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ORIGINAL RESEARCH

Efficacy Of Intraoperative Dexmedetomidine Infusion on Emergence Agitation and Quality of Recovery after Functional Endoscopic Sinus Surgery

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ABSTRACT

Background: Emergence agitation has potential to harm both patients and caregivers. This is more often witnessed in patient undergoing otolaryngology operations under general anesthesia with volatile anesthetic used for maintenance.

Aim: We investigated the effects of intra-operative dexmedetomidine infusion on emergence agitation and quality of recovery after functional endoscopic sinus surgery in adult patients.

Materials and Methods: One hundred patients undergoing functional endoscopic sinus surgery were randomized into two groups. The dexmedetomidine group (Group D, n = 50) received dexmedetomidine infusion at a rate of 0.4 mcg/kg/hr from induction of anaesthesia until extubation, while the control group (Group C, n = 50) received volume-matched normal saline infusion as placebo. Propofol (2 mg/kg) and fentanyl (2 mcg/kg) were used for induction of anaesthesia, and sevoflurane was used for maintenance of anaesthesia. The incidence of agitation, haemodynamic parameters, and recovery characteristics were evaluated during emergence. A 40-item quality-of-recovery questionnaire (QoR-40) was provided to patients 24 hours after surgery.

Results: The incidence of agitation was lower in Group D than Group C (28 vs 56 %, P = 0.018). Mean arterial pressure and heart rate were more stable intra-operatively and during emergence in Group D than in Group C ($P < 0.05$). Time to extubation, nausea and vomiting, and pain scores were similar between the groups. Global QoR-40 score at 24 hours after surgery was higher in Group D (mean 174.7 ± 6.99) compared with Group C (mean 169.4 ± 9.91) ($P < 0.05$).

Conclusion: Intra-operative infusion of dexmedetomidine provided smooth and hemodynamically stable emergence. It also improved quality of recovery after nasal surgery.

Keywords: General Anaesthesia, Complications, Emergence Agitation, Pharmacology, Dexmedetomidine, Postoperative Nausea and Vomiting, Pain Score, Quality of Recovery

INTRODUCTION

Emergence agitation (EA), also called as emergence excitement, emergence delirium or post anaesthetic excitement is a well-recognized clinical phenomenon occurring in the immediate post-operative period following general anaesthesia. It has been considered a common post anaesthetic problem in children and adults since 1960.[1,2,3] Though it is most often seen in children and elderly, with literature focused on this population, it can affect all age groups.[4] The incidence reported in paediatric population is 12 - 13 % and about 10-15 % in geriatric age group.[4]

Dexmedetomidine (Dex) is a selective α_2-receptor agonist and has sympatholytic, analgesic, and sedative properties.[5] Infusion of dexmedetomidine reduces agitation from general anaesthesia in children[6,7] and from ventilator weaning in ICU patients.[8,9] It has been shown to reduce opioid consumption, pain intensity, stress response and thus improve quality of recovery after surgery.[10,11] So the present study was designed to evaluate the efficacy of intra-operative dexmedetomidine infusion on level of agitation and quality of recovery when used as an infusion in adults undergoing functional endoscopic sinus surgery (FESS).

MATERIALS AND METHODS

This was a prospective, randomized, double blinded, placebo-controlled study, conducted over a period of 12 months at a tertiary care centre in South India, conducted after obtaining approval from the institutional review board and the ethics committee, and written informed consent from the patients. It was conducted among 100 American Society of Anaesthesiologists (ASA physical status I-II) patients who underwent elective functional endoscopic sinus surgery requiring nasal packing under general anaesthesia. The study participants were randomly allocated into two groups, group C and Group D, by a computer-generated randomization chart.

SAMPLE SIZE ESTIMATION

For calculation of sample size, primary end point mean difference of agitation level was considered between groups.

Sample size formula:

$$n = \left(\sigma \frac{Z_{1-\alpha/2} + Z_{1-\beta}}{\mu_C - \mu_D}\right)^2$$

Where,

σ is standard deviation = 1.24

z is standard normal variate

μ is expected mean

μC = 4.5 (Mean of Group C)

μD = 4.0 (Mean of Group D)

α is Type I error = 5 %

β is Type II error, meaning 1−β is power = 80 %

Calculated sample size 97 and rounded to 100. For each treatment group, sample size of 50 were considered.

INCLUSION CRITERIA

ASA I and ASA II patients of either sex, aged between 20-60 years of age who underwent FESS under general anaesthesia requiring nasal packing on each side for 24 hours post surgery.

EXCLUSION CRITERIA

Patients with uncontrolled hypertension and diabetes mellitus, kidney, liver disease, heart block greater than first degree, cognitive impairment, on chronic antipsychotic medication, BMI $\geq$ 30kg/m², patients allergic to monoamine oxidase inhibitors, adrenergic blocking agents or clonidine and pregnant women.

STUDY PROCEDURE

Group D patients received dexmedetomidine infusion at a rate of 0.4 mcg/kg/hr from the beginning of induction of anaesthesia until extubation. Dexmedetomidine was diluted with normal saline to a concentration of 4 mcg/ml in 50 ml. Group C patients received volume matched normal saline infusion as placebo. The quality of recovery was assessed 24 hour after surgery in the ward, using a 40-item quality-of-recovery questionnaire (QoR-40).[12] Five dimensions of recovery are included within the QoR-40: emotional state (9 items), physical comfort (12 items), psychological support (7 items), physical independence (5 items), and pain (7 items). Each item is graded on a five-point score, and global scores range from 40 (extremely poor quality of recovery) to 200 (excellent quality of recovery).

STATISTICAL ANALYSIS

Descriptive and inferential statistical analysis was carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented as count and per cent. Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher's exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Statistical Package for Social Sciences (SPSS) 15.0, MedCalc 9.0.1 and R software version 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate tables.

RESULTS

There was no statistically significant difference between the two groups and both groups were comparable with respect to age, gender, weight, height, BMI, ASA grade distribution, or the mean duration of surgery.

	Group						p Value
	C			D			
	N	Mean	S D	N	Mean	S D	
0 min	50	76.4	10.19	50	76.4	8.86	0.983
10 minutes	50	70.9	8.65	50	68.8	8.04	0.203
30 minutes	50	66.68	7.34	50	64.2	6.18	0.0729
End of surgery	50	80.7	8.12	50	77.5	10.26	0.0889
At extubation	50	95.7	9.49	50	90.78	10.12	0.0134
2 mins. after extubation	50	86.46	7.28	50	82.58	8.37	0.0151

Table 1: Comparison of Heart Rate between Two Groups

The baseline heart rate was comparable between the two groups. Heart rate after 10 min, 30 min and at the end of surgery (time of nasal packing) were similar between the two group (P

> 0.05), with no statistical significance. Whereas at extubation and 2 mins. after extubation, heart rate was lower in Group D than Group C (P < 0.05) and was statistically significant.

Time	Group						p Value
	C			D			
	N	Mean	S D	N	Mean	S D	
0 min	50	130.8	7.61	50	131.9	8.00	0.475
10 minutes	50	93.68	5.81	50	92.38	8.40	0.370
30 minutes	50	91.72	7.34	50	88.88	8.32	0.0734
End of surgery	50	103.9	8.70	50	100.72	7.56	0.0552
At extubation	50	125.64	6.88	50	121.9	11.03	0.0447
2 mins. after extubation	50	134.6	6.89	50	131.5	7.36	0.0355

Table 2: Comparison of Systolic Blood Pressure between Two Groups

The SBP was comparable at baseline, at 10 min and at 30 min after induction in both the groups (P > 0.05). Whereas it was lower in group D compared to group C at end of surgery, at extubation and 2 min after extubation and the difference was statistically significant (P < 0.05).

Time	Group						p value
	C			D			
	N	Mean	S D	N	Mean	S D	
0 min	50	78.26	5.00	50	79.78	4.86	0.127
10 minutes	50	58.6	6.71	50	58.8	5.18	0.881
30 minutes	50	60.0	10.34	50	58.0	8.26	0.288
End of surgery	50	67.9	7.14	50	65.2	4.14	0.023
At extubation	50	65.50	6.75	50	63.0	4.47	0.031
2 mins. after extubation	50	65.36	6.47	50	62.86	4.21	0.024

Table 3: Comparison of Diastolic Blood Pressure between Two Groups

The DBP was comparable at baseline, 10 min, and 30 min after induction (P > 0.05), whereas it was significantly lower in group D compared to group C at end of surgery, at extubation and 2 min after extubation. (P < 0.05).

Time	Group						p Value
	C			D			
	N	Mean	S D	N	Mean	S D	
0 min	50	95.76	4.97	50	97.18	4.02	0.1197
10 minutes	50	70.32	5.44	50	70.0	5.14	0.7631
30 minutes	50	70.6	8.05	50	68.3	7.13	0.1337
End of surgery	50	79.92	6.08	50	77.10	3.46	0.0053
At extubation	50	94.5	5.14	50	88.16	5.03	< 0.001
2 mins. after extubation	50	88.4	5.42	50	85.78	4.07	0.0066

Table 4: Comparison of Mean Blood Pressure between Two Groups

The mean arterial pressure (MAP) was comparable at baseline, at 10 mins. after induction and at 30 min after induction where as it was significantly lower in group D compared to group C, at end of surgery, at extubation and 2 min after extubation, and the difference of which was highly significant (P < 0.01).

	Group						p Value
	C			D			
	N	Mean	S D	N	Mean	S D	
Agitation level (grade)	50	4.5	1.23	50	3.9	1.18	0.018

Table 5: Comparison of Agitation Level between Two Groups

Agitation Score	Group C		Group D		p value
	No	%	No	%	
≥ 5	28	56.0	14	28.0	0.006
≤ 4	22	44.0	36	72.0	

Table 6: Comparison of Agitation Score Between Two Groups

Agitation score between two groups was found to be statistically significant with P < 0.05. It was found that 56 % of Group C patients showed emergence agitation compared to Group D who demonstrated 28 %. 1 patient in Group D and 2 patients in Group C showed dangerous agitation (score of 7). In group C, 7 patients were very agitated as compared to 4 patients in Group D (score of 6). All these patients were treated with fentanyl and none of them required propofol to treat the emergence agitation.

The mean time for verbal response in Group D was higher (11.5 min ± 1.16) than Group C (10.9 min ± 1.40) and it was statistically significant (P = 0.022). But it did not affect the time for extubation, and it was comparable in between the groups. (P = 0.870).

Residual sedation (agitation score ≤ 3) was found in 8 % patients in Group D whereas none of the patients in Group C had any residual sedation. This difference was not significant (P = 0.1176). However, these 4 patients in Group D did not require any other kind of intervention.

The NRS score was comparable in both the groups at all the time intervals and hence statistically insignificant (P > 0.05).

10 patients in Group C and 4 patients in Group D had severe nausea which required antiemetics, but this difference was not statistically significant (P > 0.05). None of the patients in either group had any nausea or vomiting at 30 min, 60 min, 90 min and 120 minutes.

	Group						p Value
	C			D			
	N	Mean	S D	N	Mean	S D	
Emotional state				50	39.3	3.25	0.053
Physical comfort				50	38.0	3.37	0.088
Psychological support	50	32.3	1.60	50	48.9	4.41	0.498
Physical independence	50	21.0	2.78	50	21.4	2.79	0.497
Pain	50	29.2	4.99	50	31.0	1.92	0.019
Global QoR-40	50	169.4	9.91	50	174.7	6.99	0.003

Table 7: Comparison of Quality of Recovery between Two Groups

The mean global QoR-40 score at 24 h after surgery in Group D (174.7 ± 6.99) was significantly higher than the score for Group C (169.4 ± 9.91) (P = 0.003). Group D, particularly demonstrated higher scores in pain dimension compared with Group C (P = 0.019).

DISCUSSION

The intraoperative MAP tended to be lower in group D compared to Group C, however there were no significant differences between the groups, this is similar to that seen by Kim SY et al.[13] The systolic and diastolic blood pressure values also showed a similar trend as the MAP. The property of dexmedetomidine to decrease blood pressure explains the lower MAP in group D. Maintenance of dexmedetomidine until extubation provided more stable haemodynamic changes during emergence in our study, as also observed by Kim SY et al. and Goksu S et al., using saline and dexmedetomidine as the test drugs in patients undergoing functional endoscopic sinus surgery.[13,14] Requirement of ephedrine for hypotension was not different between the groups and none of the patients in either group had any episodes of bradycardia. 3 patients in Group C had tachycardia and required esmolol intra-operatively,

whereas none of the patients in Group D had tachycardia. Previous studies done by Patel A et al. and Erdil F et al. comparing fentanyl and dexmedetomidine also shows results similar to our study with respect to hemodynamic stability.[15]

The incidence of EA in the present study was 56 % in the control group (group C) whereas it was 28 % in the dexmedetomidine group (group D) with a mean agitation level (grade) of 4.5 ± 1.23 in Group C and 3.9 ± 1.18 in Group D (P value = 0.018). This observation is comparable to those seen in the studies conducted by Kim SY et al.[13] (52%), Yu D et al. (55.4 %),[16] Khurshid H et al.[17] (50 %). In the present study, patients who were expected to have a higher risk of EA, i.e., those requiring nasal packing, use of tracheal tube, benzodiazepine premedication and inhalational agents, were included. Hence as expected, in group C the incidence of EA was higher (56 %) similar to the previously reported results which varies from 22.2 % to 55.4 %.[18] Kim SY et al. in their study reported the incidence of EA as 22.2 %.[13] Most of their patients received TIVA with propofol and remifentanil. Total intravenous anaesthesia is known to be protective against EA, hence this may be one of the reasons for observing a lower incidence in this study compared to present one.

The time to verbal response in group D was 11.5 ± 1.16 min v/s 10.9 ± 1.40 min in Group C ($P < 0.05$). Even though time to verbal response was significantly longer in Group D, time to extubation was not affected significantly (group D v/s group C, 12.9 ± 1.27 v/s 12.9 ± 1.16, $P > 0.05$). The longest time to extubation was not more than 15 minutes, which is not clinically significant, and the delay did not produce any clinical problem. These results were similar to that seen by Kim SY et al..[13] Along with significant longer time to eye opening to verbal stimuli Khurshid H et al.[17] also observed a higher time to extubation in the dexmedetomidine group which was significant. This observation by Khurshid H et al.[17] was similar to Patel A et al.,[6] who compared dexmedetomidine with fentanyl.

In our study, NRS for pain were similar between the two groups. 4 patients in group D and 10 patients in group C required rescue fentanyl in PACU. The observations made in the current study are similar to studies done before by Kim SY et al. and Khurshid H et al. who had used the same NRS for serial assessment of pain.[13,17] In a study done by Tufanogullari B et al. there was no statistical difference between the pain scores.[10]

Only 4 patients required antiemetics in Group D as compared to 10 patients in Group C in the PACU. Similar results were observed in the study done by Kim SY et al. who in their study had an incidence of nausea and vomiting of 6 % in dexmedetomidine group as compared to 9 % the saline group and the difference was not statistically significant.[13]

Global QoR-40 scores were significantly higher in Group D compared with Group C. Among the five dimensions in the QoR-40, pain was the most significantly improved among Group D patients. The effect of intra-operative dexmedetomidine infusion on patient-perceived quality of recovery has been investigated in only a few studies. Results similar to our study has been shown by Kim SY et al after nasal surgery when compared to placebo.[13]

Bekker A et al. were of the opinion that even after major spinal surgery, 0.5 mcg kg/hr of dexmedetomidine was associated with improved quality of recovery as measured by the 40-item questionnaire that was used in our study.[11] In patients with non-small cell lung cancer requiring VATS, in which a nine-item questionnaire was used for assessing quality of recovery by Lee SH et al., 1.0 mcg/kg of dexmedetomidine for 20 minutes before the termination of surgery was associated with improved quality of recovery.[19] However after laparoscopic bariatric surgery, in which a nine-item questionnaire was used for assessing quality of recovery by Tufanogullari B et al., 0.2 – 0.8 mcg/kg/hr of dexmedetomidine was not associated with improved quality of recovery.[10]

LIMITATION(S)

The present study was conducted on ASA grades I and II patients with a small sample size based on the incidence of emergence agitation, which may not be enough to check quality of recovery. A preoperative QoR-40 questionnaire was not used in our study. The possibility of effects of pain and preoperative anxiety on emergence agitation could not be ruled out. Also it is uncertain whether the beneficial effects of dexmedetomidine persisted beyond 1 day after nasal surgery. So, further studies with inclusion of higher ASA grade and larger sample size, where follow up are done beyond 24 hrs post surgery will be required to extrapolate our findings.

CONCLUSION

Maintenance of intra-operative dexmedetomidine infusion (0.4 mcg/kg/hr) until extubation provided smooth and hemodynamically stable emergence without complications after functional endoscopic sinus surgery. Furthermore, it improved the quality of recovery 1 day after surgery.

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