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Effects of intra-operative administration of intravenous dexmedetomidine on incidence of emergence phenomenon after general anaesthesia in adults; An observational study

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ABSTRACT

Background: The occurrence of emergence agitation (EA) is the most common and practical problem faced in the immediate post-operative period during the process of Extubation under General Anaesthesia. Dexmedetomidine, an α^2 adrenoceptor agonist is an excellent drug that has been shown effective to decrease the preoperative anxiety and smooth induction and emergence. **Aims and Objectives:** To assess the effect of intravenous dexmedetomidine primarily on EA and other complications that may occur during emergence from general anesthesia. **Materials and Methods:** 80 patients of either gender aged 18–65 years with ASA status I and II, undergoing various elective general and urological surgeries under general anesthesia were included in the study. Patients receiving adjuvant drug dexmedetomidine, were labelled as Group D (n = 40) and those who didn't receive any adjuvant were labelled as group C (n = 40). Dexmedetomidine was given at 1 μg/kg and then maintained at infusion of 0.4 μg/kg/h till the end of the surgery for group D. The hemodynamic parameters and SpO_2 were measured during the intraoperative period at various intervals of time till the end of surgery and also on arrival to the recovery room till patient was discharged from post-anesthesia care unit in both the groups. **Results:** The use of IV dexmedetomidine has proved significantly effective in prevention of incidence of EA with the overall incidence of agitation of 7.5% in Group D as compared to 42.5% in group C. **Conclusion:** Intraoperative administration of intravenous dexmedetomidine decreased the incidence of EA and other emergence phenomena like cough, pain and PONV with stable hemodynamics, safety profile, good analgesic properties and opioids sparing side effects.

Key words: Dexmedetomidine; Emergence agitation; General anaesthesia; Extubation

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INTRODUCTION

The smooth and safe emergence after the completion of surgery is one of the primary goals of anesthesia and during this critical phase a wide range of undesirable complications may occur. Emergence from general anesthesia involves cessation of sedatives, reversal of paralysis and extubation. At times, emergence from general anaesthesia can be extremely challenging due to occurrence of emergence phenomenon or emergence agitation (EA). Emergence phenomenon is a common complication after general anaesthesia in the post-anesthesia care unit (PACU).[1] In certain cases, it may lead to self-extubation, accidental removal of catheters, pain, and bleeding.[1,2] These changes may be detrimental to patients, particularly in those with impaired cardiac and pulmonary reserves.[3] Different studies have reported different incidences of emergence phenomenon in adult populations, ranging from 3.7% to

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21%, due to the variability in the patient population and the scale used to assess EA.[1-4] Furthermore, emergence from anesthesia is often accompanied by signs of delirium in PACU, which may be associated with worse outcomes and also further delirium in the postoperative course.[5]

Various pharmacological and non-pharmacological strategies are being used to prevent emergence phenomenon. Dexmedetomidine is a selective α2-adrenoceptor agonist with sympatholytic, analgesic, anxiolytic and sedative properties without respiratory depression.[6] Its being used intra-operatively for smooth and hemodynamically stable emergence and to improve the quality of emergence from general anesthesia.[7-9]

This hospital based observational study was conducted in a tertiary teaching hospital, and its aim was to assess the effect of intravenous dexmedetomidine primarily on EA and other complications that may occur during emergence from general anesthesia such as coughing, PONV and pain and also to assess the effect of dexmedetomidine on intra and post-operative hemodynamic parameters.

Aims and objectives

To assess the effect of intravenous dexmedetomidine primarily on emergence agitation and other complications that may occur during emergence from general anesthesia.

MATERIALS AND METHODS

This observational study was conducted in the Department of Anaesthesiology, Sher-I-Kashmir Institute of Medical Sciences from August 2020 to August 2021. After approval from Institutional Ethical Committee, a written informed consent was taken from the patients for participation in this study. Patients of either gender between age group 18–65 years with ASA status I and II, undergoing elective surgeries which include abdominal surgeries, urological surgeries and Thyroidectomies under general anesthesia with expected duration of surgery up to 3 h were included in this study. Patients allergic to dexmedetomidine, obese (body mass index >35 kg/m^2), with underlying heart block or liver diseases, on antidepressants, or with chronic pain using opioid or non-opioid analgesics were excluded from the study. Pre-anaesthetic evaluation was carried out in all the patients and the whole procedure was explained to each patient.

A total of 80 patients were included in the study. Patients receiving adjuvant drug as dexmedetomidine were labelled as Group D (n=40) and those who didn't receive any adjuvant were labelled as group C (n=40). The patients were shifted to the operating room, baseline standard monitors were connected to the patient. Preoperative baseline systolic and diastolic BP, HR, SpO_2 were recorded. Intravenous line was established. The anesthetic technique was uniform for all patients. Patients were induced with fentanyl @1–2 μg/kg, IV lidocaine @1 mg/kg, propofol@1.5–2 mg/kg and atracurium 0.5 mg/kg. After orotracheal intubation anesthesia was maintained using nitrous oxide in oxygen in a ratio of 60:40, isoflurane 1% and 0.1 mg/kg of atracurium after every 20 min.

After anesthesia induction the adjuvant drug, dexmedetomidine was started as per the discretion of the in-charge anesthesiologist. Whether the patient will receive dexmedetomidine or not was decided by the in-charge anesthesiologist according to his/her routine.

Dexmedetomidine used was in the concentration of 4 μg/mL. The anesthesiologist in-charge started the adjuvant drug 1 μg/kg via infusion pump over a period of 15 min, then maintained infusion at the rate of 0.4 μg/kg/h till the end of the surgery for group D. At the end of the surgery nitrous oxide, isoflurane and the adjuvant drug (in group D) were discontinued, defined as T_0 or "baseline of emergence process". 100% oxygen was given at 6 L/min. Inj ondensteron 0.1 mg/kg was given. The patients were reversed using neostigmine 60 μg/kg and glycopyrolate 10 μg/kg. When the patients could breathe spontaneously and followed the command to "open their eyes", they were extubated and observed for 10 min after extubation and then transferred to the recovery room.

The hemodynamic study parameters HR (beats/min), SBP, DBP, mean arterial pressure (MAP) (mmHg) and SPO_2 were measured before induction, at induction, at every 15 min after induction, till the end of surgery. These hemodynamic parameters were again recorded on arrival in the recovery room and at every 5 min till patient was discharged from PACU in both the groups.

In both the groups EA, cough, PONV, pain was recorded at T0, at extubation, 2 min, 5 min and 10 min post extubation. Patients were shifted to PACU, and above-mentioned study parameters were recorded at arrival, after every 5 min till patient was discharged from PACU. Level of agitation was assessed with the help of Riker sedation-agitation scale (RSAS) and the highest agitation score for each patient was recorded. Level of pain was measured with the help of 11-point numeric rating scale. The grade of cough was assessed using a 4-point scale (0=no cough; 3=severe, sustained for >5 s). PONV score was assessed using a 4-point scale (1=absent; 2=mild nausea; 3=severe nausea; and 4=vomiting).

The recorded data was compiled and evaluated using SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean±SD and

categorical variables were summarized as frequencies and percentages. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P<0.05 was considered statistically significant. All P-values were two tailed.

RESULTS

Comparison of demographic data

All the demographic data of both the groups were comparable in terms of age, gender, ASA status and duration of surgery. The age of the patients and gender distribution among both the groups were comparable in our study with mean age of 38.68yrs with SD±13.12 years in group D and 40.35 years with SD±12.26 years in group C and the difference being statistically insignificant (P=−0.557). The gender distribution was also comparable among the two groups with P=0.501 (Table 1).

Comparison of hemodynamic parameters

The heart rate, systolic and diastolic blood pressures were significantly lower in dexmedetomidine group compared to the group C without development of any bradycardia or hypotension. There were statistically significant lower values (P<0.05) of all the hemodynamic parameters in group D as compared to Group C, both in intra-operative period as well as the PACU (Tables 2 and 3).

Comparison of incidence of agitation, cough, pain score and PONV

Post extubation and during the PACU stay, patients were assessed for EA using RSAS. A score of 5 or > 5 was taken as agitated. In our study the overall incidence of agitation was 7.5% in D group and 42.5% in group C. The score was measured at T0, at extubation, 2 min, 5 min and 10 min post extubation and then in the recovery room every 15 min till discharge. None of the patients in either group showed any agitation at T0 and at extubation. For Group D 7.5% of patients had RSAS score >5, at 5 min post extubation, which remained same at 10 min. However, it was observed that, 40% of patients in group C had RSAS score ≥5 at 5 min post extubation and then flattened to 37.5% at 10 min post extubation. The P-value at 5 min and 10 min post extubation, were 0.001 and 0.003repectively, which were statistically significant (Table 4).

On arrival to PACU 32.5% patients in Group C had RSAS score ≥5, while only 5% in Group D had RSAS score >5 with P=0.004. Similarly, significant differences (P<0.005) were noted at other intervals of time in PACU stay and at the time of discharge from PACU (Table 4).

The incidence of cough between two groups was also observed. It was assessed using 4point ordinal scale. The results indicated that overall incidence of coughing was significantly lower in group D (32.5%) than in group in C (62.5%) with the P<0.001. Also the incidence of severe cough (grade 3) was 2.5% in group D while it was 15% in Group C with the P=0.048 (Table 4).

Table 4, also shows the comparison based on pain score, between the two groups at various intervals of time. It was assessed using Numeric pain rating scale. The results indicated that pain scores were significantly higher in

Table 1: Demographic profile of patients of both the groups

Demographic characteristics	Group D (n=40)	Group C (n=40)	P-value
Age (in years)	38.68±13.12	40.35±12.26	0.557
Gender (M/F)	42.5/57.5	50/50	0.501
ASA (I/II)	75/25	82.5/17.5	0.412
Mean duration of surgery (min)	110.7±13.92	113.2±14.85	0.883

Table 2: Comparison of hemodynamic parameters intra-operatively in both groups

Hemodynamic parameters	Group D	Group C	P-value
Heart rate			
Base line	82.98±10.91	81.48±8.20	0.489
At 15 min (post induction)	73.20±8.98	79.15±12.51	0.017*
At 30 min	70.98±10.09	78.23±12.12	0.005*
At 60 min	72.40±8.68	79.53±12.91	0.005*
At 90 min	74.71±7.36	82.97±8.47	<0.001*
At 120 min	81.64±5.64	88.40±7.13	<0.009*
SBP (mmHg)			
Base line	135.78±6.77	134.13±7.30	0.298
At 15 min (post induction)	95.78±6.96	126.33±7.09	<0.001*
At 30 min	95.45±7.59	123.30±10.00	<0.001*
At 60 min	92.55±6.28	123.25±6.93	<0.001*
At 90 min	98.13±7.13	110.73±5.27	<0.001*
At 120 min	94.29±6.52	112.53±4.27	<0.001*
DBP (mmHg)			
Base line	84.30±6.51	85.28±4.30	0.819
At 15 min (post induction)	63.03±4.70	79.85±4.75	<0.001*
At 30 min	61.60±4.58	76.18±6.37	<0.001*
At 60 min	61.73±3.89	84.23±6.38	<0.001*
At 90 min	62.42±3.73	75.05±4.59	<0.001*
At 120 min	62.64±2.68	74.20±4.00	<0.001*
MAP (mmHg)			
Base line	101.46±5.75	101.56±4.43	0.875
At 15 min (post induction)	73.95±3.71	95.35±4.55	<0.001*
At 30 min	72.89±4.31	91.89±6.87	<0.001*
At 60 min	72.00±3.12	97.23±5.34	<0.001*
At 90 min	74.33±4.25	86.95±3.55	<0.001*
At 120 min	101.46±5.75	101.56±4.43	0.875

MAP: Mean arterial pressure, *Statistically significant

Table 3: Comparison of hemodynamic parameters of both the groups in PACU

Hemodynamic parameters	Group D	Group C	P-value
Heart rate (bpm)			
On arrival	84.28±8.42	94.60±6.71	<0.001*
At 5 min	88.60±8.35	98.55±6.60	<0.001*
At 10 min	83.70±7.58	93.33±6.43	<0.001*
At 15 min	76.65±7.05	89.38±5.45	<0.001*
At discharge	84.68±6.87	91.15±5.99	<0.001*
SBP (mmHg)			
On arrival	118.48±4.91	128.70±4.39	<0.001*
At 5 min	125.98±6.10	134.45±5.93	<0.001*
At 10 min	119.63±5.79	128.25±6.06	<0.001*
At 15 min	116.63±4.94	127.45±6.08	<0.001*
At discharge	122.13±5.80	130.48±6.20	<0.001*
DBP (mmHg)			
On arrival	76.68±3.37	83.48±2.28	<0.001*
At 5 min	80.58±3.73	86.13±3.95	<0.001*
At 10 min	78.93±4.05	84.58±4.11	<0.001*
At 15 min	75.65±4.10	81.63±3.61	<0.001*
At discharge	74.35±4.38	82.05±2.93	<0.001*
MAP (mmHg)			
On arrival	90.61±2.91	98.55±2.14	<0.001*
At 5 min	95.71±3.21	102.24±3.28	<0.001*
At 10 min	92.49±3.67	99.14±3.48	<0.001*
At 15 min	89.31±3.42	96.90±3.45	<0.001*
At discharge	90.28±3.86	98.19±2.84	<0.001*

MAP: Mean arterial pressure, *Statistically significant

Table 4: Effects of use of Intra-operative Dexmedetomidine on incidence of agitation, cough, pain score and PONV

Parameter	Group D (%)	Group C (%)	P-value
Incidence of agitation			
At extubation (T0)			
2 min post extubation	2.5	30	<0.002*
5 min post extubation	7.5	40	<0.001*
10 min post extubation	7.5	37.5	<0.003*
On arrival in PACU	5	32.5	<0.004*
At 5 min	5	27.5	<0.015*
At 10 min	5	32.5	<0.004*
At 15 min	2.5	25	<0.009*
At discharge	2.5	15	<0.034*
Incidence of cough			
Any cough (Grade ≥1)	32.5	62.5	<0.001*
Severe cough (Grade 3)	2.5	15.0	0.048*
Pain score			
At extubation	0	0.48±0.68	<0.001*
2 min post extubation	0.23±0.42	0.73±0.91	0.002*
5 min post extubation	0.35±0.48	1.18±1.22	<0.001*
10 min extubation	0.43±0.64	1.73±1.50	<0.001*
On arrival in PACU	0.43±0.64	1.63±1.71	<0.001*
At 5 min	0.55±0.88	1.25±1.66	0.021*
At 10 min	0.75±1.19	0.53±1.04	0.371
At 15 min	0.75±1.28	0.48±0.55	0.251
At discharge	0.53±0.93	0.50±0.72	0.893
PONV			
No nausea	72.5	37.5	0.012*
Mild nausea	17.5	35.0	0.012*
Severe nausea	10.0	20.0	0.012*
Vomiting	0.0	7.5	0.012*

P<0.005- significant, *Statistically significant

group C than in group D with P<0.001 at all intervals of time till up to 5 min in PACU with the P=0.021 at 5 min in PACU, and thereafter the pain scores among the two groups remained comparable during the stay in PACU up to discharge from the PACU.

Our results also showed a significant reduction in PONV in patients in group D, as compared to Group C with the P=0.012. The results showed that only 27.5% of group D had mild or severe nausea, while 55% in group C had mild or severe nausea. Also, no patient in Group D had vomiting, while 3 patients in Group C had vomiting (Table 4).

The requirement of rescue analgesia between the two groups was also observed in our study. It showed 62.5% of patients in Group C required rescue analgesia while only 12.5% in group D required rescue analgesia and the difference being statistically significant (Table 5).

DISCUSSION

Emergence from general anesthesia is not simply the reverse process of induction. The knowledge of its complex mechanisms is mandatory for avoiding or limiting number of complications including altered mental status, coughing, which may induce an increase in intracranial and intraocular pressures, respiratory events like laryngospasm, hypertension, tachycardia and the occurrence of EA.[10]

EA is multi-factorial and one possible mechanism is variation in neurologic recovery rate in different brain areas.[11] Surgery-induced neuro inflammation may be another cause of this functional change within the brain.[12] Moreover, the association of EA with other factors, such as pain, inhalational anesthetics, preoperative anxiety, male gender, age, and type of surgical procedures, has been suggested.[1-4]

Dexmedetomidine because of its unique properties offers its promising use in wide spectrum of clinical settings, ICU and now making its way through fast-tracking anesthesia regimens and offers anesthetic sparing and hemodynamic stabilizing effects. It is a new generation, highly selective α2-adrenergic receptor agonist that is associated with sedative and analgesic sparing effects, reduced delirium and agitation, perioperative sympatholysis.[13]

Table 5: Requirement of rescue analgesia between the patients of two groups

Rescue analgesia needed	Group D	Group C	P-value
Yes	12.5	62.5	<0.001*
No	87.5	37.5	<0.001*

*Statistically significant

This study was intended to determine the role of dexmedetomidine on EA and other complications that may occur during emergence from general anesthesia such as coughing, haemodynamic variations, PONV and pain. All the demographic parameters in both the groups of our study were comparable (Table 1) with no statistical significance.

In a study conducted by Kim et al., (2013), the results suggested that the incidence of agitation was lower in patients in group receiving dexmedetomidine than the group in controls (28 vs. 52%, P=0.014). They concluded that intra-operative infusion of dexmedetomidine provided smooth and hemodynamically stable emergence and also improved quality of recovery surgery.[7] Similarly Polat et al., (2015) who in their study compared three groups one receiving ramifentanil, other receiving dexmedetomdine and the third as a control group receiving normal saline(placebo) in their study found that the incidence of EA was significantly lower in group R (ramifentanil) and group D.[14] Similarly in various other studies where dexmedetomidine has been used either as premedication, 1 μg/kg intranasal 45 min before induction,[15] or loading dose 2 μg/kg followed by maintenance of 0.7 μg/kg/h and at dose of 0.3 μg/kg iv 10 min before discontinuation of anesthetics[16] has all showed decreased incidence of EA. All these studies have results consistent with the result of our study.

Although many studies showed similar results, a randomized controlled study conducted by Ham et al., (2014), found that that addition of a single dose of dexmedetomidine (1 μg/kg) to low-dose remifentanil infusion did not attenuate EA in intubated patients after orthognathic surgery compared with low-dose remifentanil infusion alone. However, single-dose dexmedetomidine suppressed coughing, hemodynamic changes, and pain during emergence and recovery phases, without respiratory depression.[17] So it indicates that single dose of dexmedetomidine is not enough to attenuate EA, therefore a continuous infusion was used in our patients which was helpful in attenuating EA.

Though the primary objective of this study was to assess the effect of intravenous dexmedetomidine on emergence delirium and recovery profile of patients emerging from general anesthesia by evaluating cough, post-operative nausea, vomiting and pain scores; the effect of dexmedetomidine on hemodynamic parameters both intra and post operatively, were also observed.

Regarding the hemodynamic parameters it was observed that the heart rate, systolic and diastolic blood pressure showed a statistically significantly lower values in dexmedetomidine group compared to the group C without development of any bradycardia or hypotension and this trend continued in PACU till discharge of the patient from PACU area with the P<0.001 (Tables 2 and 3). Similar observations were also noted in readings of systolic, diastolic and MAP measurements with statistically significant difference (P<0.001) between the two groups, the trend of which continued in PACU till the discharge of patient from PACU (Tables 2 and 3).

This can be explained by the fact that dexmedetomidine is a highly selective α 2-adrenoceptor agonist, with hemodynamic stability, analgesic and sympatholytic affects, it also maintains adequate organ perfusion. It attenuates the stress responses during surgery and maintains intraoperative hemodynamics.[18] In agreement with the results of the present study, a study by Rao et al.,[19] showed that patients who underwent elective surgeries under general anesthesia and had received a loading dose of dexmedetomidine 1 μg/kg and then continuous infusion of 0.5 μg/kg/h had a stable intra-operative hemodynamics. Many other studies as conducted by Kang et al.,[20] Yacout et al.,[21] also showed similar results.

Assessing the pain using numeric pain rating scale showed that the pain scores were significantly higher (P<0.001) in group C than in group D, thereby significantly increasing the requirement of rescue analgesia in group C (62.5%) than in group D (12.5%) (Tables 4 and 5). Similarly, in a study done by Bielka et al., they reported that the use of intra-operative dexmedetomidine infusion is safe and effective for improving analgesia during and after elective laparoscopic cholecystectomy, thus supporting the evidence that dexmedetomidine appears to significantly reduce the severe postoperative pain, prolongs the time to rescue analgesia and decrease the overall requirements of analgesics.[22] However, Rebecca et al., in a retrospective study found that Intra-operative use of dexmedetomidine during posterior spinal fusion for adolescent idiopathic scoliosis appeared to have no effect on postoperative pain scores.[23] The possible reason might be that both groups received intrathecal morphine and iv ketamine intra-operatively that masked the analgesic effect of dexmedetomidine.

Attenuation of cough, and other hemodynamic changes at the time of emergence in children and adults has also been seen with dexmedetomidine.[7,24] Although, there has been conflicting results regarding the efficacy of dexmedetomidine as a cough suppressant, we in this study found that the overall incidence of coughing was significantly lower in group D as compared to group C (Table 4). A study done by Guler et al., stands in concordance with our results of dexmedetomidine attenuating the airway reflexes during extubation.[25] While

the superiority of dexmedetomidine over ramifentanil still remains debatable[26] many studies have shown dexmedetomidine being superior to fentanyl for cough suppression during extubation.

The incidence of PONV, showed a statistically significant reduction in group D, as compared to Group C. The results of this study are also in accordance with the study done by Wang et al., who in their meta-analysis indicated that perioperative dexmedetomidine decreased postoperative nausea and shivering in laparoscopic surgical patients.[27] The possible reason for the reduced PONV may be attributed to the direct antiemetic properties of alpha 2 agonist through inhibition of catecholamine by parasympathetic tone. Administration of Dexmedetomidine reduces the perioperative fentanyl consumption which may also explain the reason for decrease PONV.[28]

Limitations of the study

The patients not followed after being discharged from PACU and the sample size was small.

CONCLUSION

In our study we found that intraoperative administration of intravenous dexmedetomidine decreased the incidence of EA and other emergence phenomena like cough, pain and PONV. It also provided stable hemodynamics both intra and post operatively. The safety profile of dexmedetomidine with good analgesic properties, opioids sparing side effects and a stable hemodynamics will led to more preferential usage of dexmedetomidine in modern day anaesthesia practice.

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GJB- Definition, review of literature, implementation of study protocol, data collection, data analysis; **INN-** Concept, design of protocol, manuscript preparation, manuscript review; **AQL-** Design of study, statistical analysis and interpretation; **FM-** Design of study, prepared first draft of manuscript, revision of manuscript and submission of article; **FAG-** Review manuscript; **AHM-** Implementation of study protocol, data collection; **RQ-** Coordination, preparation of table and editing and manuscript revision.

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