least 9. The discharge time was defined as the period of time from the end of the surgical procedure till the patients fulfilled the discharge criteria from PACU.

The criteria for discharge f rom PACU were return of vital signs and level of consciousness to baseline, and the ability to ambulate without help and to tolerate clear fluids without nausea and vomiting.

Postsurgical recovery was evaluated using a modified Aldrete score at 10 min in the recovery room. Postsurgical pain was assessed every 10 min in the recovery room using FLACC Behavioural pain assessment scale.

The primary outcome of the study was to compare the two groups in terms of postoperative recovery time by modified Aldrete recovery score, to assess postoperative pain by FLACC behavioural pain assessment scale, to assess intraoperative hemodynamics, to assess quality of the surgical field and to assess the need for rescue analgesia and antiemesis in the PACU.

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired 't' test. Categorical variables were analysed with the Chi square test and Fisher exact test. Statistical significance was taken as $p < 0.05$.

RESULTS:

Forty patients were enrolled with twenty patients in each group who completed the study.

Regarding the patients' demographic data and the operative time there was no statistical significance between both the groups. (Figure 1)

With regards to the intraoperative heart rate, it was statistically significant and lower in the Dexmedetomidine group when compared to the Fentanyl group at all time periods ($p<0.05$). There was a significant reduction in the values in comparison with the baseline value at all time periods in the Dexmedetomidine group, whereas in the Fentanyl group the difference was not significant. (Table 1)

As far as the intraoperative mean arterial pressure (MAP) is concerned, it was lower in the Dexmedetomidine group than in the Fentanyl group at all time periods. This decrease was statistically significant at 1 min. after intubation and throughout the surgical procedure. The MAP decreased significantly from the baseline value at all time periods in the Dexmedetomidine group while in the Fentanyl group the decrease in MAP from the baseline value was not significant during all time periods except at 1 min after induction. The quality of the surgical field intraoperatively was significantly better in the Dexmedetomidine group. (Table 2)

Considering the recovery and discharge times, Dexmedetomidine group showed significantly shorter recovery time, mean value of 564.25 seconds versus 593.00 seconds in the Fentanyl group using the MAS scoring system and significantly shorter discharge time in the Dexmedetomidine group (23.54 +/- 4.52) mins than in the Fentanyl group (28.46 +/- 5.62) mins. (Table 3)

Regarding the FLACC-BPAS (Face, Legs, Activity, Cry and Consolability – Behavioural Pain Assessment Scale) score, it is clearly evident that 95% of patients in the Dexmedetomidine group had a score of 0 whereas 70% of patients in the Fentanyl group had a score of 0 ($p= 0.0449$), i.e. a statistically significant difference of 26% between the groups and a percentage difference of 25 points. One patient in the Dexmedetomidine group and 5 patients in the Fentanyl group required just a single bolus dose of rectal Diclofenac at 10 min in the PACU. (Table 4)

Moreover, there was no statistically significant difference between both the groups regarding the need for anti-emetics in the PACU. No cases of apnoea were reported in the study groups.

Figure 1. Age Groups

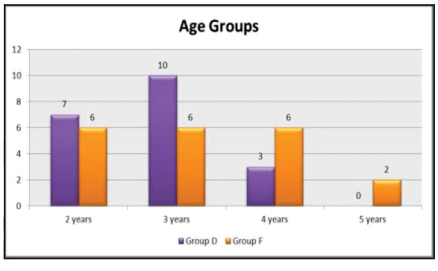

Table 1 : Intraoperative Heart Rate in Dexmedetomidine and Fentanyl groups.

Heart Rate Distribution	Group D		Group F		P value Unpaired t Test
	Mean	SD	Mean	SD	
Baseline	130.90	12.53	131.31	12.53	0.9465
1min After Induction	125.25	11.17	128.16	11.17	0.1771

1 min After Intubation	129.50	12.56	133.41	12.56	0.8468
15 min	123.60	8.59	127.81	8.59	0.8722
30 min	121.95	8.63	125.86	8.63	0.8304
45 min	120.95	10.17	124.06	10.17	0.8617
1 Hr	118.20	10.44	122.76	10.44	0.5486
1.30 Hr	114.65	11.46	118.31	11.46	0.3355
2 Hr	110.20	11.98	115.61	11.98	0.8602
2.5 Hr	106.70	9.98	111.81	9.98	0.7148
3 Hr	107.70	9.91	110.71	9.91	0.5463
3.5 Hr	108.82	11.01	112.07	11.01	0.5797
4 Hr	109.67	0.00	111.76	0.00	0.4438
4.15 Hr	100.00	0.00	112.16	0.00	0.7787
Post Operative	108.60	8.27	112.81	8.27	0.3159

Table 2 : Intraoperative MAP in Dexmedetomidine and Fentanyl Groups

Mean Arterial Pressure Distribution	Group D		Group F		P value Unpaired t Test
	Mean	SD	Mean	SD	
Baseline	79.55	3.72	81.16	3.72	0.2849
1min After Induction	72.40	4.33	77.21	4.33	0.08
1 min After Intubation	79.20	3.56	83.27	3.56	0.7917
15 min	76.65	5.17	80.05	5.17	0.9328
30 min	75.10	5.83	78.00	5.83	0.8389
45 min	73.80	5.36	76.00	5.36	0.5012
1 Hr	72.55	5.84	75.11	5.84	0.771
1.30 Hr	71.10	6.53	73.84	6.53	0.8496
2 Hr	69.55	6.26	72.21	6.26	0.3226
2.5 Hr	69.80	4.18	70.69	4.18	0.6827
3 Hr	70.40	4.43	72.42	4.43	0.8866
3.5 Hr	68.53	4.65	73.80	4.65	0.7812
4 Hr	72.00	0.00	84.16	0.00	>0.9999
4.15 Hr	80.00	0.00	88.16	0.00	0.9999
Post Operative	68.95	5.38	74.69	5.38	0.6199

Table 3 : Postoperative recovery times

Postoperative Recovery Time by MAS Distribution	Group D	Group F
Mean	564.25	593.00
SD	50.27	51.33
P value Unpaired t Test		0.0441

Table 4 : FLACC – Behavioural Pain Assessment Scale

FLACC- BPAS Status	Group D	%	Group F	%
Score 0	19	95.00	14	70.00
Score 1	1	5.00	6	30.00
Total	20	100.00	20	100.00
P value Fishers Exact Test			0.0449	

DISCUSSION :

Dexmedetomidine, due to its short half life of 8 mins and a terminal half life of 3.5 hrs, provides easy titration, quick recovery and less adverse events. It also provides adequate sedation with good cardiovascular and respiratory stability (11,12). The alpha-2 adrenoceptors exist in the dorsal horn neurons of the spinal cord and release endogenous opiate substances. Therefore, alpha-2 adrenergic agonists may be used in pain management and may decrease intraoperative opioid requirements (13).

The significant finding in this study was that Dexmedetomidine displayed a significant reduction in intraoperative HR and MAP more than Fentanyl. However, the intraoperative reduction in hemodynamic parameters in both the groups was within 20% from the baseline values. It also showed that Dexmedetomidine has remarkably better surgical quality scale and shorter recovery and discharge times than Fentanyl.

Gupta N et al did a comparative study between Dexmedetomidine and volume matched saline (placebo) and found that the Dexmedeto midine group had reduced postoperative pain and shorter recovery time. (14)

Mohammed Hafiz El Saeid et al who compared the IV infusion doses of Dexmedetomidine 0.4 mcg/kg/hr vs Fentanyl 1 mcg/kg/hr, observed hat postoperative pain was not significantly

different between the two groups. But they found that the postoperative recovery time was significantly shorter in the Dexmedetomidine group in addition to providing a better surgical field than Fentanyl group. They also observed that the Dexmedetomidine group showed a reduction in HR and MAP than the Fentanyl group and Dexmedetomidine was better in inducing deliberate hypotension which was statistically significant. (15)

Passaint Fahim Hassan, Amany Hassan Saleh et al who compared the effect of 0.4 mcg/kg/hr of Dexmedetomidine continuous infusion versus 10 mg/kg/hr Magnesium sulphate continuous infusion in providing better quality of surgical field and observed that Dexmedetomidine had superior effect on the surgical field. (16)

Goyal S et al who compared the effect of 0.25 mcg/kg/hr maintenance dose of Dexmedetomidine versus Fentanyl 0.5 mcg/kg/hr, observed that Dexmedetomidine had better recovery profile as well as a reduced need for postoperative pain management than Fentanyl. They also observed that the mean intraoperative hemodynamics (HR and MAP) was less in Dexmedetomidine group compared to Fentanyl group with significant p value. (17)

As a limitation to this study, only a subjective scoring system could be used to assess the quality of the surgical field and BIS monitor could not be used to assess the depth of anaesthesia. Further studies are needed to compare the efficacy of Dexmedetomidine with other commonly used agents during cochlear implant surgeries in paediatric population.

CONCLUSION:

Dexmedetomidine administration in cochlear implantation in pediatric patients appears to be a better alternative to fentanyl, since it produces quick postoperative recovery along with reduced postoperative pain and a lesser need for rescue analgesia with better quality of the surgical field. Dexmedetomidine was well tolerated with no clinically significant adverse effects on blood pressure and heart rate.

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Nil.

Conflicts of interest:
There are no conflicts of interest.

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