ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

A triple blind, randomised, placebo controlled, add-on trial to assess the efficacy and safety of dexmedetomidine in facilitation of general anaesthesia in patients undergoing elective spine surgery

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Submission: 10-11-2020 Revision: 30-01-2021 Publication: 01-03-2021

ABSTRACT

Background: Dexmedetomidine is a centrally acting sympatholytic drug acting as an agonist on alpha2 receptors. Of late, the drug has become popular in anaesthesia because of its sedative, analgesic and anti-adrenergic effects. **Aims and Objectives:** We conducted a single centre, randomised, placebo controlled, triple blinded add-on trial to assess the efficacy and safety of the drug as an adjuvant in general anaesthesia (GA) during elective spine surgery. **Materials and Methods:** Anaesthesia was induced and maintained using standard method in all the patients (N = 60). Concomitantly, patients in the treatment arm (n = 30) and control arm (n = 30) were infused with dexmedetomidine and normal saline respectively. The anaesthetic sparing effect, hemodynamic stability, and adverse events of dexmedetomidine were assessed using pre-defined outcome parameters. **Results:** Anaesthetic Sparing Effect: Dexmedetomidine produced statistically significant reduction in the requirement of propofol and fentanyl during GA ($p < 0.001$). There was no significant difference in requirement of rocuronium ($p = 0.25$). Hemodynamic Stability: The cardiovascular stimulation during surgery, in general, and during stress of artificial endotracheal access, in particular, were attenuated in the treatment arm. The heart rate (HR) and mean arterial pressure (MAP), in the control and treatment arm became greater and lesser than the baseline value respectively, at all the time points following induction. The HR and MAP remained close to baseline values during intubation and extubation in the treatment arm but surged significantly in the control arm ($p < 0.001$). Adverse Events: The number of episodes of hypotension, hypertension and bradycardia in the control arm was 1, 18 and 1 respectively. In the treatment arm, 2 episode each of hypotension and bradycardia and none of hypertension occurred. **Conclusion:** Dexmedetomidine, which is being increasingly used as an adjuvant in GA in various types of surgeries, also plays an auxiliary role in facilitation of GA in spine surgery. It decreases requirement of the primary anaesthetic agents, and also mitigates intra-operative cardiovascular instability without causing any significant adverse effect.

Key words: Dexmedetomidine; General Anaesthesia; Spine surgery; Adverse effects

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v12i3.32831

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Dexmedetomidine, an alpha-2 agonist, was first approved by Food and Drug Administration (FDA) at the end of 1999 for use in humans as a short-term medication (<24 hours) for analgesia and sedation in the critical care units.[1] It not only possesses hypnotic and sedative properties but has also analgesic and para-sympathetic

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actions with comparatively lesser effect on respiratory depression.[1] In addition, the drug has the ability to reduce both the anaesthetic and opioid analgesic requirements during the perioperative period.[2] Owing to the beneficial actions, the molecule is becoming increasingly popular as an add-on drug for smooth and stable anaesthesia in many critical and prolonged surgeries. Though numerous trials have been conducted in which the use of dexmedetomidine have been demonstrated to reduce requirements of anaesthetic agents and post-operative opioid analgesics,[3] there is limited data on the use of this drug in spinal surgery. Spinal surgery involves but is not limited to nerve root or cord decompression, laminectomy, laminoplasty and disc arthroplasty.[4] Hemodynamic stability is also necessary during spinal surgery to minimise blood loss and ensuring an equilibrium between spinal cord perfusion and a bloodless surgical window.[5] Dexmedetomidine not only has an anaesthetic sparing effect, it can also have a better cardiovascular safety during surgery due to its sympatholytic effect.[3] Therefore, the present study was designed as randomized, triple blind, parallel group, placebo controlled, single-centre study to evaluate the anaesthetic sparing effect, hemodynamic stability and adverse effects of the intraoperative infusion of dexmedetomidine in patients undergoing elective spine surgery.

MATERIALS AND METHODS

Study population

The patients admitted in a teaching hospital for elective spine surgery under general anaesthesia were screened for inclusion in the study based on predefined eligibility criteria. Patients of either gender in the age group of 30-60 years with expected duration of surgery of 1.5-2.5 hours and falling under American Society of Anaesthesiology (ASA) physical status I or II, were included. The exclusion criteria were 1. Patients having any severe systemic illness. 2. Long term use of certain medications. 3. Psychiatric illness. 4. Alcohol/drug abuse. 5. Patients on chronic opioid analgesic, tri cyclic anti-depressant (TCA), clonidine, mono-amine oxidase inhibitor (MAOI) therapy. 6. Heavy smoking habit. 7. Pregnancy and breast-feeding mothers. 8. History of allergic reactions to any drug. 9. Abnormal preoperative electrolyte concentrations. 10. Participation in any other clinical trial within 3 months. 11. Failure to get informed consent. The study was approved by Institutional Ethics Committee, Calcutta National Medical College & Hospital, Kolkata. Informed written consent was taken from each participant.

Study design

The current study was designed as a prospective, interventional, randomized, placebo controlled, triple blinded trial with two parallel treatment groups. 60 patients were randomly allocated into two equal groups: - group D (patients received dexmedetomidine 1μg/kg in 10 mins, followed by 0.5 μg/kg/hr) and group C (control group-patients received equal volume of 0.9% normal saline in the same manner) according to a computer-generated random number table using block randomisation in blocks of 6. Allocation concealment was achieved by placing the randomization sequence for each subject in sequentially numbered sealed brown envelopes. Randomisation and allocation concealment were carried out by an independent researcher who was oblivious to the ongoing research. The independent researcher supplied the drug or the placebo in identical looking 50 ml syringe containing same volume of fluid and identified only by the computer-generated random number sequence. The participants, the anaesthetist and other health care professionals involved in treatment, and the researcher collecting the data were oblivious to the treatment allocation. Data was analysed by an independent statistician not involved in patient care and also oblivious to treatment allocation. The statistician was maximally exempted of any assessment bias as the key to the dichotomous coding of the treatment and placebo arms were kept unknown. Unblinding for any stakeholder was done only when data analysis was complete and the results were finalised and secured from alteration. The study was conducted from July 2011 to June 2012.

Outcome measures

Primary outcome measures

- Dose of propofol required for induction and maintenance of anaesthesia during the surgery

Secondary outcome measures

- Total dose of fentanyl and rocuronium required during the intra-operative period
- Heart rate and mean arterial pressure during the intra-operative period
- Adverse events during and after anaesthesia.

Sample size

Sample size estimation was done by using Win Pepi software (version 11.15, J.H.Abramson, July 1, 2011). Assuming a study power of 90% and probability of type 1 error to be 5%, it was observed that a total of 55 patients will be required to detect a significant difference of 1.2 (pooled standard deviation 3) of the mean doses of total requirement of propofol consumption (mg/kg) throughout the surgery period. Considering that 4-5 patients may not be included in the final analysis due to unforeseen situations, we included a total of 60 patients (30 patients in each group) for this trial.

Procedure

Pre-operative

The patients were directed to take light dinner on the preoperative day and were not allowed to take food or water since morning on the operative day. Adequate sleep and allay of anxiety were ensured in all patients with oral diazepam 10 mg and oral midazolam 7.5 mg (with one-or two sips of water) on the pre-operative night and 2 hours before operation respectively.

Operative

A final assessment of operative fitness was done before the start of surgery. A standard protocol for anaesthesia was obeyed for each patient. Pre-medication with intravenous glycopyrrolate (0.2 mg) and ranitidine (50 mg) was done. Adequate hydration and oxygenation were ensured for each patient as per protocol. Injection fentanyl (2 mcg/Kg body weight) was given 3 minutes before induction with intravenous propofol administered at a rate of 20 mg/5 seconds. The treatment/control preparation was also started 3 minutes before induction at the pre-determined rate of 1.5 ml/kg/hr for 10 min, followed by infusion of 0.12 ml/kg/hr. Endotracheal intubation was facilitated by muscle relaxant rocuronium bromide in a dose of 0.9 mg./kg. The level of anaesthesia was monitored clinically and with Bi-spectral Index (BIS). The BIS electrodes were placed on the forehead and on the lateral angle of orbit and connected to A-2000 BIS monitoring system. Maintenance of anaesthesia was achieved with by N2O 66% in oxygen 33%, and injection propofol at 5 mg/kg/hr which was titrated to maintain a BIS value in the range of 40-60. Inadequate analgesia defined as an increased of HR and MAP of more than 20% of baseline was managed with a bolus dose of fentanyl 0.5 μgm/kg body weight or propofol 20 mg for BIS of 40-60 and >60 respectively. Muscle relaxation was maintained by intermittent bolus doses of rocuronium bromide with constant neuromuscular (TOF responses) monitoring. Propofol requirement was adjusted to maintain a constant BIS value within 40-60. Adverse effects of bradycardia (defined as symptomatic bradycardia with HR <60 beats/minute) and hypotension (defined as MAP < 20% of pre induction value or systolic BP < 90mm of Hg in two consecutive readings taken 3 min apart) were monitored and treated. On completion of surgery, anaesthesia reversal was done as per standard anaesthetic care.

Post-operative

The patients were observed for any adverse events or side effects during the postoperative period and appropriately treated if required. Postoperatively, all patients were monitored in the recovery room for first 24 hrs. Patients were assessed for pain after shifting to post anaesthetic care unit from operation theatre and provided pain relief with standard analgesics.

Assessment of outcome parameters

Anaesthetic sparing effect

The anaesthetic sparing effect of dexmedetomidine was assessed by comparing the requirement of propofol for induction and maintenance of anaesthesia in the two arms. In addition, the total intra-operative requirement of fentanyl and rocuronium was also compared in the two groups.

Hemodynamic stability

Heart rate and mean arterial pressure in the two arms during the operative period were recorded at multiple time points and compared within and between the groups.

Adverse events

The number of adverse events of hypotension, bradycardia and hypertension were recorded in both the groups and compared.

Statistical analysis

Discrete categorical data were presented as n (%) and median. Continuous data were given as mean (±SD). Fisher's exact test was employed to test the association of study characteristics between the two treatment groups for categorical variables. As the continuous data were not passing the normality test, non-parametric statistics were performed. Nonparametric Mann-Whitney test was employed to find the significant difference ($p<0.05$) between the two groups (intergroup comparison). Friedman's ANOVA test followed by Dunn's Multiple Comparison test as post hoc test was employed to find intragroup differences between outcome parameters at multiple time points. The computer software graph pad instat version 3.06.was used for all the statistical analysis.

RESULTS

Baseline characteristics

The demographic and clinical characteristics of the patients in the two arms are shown in Table 1. All patients were compliant with the treatment protocol after randomization. There was no statistically significant difference between the two arms with respect to the baseline characteristics.

Anaesthetic sparing effect

There was statistically significant greater requirement of propofol, and fentanyl during the intraoperative in Group C compared to Group D (P<.0.001 for both the drugs). However, the dose of rocuronium required for intraoperative muscle relaxation was not statistically or clinically different between the two groups (P=0.25). The requirement of the three drugs during the intraoperative period is shown in Table 2.

The requirement of the drugs in mg/Kg body weight is expressed as mean± Standard deviation.

Hemodynamic stability

Comparison of heart rate

Intergroup comparison

Apart from the preoperative heart rates which were very similar (p=0.55) in the two groups, the heart rate in group D was significantly (P<0.001) less than that of group C at all observed time points in the intra-operative period. The differences in the heart rate between the two groups were maximum during intubation and extubation. (Table 3, Figure 1).

Intragroup comparison

The heart rates in group D after induction and during maintenance were significantly less compared to baseline (P<0.001) at all time points. No significant increase in heart rates occurred during intubation or extubation and were very close to baseline values on both the occasions. In group C, heart rates were higher than baseline value at all time points, becoming statistically significant during intubation and extubation and showed two peaks- one at 1 minute after intubation and the other at 1 minute after extubation (p=0.001 and 0.01 respectively) (Table 3, Figure 1).

Comparison of Mean Arterial Pressure (MAP)

Intergroup comparison

The results of intergroup comparison of MAP between the two groups were similar to comparison of heart rates. Likewise, the preoperative MAPs were close to each other (p=0.42) in the two groups, and significantly

Table 1: Comparison of baseline characteristics in the two treatment arms. Continuous data are expressed as mean±Standard deviation and categorical data are expressed as counts

Sl. No.	Variable	Group D (n=30)	Group C (n=30)	*P* value
01	Age in years	42.54±6.70	41.94±3.75	0.25
02	Body weight in Kgs	57.4±6.80	54.74±5.71	0.25
03	Gender (Male/Female)	21/9	19/11	0.78
04	Height in Cms	158.97±5.57	157.6±6.34	0.39
05	ASA-PS grade (Grade I/Grade II)	20/10	18/12	0.78
06	Duration of surgery in minutes	135±11.21	129.5±14.16	0.13
07	Type of Surgery (MD/PI)	16/14	18/12	0.79

ASA-PS- American Society of Anaesthesiology- Physical Status, MD- Microdiscectomy, PI-Pelvic Instrumentation

Table 2: Comparison of the intra-operative requirement of the anaesthetic drugs in the two treatment arms

Sl. No.	Variable	Group D	Group C	*P* value
01	Induction dose of propofol	1.24±0.23	1.99±0.17	<0.0001
02	Maintenance dose of propofol	2.52±0.32	4.11±0.58	<0.0001
03	Total dose of propofol	6.88±0.78	10.87±1.81	<0.0001
04	Total dose of fentanyl	2.61±0.26	4.38±0.66	<0.0001
05	Total dose of rocuronium	1.77±0.16	1.72±0.17	0.25

The requirement of the drugs in mg/Kg body weight is expressed as mean± Standard deviation.

Table 3: Comparison of heart rate (beats/min) in the intraoperative period between the two treatment arms

TIME PERIOD IN MINUTES	GROUP D MEAN (SD)	GROUP C MEAN (SD)	*P* value
Pre-operative (HR1)	76.6 (5.53)	77.6 (5.01)	0.55
After infusion (HR2)	69.37 (5.62)	84.4 (11.14)	<0.0001
1 min after induction (HR3)	68.34 (6.54)	84.7 (15.43)	<0.0001
1 min after intubation (HR4)	77.84 (8.75)	108.2 (9.17)	<0.0001
10 min (HR5)	71(6.42)	89.14 (10.74)	<0.0001
20 min (HR6)	70 (7.51)	88.47 (9.3)	<0.0001
30 min (HR7)	71.04 (7.17)	84.87 (9.06)	<0.0001
40 min (HR8)	70.87(8.52)	85.14 (10.54)	<0.0001
60 min (HR9)	70.54 (7.82)	84.74 (9.76)	<0.0001
80 min (HR10)	69.87 (8.35)	83.07 (10.64)	<0.0001
100 min (HR11)	69.1 (6.95)	82.27 (9.69)	<0.0001
120 min (HR12)	70.48 (7.66)	85.37 (10.99)	<0.0001
130 min (HR 13)	70 (4.12)	84.78 (8.54)	<0.001
1 min after extubation (HR14)	79.27 (6.61)	103.67 (8.64)	<0.0001
3 min after extubation (HR15)	74.62 (6.46)	92.94 (7.32)	<0.0001

(P<0.001) less in group D at all other observed time points in the intra-operative period. Similarly, the differences in the MAPs between the two groups were maximum during intubation and extubation (Table 4, Figure 2).

Intragroup comparison

The intragroup pattern of change in MAP between the two groups was also analogous to their respective change in heart rates. The MAPs in group D after induction was less than the baseline MAP at all intraoperative time points and reached statistical significance at all the time points except at 1 minute after intubation and 1 minute after extubation. In contrast, in group C, the MAPs were higher than the baseline MAP at all intra-operative time points and was statistically significant during intubation and extubation. Two peaks of increase in MAP was observed- one at 1 minute after intubation and the other at 1 minute after extubation (Table 4, Figure 2).

Adverse events

The number (percentage) of adverse events of hypotension, hypertension and bradycardia in group C was 1(3%), 18(60%) and 1(3%) respectively. 2 (6%) incidences each of hypotension and bradycardia was seen in group D. No event of rise of blood pressure occurred in group D.

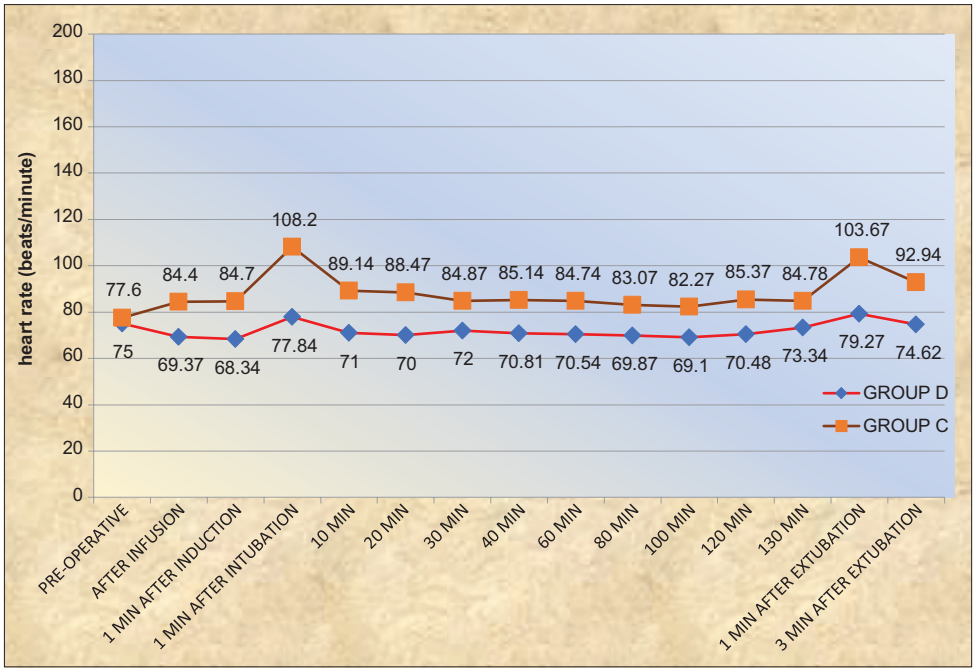

Figure 1: Time series graph showing the heart rate (beats/min) at incremental time points in the intraoperative period in the two treatment arms

Table 4: Comparison of mean arterial blood pressure (MAP) in mm of Hg at different time points in the intra-operative period between the two treatment arms

TIME PERIOD IN MINUTES	GROUP D MEAN (SD)	GROUP C MEAN (SD)	*P* value
Pre-operative (MAP1)	93.41 (6.4)	91.46 (6.21)	0.42
After infusion (MAP2)	86.17 (5.9) *	96.21 (8.28)	<0.0001
1 min after induction (MAP3)	79.05 (5.94) ***	91.64 (6.92)	<0.0001
1 min after intubation (MAP4)	93.18 (10.28)	113.27 (5.81) ***	<0.0001
10 min (MAP5)	85.6 (7.14) *	99.83 (8.28) **	<0.0001
20 min (MAP6)	84.93 (7.0) **	98.92 (5.81) *	<0.0001
30 min (MAP7)	86.08 (6.69) *	97.31 (4.98)	<0.0001
40 min (MAP8)	85.69 (5.69) *	97.57 (4.68)	<0.0001
60 min (MAP9)	84.5 (5.76) **	97.50 (6.64)	<0.0001
80 min (MAP10)	84.7 (5.59) **	97.33 (7.34)	<0.0001
100 min (MAP11)	83.16 (6.22) ***	96.35 (6.47)	<0.0001
120 min (MAP12)	83.94 (5.67) ***	98.24 (5.49)	<0.0001
130 min (MAP13)	82.5 (5.49) **	98.37 (5.34)	<0.0001
1 min after extubation (MAP14)	91.05 (8.86)	112.34 (8.46) ***	<0.0001
3 min after extubation (MAP15)	85.24 (6.82) **	102.64 (7.38) ***	<0.0001

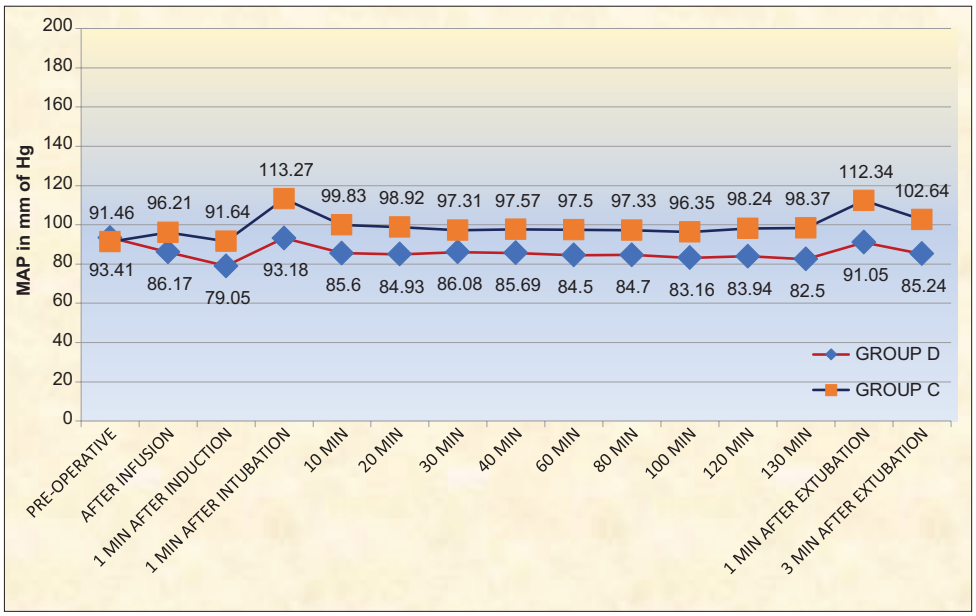

Figure 2: Time series graph showing the Mean Arterial Pressure (MAP) at incremental time points in the intraoperative period in the two treatment arms

DISCUSSION

The primary aim of our study was to assess the adjuvant role of dexmedetomidine in general anaesthesia in patients undergoing elective lumbar spine surgery. In addition, we also evaluated the hemodynamic stability and safety of the drug in the same set of patients. The results of our study support the auxiliary use of drug in general anaesthesia to mitigate the requirement of the primary anaesthetic and analgesic agents with better hemodynamic stability and safety. The use of dexmedetomidine is not new in anaesthesia and the scientific evidence in favour of the drug as a useful adjunct is becoming stronger. We discuss the results of our study vis-à-vis the existing literature under the following headings.

Anaesthetic sparing action

Our result demonstrated a highly significant reduction in consumption of propofol during induction and also in maintenance of anaesthesia. Fentanyl requirement was also found to be lower in dexmedetomidine receiving group. However, consumption of rocuronium was comparable in both the groups. Shabaz and Arain in 2002, used an initial loading dose of 1 µgm /kg for 10 mins period before induction followed by 0.4µgm /kg/hr continuous infusion to the end of surgery and observed reduced anaesthetic requirements, less morphine sulfate consumption with lower pain scores in the postoperative period.[6] Gurbet A and Turker G 11 in 2006 used a loading dose of dexmedetomidine 1 µgm /kg iv during induction of anaesthesia, followed by a continuous infusion at a rate of 0.5µgm /kg/hr throughout the operation. They reported that intraoperative use of dexmedetomidine infusion reduces perioperative analgesic requirements.[7] In our study, we also used the loading infusion of dexmedetomidine at 1µgm /kg followed by continuous infusion of 0.5µgm / kg/hr throughout the intraoperative period and observed decreased anaesthetic as well as perioperative analgesic requirements. We found the dose of propofol needed for induction was reduced significantly (37.69%) in the patients receiving dexmedetomidine (p value<0.0001), as also found by Aanta and co-workers, demonstrating the anaesthesia potentiating effects of the drug.[8] This finding also corroborates with the result of earlier study by Peden et al. in 2001, where they demonstrated 40% decrease in induction dose of propofol.[9] The requirement of propofol for maintenance of anaesthesia during the entire surgical procedure was markedly reduced (38.69%) in dexmedetomidine treated group (p value<.0001). This observation is consistent with the finding obtained in study conducted by Nkanyezi E et al. in 2008. [10] In their study, addition of dexmedetomidine infusion to a propofol-remifentanil anaesthetic combination during spinal fusion decreased propofol infusion requirement by about 30%. The amount of rocuronium was comparable between the groups (p value 0.24). This result does not corroborate with the previous study performed by Pekka O Talke et al in 1999, in which they found that rocuronium concentration increased and the T1 response decreased during the dexmedetomidine administration.[11] In a recent trial, the use of intranasal dexmedetomidine was found to reduce the requirement of propofol and remifentanil during anaesthesia, but less than that of intravenous dexmedetomidine administered at the same dose. [12]

Hemodynamic stability

Dexmedetomidine loading infusion attenuated the hemodynamic responses to laryngoscopy, tracheal intubation and extubation. In dexmedetomidine receiving group there was steady and smooth reduction of MAP and HR, with no episodes of severe hypotension or bradycardia. Tracheal intubation is associated with increases in arterial pressure, heart rate and plasma catecholamine concentrations. Increase in MAP and HR observed in the control group in the present study, were similar to those reported in earlier studies.[13] In the present study, loading infusion with dexmedetomidine 1μgm/kg attenuated but not totally obtunded the cardiovascular response to tracheal intubation after induction of anaesthesia. In patients undergoing general or gynaecological surgery, numerous studies have shown that dexmedetomidine blunts cardiovascular response to intubation and our findings are in accordance with them.[14,15] Administration of dexmedetomidine infusion resulted in improve intraoperative haemodynamic stability. The intraoperative haemodynamic stability is of utmost importance in lumbar spine surgeries to reduce blood loss and also to prevent spinal cord ischemia. Tanskanen et al. stated that dexmedetomidine used as an anaesthetic adjuvant, provided perioperative haemodynamic stability when compared to fentanyl without postoperative respiratory depression.[16] The haemodynamic responses emerging from anaesthetic and extubation were blunted with dexmedetomidine. Dexmedetomidine have also been used as a supplement to isoflurane for vitreoretinal surgeries, without causing undue haemodynamic fluctuation and had been shown to decrease the excitatory response during extubation with acceptable reduction of intraocular pressure.[17] In an experimental study, it was observed that the level of stress hormones in the intraoperative and post-operative period is less in dexmedetomidine group compared to placebo.[18] The agonistic action of the molecule on the neuronal alpha-2 receptors is deemed to subdue the adrenergic surge that produce a state of sustained and consistent hemodynamic stability during surgery. The attenuation of sympathetic drive continues during anaesthetic emergence and a similar hemodynamic stability is observed during extubation without prolonging the time to extubation.[19]

Safety

Dexmedetomidine was well tolerated and no serious side effects or adverse reactions occurred in our study. In addition to this beneficial property of α2 agonists, it had been reported to increase the risk of hypotension and bradycardia.[15] These effects have most often been seen in young healthy volunteer on rapid and large bolus doses administration.[15,20] In our study, bradycardia was observed in two patients receiving dexmedetomidine, with no fall in blood pressure, which responded promptly to i.v. glycopyrrolate 0.1 mg. This finding is consistent with the lower incidence of side effects in the study performed by Keniya VM et al in 2011.[21]

Limitations of the study

There were certain limitations as the present study was carried out in ASA I/II patients, but the usefulness can be of immense help in high risk cardiac patients who were not our study population. We could not measure the plasma concentration of propofol, fentanyl and rocuronium of both the groups. Patient controlled analgesia device which can provide better assessment of analgesic requirement could not be used in our study because of non-availability.

CONCLUSION

Perioperative use of dexmedetomidine reduces the requirements of propofol and fentanyl, attenuate the haemodynamic response to tracheal intubation and extubation and additionally provides haemodynamic stability throughout the intraoperative period in lumbar spine surgery. Therefore, with proper precaution, patient selection and judicious dose, perioperative use of dexmedetomidine has anaesthetic and opioids sparing effect without causing any significant adverse events.

ACKNOWLEDGEMENT

The authors sincerely thank the Department of Anaesthesiology and Neuro-surgery for support and co-operation all throughout the conduct of the study.

REFERENCES

1. Keating GM, Hoy SM and Lyseng-Williamson KA. Dexmedetomidine: a guide to its use for sedation in the US. Clin. Drug Investig. 2012; 32:561-567.
   https://doi.org/10.1007/BF03261910
2. Tang C and Xia Z. Dexmedetomidine in perioperative acute pain management: a non-opioid adjuvant analgesic. J. Pain Res. 2017; 10:1899-1904.
   https://doi.org/10.2147/JPR.S139387
3. Davy A, Fessler J, Fischler M and LE Guen M. Dexmedetomidine and general anesthesia: a narrative literature review of its major indications for use in adults undergoing non-cardiac surgery. Minerva Anestesiol. 2017; 83:1294-1308.
4. Latka D, Miekisiak G, Jarmuzek P, Lachowski M and Kaczmarczyk J. Treatment of lumbar disc herniation with radiculopathy. Clinical practice guidelines endorsed by The Polish Society of Spinal Surgery. Neurol. Neurochir. Pol. 2016; 50:101-108.
   https://doi.org/10.1016/j.pjnns.2015.12.001
5. Kawano H, Manabe S, Matsumoto T, Hamaguchi E, Kinoshita M, Tada F, et al. Comparison of intraoperative blood loss during spinal surgery using either remifentanil or fentanyl as an adjuvant to general anesthesia. BMC Anesthesiol. 2013; 13:46.

https://doi.org/10.1186/1471-2253-13-46

6. Arain SR and Ebert TJ. The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. Anesth. Analg. 2002; 95:461-466.
   https://doi.org/10.1097/00000539-200208000-00042
7. Gurbet A, Basagan-Mogol E, Turker G, Ugun F, Kaya FN and Ozcan B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Can. J. Anaesth. 2006; 53:646-652.
   https://doi.org/10.1007/BF03021622
8. Aantaa R, Kanto J, Scheinin M, Kallio A and Scheinin H. Dexmedetomidine, an alpha 2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynecologic surgery. Anesthesiology. 1990; 73:230-235.
   https://doi.org/10.1097/00000542-199008000-00007
9. Peden CJ, Cloote AH, Stratford N and Prys-Roberts C. The effect of intravenous dexmedetomidine premedication on the dose requirement of propofol to induce loss of consciousness in patients receiving alfentanil. Anaesthesia. 2001; 56:408-413.
   https://doi.org/10.1046/j.1365-2044.2001.01553.x
10. Ngwenyama NE, Anderson J, Hoernschemeyer DG and Tobias JD. Effects of dexmedetomidine on propofol and remifentanil infusion rates during total intravenous anesthesia for spine surgery in adolescents. Paediatr. Anaesth. 2008; 18:1190-1195.
    https://doi.org/10.1111/j.1460-9592.2008.02787.x
11. The Effects of Dexmedetomidine on Neuromuscular Blockade in Human Volunteers [Internet]. [cited 2020 Nov 6]; Available from: https://insights.ovid.com/anesthesia-analgesia/asag/1999/03/000/effects-dexmedetomidine-neuromuscular-blockade/31/00000539
12. Wu X, Hang L-H, Wang H, Shao D-H, Xu Y-G, Cui W, et al. Intranasally Administered Adjunctive Dexmedetomidine Reduces Perioperative Anesthetic Requirements in General Anesthesia. Yonsei Med. J. 2016; 57:998-1005.
    https://doi.org/10.3349/ymj.2016.57.4.998
13. Shribman AJ, Smith G and Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br. J. Anaesth. 1987; 59:295-299.
    https://doi.org/10.1093/bja/59.3.295
14. Aho M, Erkola O, Kallio A, Scheinin H and Korttila K. Dexmedetomidine infusion for maintenance of anesthesia in patients undergoing abdominal hysterectomy. Anesth. Analg. 1992; 75:940-946.
    https://doi.org/10.1213/00000539-199212000-00012
15. Lawrence CJ and De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. Anaesthesia. 1997; 52:736-744.
    https://doi.org/10.1111/j.1365-2044.1997.169-az0303.x
16. Tanskanen PE, Kyttä JV, Randell TT and Aantaa RE. Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumour surgery: a double-blind, randomized and placebo-controlled study. Br. J. Anaesth. 2006; 97:658-665.
    https://doi.org/10.1093/bja/ael220
17. Lee YYS, Wong SM and Hung CT. Dexmedetomidine infusion as a supplement to isoflurane anaesthesia for vitreoretinal surgery. Br. J. Anaesth. 2007; 98:477-483.
    https://doi.org/10.1093/bja/aem040
18. Kim MH, Lee KY, Bae SJ, Jo M and Cho JS. Intraoperative dexmedetomidine attenuates stress responses in patients undergoing major spine surgery. Minerva Anestesiol. 2019; 85:468-477.
    https://doi.org/10.23736/S0375-9393.18.12992-0
19. Jo YY, Kim HS, Lee KC, Chang YJ, Shin Y and Kwak HJ. CONSORT the effect of intraoperative dexmedetomidine on hemodynamic responses during emergence from nasotracheal intubation after oral surgery. Medicine (Baltimore) 2017;96: e6661.
    https://doi.org/10.1097/MD.0000000000006661
20. Ebert TJ, Hall JE, Barney JA, Uhrich TD and Colinco MD. The Effects of Increasing Plasma Concentrations of Dexmedetomidine in Humans. Anesthesiology. 2000; 93:382-394.
    https://doi.org/10.1097/00000542-200008000-00016
21. Keniya VM, Ladi S and Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J. Anaesth. 2011; 55:352-357.
    https://doi.org/10.4103/0019-5049.84846

Author's Contribution:
MR, CKD, AA - Concept and design of the study; prepared first draft of manuscript; **MR, CKD, AA, SNA -** Interpreted the results; reviewed the literature and manuscript preparation; **SNA, CKD, MR -** Statistically analysis and interpretation of results, preparation of manuscript and revision of the manuscript.

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Source of funding: None, **Conflict of Interest:** None.