Original Article

A comparative study of dexmedetomidine–propofol and fentanyl-propofol on perioperative haemodynamics, propofol requirement and post-operative recovery profile in patients undergoing elective abdominal surgeries - A prospective randomised double-blind study

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Abstract

Background: Dexmedetomidine is gaining popularity for its sympatholytic, sedative and haemodynamic stabilising properties, without significant respiratory depression.

Methods: A prospective randomised double-blind study was conducted on 60 patients belonging to American Society of Anesthesiologists (ASA) Grade I and II undergoing elective abdominal surgeries who were randomised to receive either dexmedetomidine (Group D-P) or fentanyl (Group F-P) 10 Min prior to induction. Induction was done with midazolam along with propofol in 20 mg aliquots until bispectral index (BIS) value drops below 60. Infusion of one of the study drugs was continued along with propofol infusion which was titrated to maintain BIS around 40–60. Vecuronium to provide muscle relaxation and bolus doses of fentanyl were given whenever additional analgesia was needed. Intra-operative propofol, vecuronium and additional fentanyl requirement, time from discontinuation of anaesthetic drugs to extubation, time from the end of surgery to achieve a Ramsay sedation score of 2 and to the first post-operative analgesic request were recorded. Post-operatively, patients were monitored till 24 h for any adverse events.

Results: A significant decrement in heart rate was observed in the D-P group in comparison to the fentanyl group. The D-P group was found to have required less propofol for induction, limited additional fentanyl requirement, less time required for extubation and a delay in request for first post-operative analgesia which was statistically significant.

Conclusions: Propofol–dexmedetomidine provides better haemodynamic stability with lesser intraoperative propofol and fentanyl requirement, early cognitive recovery and longer postoperative analgesia when compared to propofol–fentanyl.

Keywords: Bispectral index, dexmedetomidine, post-operative recovery

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INTRODUCTION

Ideally, general anaesthesia should provide quick and pleasant induction; till recently, inhalational agents have been the choice for maintenance of anaesthesia as the anaesthesiologists are able to titrate the concentrations of the volatile agents to a finest degree. Despite these advantages, inhalational agents had their own drawbacks and shortcomings. Total intravenous anaesthesia (TIVA) has many advantages over inhalational anaesthesia in terms of better haemodynamic stability and recovery profile, lesser incidence of post-operative nausea and vomiting[1] and no operating room pollution.

Propofol (2,6-diisopropylphenol) is a short-acting intravenous anaesthetic agent that is widely used for TIVA to induce and maintain anaesthesia, as well as for sedation. Fentanyl, an opioid, relieves pain and reduces somatic and autonomic responses to airway manipulation.[2] Dexmedetomidine is an alpha-2 adrenergic receptor agonist used for sedation and analgesia and as an adjunct in anaesthesia to reduce anaesthetic requirements in procedures requiring TIVA.[3]

In the present study, we compared dexmedetomidine–propofol and fentanyl–propofol on perioperative haemodynamics, propofol requirement and post-operative recovery profile.

MATERI AL AND METHODS

A prospective randomised double-blind study was conducted in patients who underwent elective abdominal surgeries in surgical gastroenterology operation theatre of Sri Venkateswara Institute of Medical Sciences (SVIMS), a tertiary care teaching Hospital in Tirupati, South India. The study was approved by the Institutional Ethics Committee. Written informed consent was taken from all study participants before conduct of the study. Sixty patients belonging to American Society of Anesthesiologists (ASA) grade I and II were randomised to receive either dexmedetomidine 1 μg/kg (group D-P)[4] or fentanyl 2 μg/kg (group F-P) 10 min prior induction. Induction was done with midazolam along with propofol in 20 mg aliquots until the bispectral index (BIS) value drops below 60.[5] Infusion of one of the study drugs either dexmedetomidine 0.5 μg/kg/h[6] or fentanyl 1 μg/kg/h[7] was continued during maintenance along with propofol infusion 3–9 mg/kg/h which was titrated to maintain BIS around 40–60.[8] Vecuronium was used to provide muscle relaxation and bolus doses of fentanyl 0.5 mcg/Kg[9] were given whenever additional analgesia was needed. At the end of the surgery, residual neuromuscular blockade was reversed and was extubated. Intra-operative propofol, additional fentanyl requirement, time from discontinuation of anaesthetic drugs to extubation, time from the end of surgery to achieve a Ramsay sedation score[10] of 2 and to the first post-operative analgesic request using numerical rating scale[11] (>4) were recorded. Post-operatively, patients were monitored till 24 h after completion of the surgery for any adverse events.

Statistical analysis

All collected data were entered in Microsoft Excel worksheet (Microsoft Corp, Redmond, WA) and double checking was done for any clerical errors. The variables with normal distribution were expressed as mean with standard deviation. The variables that were not normally distributed were expressed as median with range. Proportions were reported with 95% confidence intervals. Continuous data were analysed with unpaired Student's *t*-test or Mann–Whitney *U* test as appropriate. Categorical data were analysed with proportion, Chi-square test, or Fisher's exact test as appropriate. Repeated-measure analysis of variance (ANOVA) was used to compare measurements over time as appropriate. A $P < 0.05$ was considered statistically significant. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 17 (IBM Corp Somers NY, USA) statistical software.

RESULTS

Patients in the two groups were comparable demographically (Table 1). There was a variation of heart rate (HR) between the two groups at all time intervals (Table 2). Mean baseline HR in Group D-P was 79.70 ± 12.6 and in Group F-P is 83.5 ± 13.9 ($P = 0.276$).

Table 1: Comparison of demographic data between the study groups

Variables	Group D-P (*n*=30)	Group F-P (*n*=30)	*P*-value
Age (years)*	42.8±11.1	47.1±11.9	0.158
Gender†			
Male	17	14	0.438
Female	13	16	
Weight (kg)*	52.4±12.0	50.1±10.9	0.434
BMI (kg/m^2)*	21.3±2.42	20.8±2.9	0.513
ASA Grade	23/7	20/10	0.390
I			
II			
Duration of surgery (min)	206.8±26.4	198.1±31.5	0.253

*Data are presented as mean standard deviation
†Data are presented as No.s
n=No. of patients; BMI=Body mass index; ASA=American Society of Anesthesiologists; D-P=Dexmedetomidine-propofol group; F-P=Fentanyl-Propofol group

Table 2: Comparison of heart rate between the study groups

Heart rate (beats/min)	D-P Group (*n*=30)	F-P Group (*n*=30)	*P*-value
Baseline	79.7±12.6	83.5±13.9	0.276
Before induction	73.8±10.3	81.4±12.7	0.014
Before intubation	72.0±7.3	79.3±12.7	0.008
At 5 min	76.5±11.8	82.3±13.0	0.075
At 15 min	73.7±8.7	82.0±15.8	0.014
At 30 min	72.3±10.21	80.1±14.2	0.018
At 60 min	71.8±9.6	80.1±15.3	0.014
At 90 min	72.5±10.1	78.9±13.9	0.049
At 120 min	72.7±10.1	75.5±9.9	0.278
At 150 min	70.1±8.0	75.4±9.57	0.026
At 180 min	68.65±7.39	74.66±8.85	0.012
At 210 min	68.76±5.81	77.00±12.56	0.021
At 240 min	65.33±8.50	70.00±7.87	0.486

n=No. of patients; D-P=Dexmedetomidine-propofol group; F-P=Fentanyl-propofol group

Post-intubation HR increased in both the groups which gradually decreased thereafter. Highest mean HR recorded was at 5 Min (i.e., post-intubation) in both the groups.

There was a variation of systolic blood pressure (SBP) between the two groups at all time intervals (Table 3). However, this difference is not statistically significant. Mean baseline SBP in Group D-P was 123.2 ± 15.8 mm of Hg and in Group F-P was 125.2 ± 18.2 mm of Hg (P = 0.652). There was a variation of diastolic blood pressure (DBP) between the two groups at all time intervals (Table 4). However, this difference is not statistically significant. Mean baseline DBP in Group D-P was 76.9 ± 12.2 mm of Hg and in Group F-P was 77.9 ± 9.7 mm of Hg (P = 0.727). Mean arterial blood pressure (MABP) showed difference at all time intervals in between both the groups (Table 5). However, this difference is not statistically significant. Baseline MABP in Group D-P was 86.6 ± 11.9 mm of Hg and in Group F-P was 88.8 ± 10.5 mm of Hg (P = 0.458).

Table 3: Comparison of systolic blood pressure between the study groups

Systolic BP (mm Hg)	D-P Group (*n*=30)	F-P Group (*n*=30)	*P*-value
Baseline	123.2±15.8	125.2±18.2	0.652
Before induction	119.5±13.6	117.5±14.7	0.598
Before intubation	110.9±19.5	107.2±16.1	0.421
At 5 min	117.2±11.8	120.6±16.4	0.360
At 15 min	116.6±14.9	117.6±16.0	0.803
At 30 min	122.0±12.4	117.9±14.6	0.242
At 60 min	123.1±16.5	120.4±14.0	0.498
At 90 min	119.2±17.0	117.5±14.5	0.667
At 120 min	121.7±15.1	118.4±15.3	0.409
At 150 min	120.3±13.7	119.4±14.4	0.803
At 180 min	119.3±13.6	115.9±11.1	0.340
At 210 min	119.8±11.3	113.8±9.6	0.132
At 240 min	115.3±5.0	115.3±4.0	>0.99

n=No. of patients; D-P=Dexmedetomidine-propofol group; F-P=Fentanyl-Propofol group; BP=Blood pressure

Table 4: Comparison of diastolic blood pressure between the study groups

Diastolic BP (mm Hg)	D-P Group (*n*=30)	F-P Group (*n*=30)	*P*-value
Baseline	76.9±12.2	77.9±9.7	0.727
Before induction	75.4±13.2	75.2±12.4	0.960
Before intubation	74.9±15.3	68.7±11.5	0.080
At 5 min	77.9±9.5	76.9±9.8	0.670
At 15 min	76.1±13.9	74.4±9.3	0.587
At 30 min	77.6±9.2	74.9±11.7	0.336
At 60 min	77.4±11.8	76.5±11.9	0.761
At 90 min	77.9±13.8	73.7±12.5	0.218
At 120 min	79.0±10.7	73.4±12.1	0.062
At 150 min	78.2±9.1	76.6±11.0	0.553
At 180 min	78.5±11.6	75.6±11.2	0.379
At 210 min	77.4±8.9	71.7±12.3	0.150
At 240 min	76.0±5.2	82.3±6.5	0.258

n=No. of patients; D-P=Dexmedetomidine-propofol group; F-P=Fentanyl-propofol group; BP=Blood pressure

Table 5: Comparison of mean arterial blood pressure between the study groups

Mean arterial BP (mm Hg)	D-P Group (*n*=30)	F-P Group (*n*=30)	*P*-value
Baseline	86.6±11.9	88.8±10.5	0.458
Before induction	84.7±13.4	84.8±12.5	0.984
Before intubation	82.6±15.9	77.8±11.6	0.193
At 5 min	87.4±9.6	85.8±11.9	0.568
At 15 min	84.9±13.9	84.5±10.6	0.884
At 30 min	88.0±10.7	86.6±12.0	0.644
At 60 min	87.8±12.4	85.9±10.7	0.520
At 90 min	88.9±12.7	83.1±12.6	0.081
At 120 min	88.8±12.7	83.6±11.5	0.101
At 150 min	89.6±9.7	86.6±11.0	0.279
At 180 min	87.9±11.4	84.2±10.2	0.231
At 210 min	87.4±9.1	81.2±9.9	0.080
At 240 min	84.0±3.5	88.3±2.5	0.154

n=No. of patients; D-P=Dexmedetomidine-propofol group; F-P=Fentanyl-Propofol group; BP=Blood pressure

We observed a statistically significant difference in propofol consumption for induction as Group D-P (1.105 ± 0.30 mg/kg) required less propofol compared to Group F-P (1.281 ± 0.32 mg/kg) (P = 0.033) (Table 6). We also observed that propofol consumption for maintenance was lower in Group D-P (3.787 ± 1.29 mg/kg/h) compared to Group F-P (4.403 ± 1.37 mg/kg/h) (P = 0.079). Patients in both the groups received additional doses of fentanyl as boluses of 0.5 mg/kg intravenous (IV) whenever there was inadequate analgesia (defined as a rise in HR or MABP by 20% of baseline with BIS within the recommended range of 40–60). Four patients in D-P group and 12 patients in F-P group required significantly more number of additional fentanyl doses (P = 0.049).

We observed the time taken from discontinuation of anaesthetic agents to tracheal extubation to be 12.4 ± 3.1 min and 15.9 ± 4.3 min in D-P and F-P groups, respectively (P = 0.001) (Table 7). Ramsay sedation score was assessed immediately after surgery until they

Table 6: Comparison of intraoperative requirements between study groups

Variable	D-P Group (*n*=30)	F-P Group (*n*=30)	*P*-value
Total amount of propofol consumption during induction (mg/kg)	1.105±0.30	1.281±0.32	0.033
Total amount of propofol consumption during maintenance (mg/kg/h)	3.787±1.29	4.403±1.37	0.079
No. of additional doses of fentanyl required			
0	26	18	0.049
1	3	11	
2	1	1	

n=number of patients; P-D=Propofol-dexmedetomidine group; P-F=Propofol-fentanyl group

Table 7: Comparison of post-operative recovery profile between study groups

Variables	D-P Group (*n*=30)	F-P Group (*n*=30)	*P*-value
Time since anaesthetic discontinuation to tracheal extubation (min)	12.43±3.10	15.93±4.25	0.001
Time from end of surgery to Ramsay sedation score of 2 (min)	7.63±3.68	10.40±5.43	0.025
Time from end of surgery to first post-operative analgesic requirement (min)	39.10±22.18	22.10±12.59	0.001
Adverse events post-operatively bradycardia, hypotension, hypertension, tachycardia, etc.			
Yes	5	4	
No	25	26	0.718

n=number of patients; D-P=Dexmedetomidine-propofol group; F-P=Fentanyl-Propofol group

achieved a score of 2 and the time taken for the patient from the end of surgery to achieve a RSS of 2 was recorded. Patients in D-P group required a significantly shorter time (7.6 ± 3.7) compared to those in F-P group (10.4 ± 5.4 min) ($P = 0.025$).

Pain score were evaluated using a 0–10 cm NRS (starting from 0 – no pain to 10 – worst imaginable pain) every 15 min till 1 H and then at 2, 4 and 8 H after surgery and the time taken from the end of the surgery to NRS >−4 was recorded. If NRS >−4, injection tramadol 1.5 mg/kg IV bolus was given followed by activation of epidural. There was a significant delay in post-operative first analgesic request in D-P group (39.1 ± 22.2 vs. 22.10 ± 13.0 Min) than in F-P group ($P = 0.001$).

Post-operatively, patients were monitored for any adverse cardiovascular or respiratory events, nausea, vomiting, shivering or any other adverse events. Only five patients in D-P group had bradycardia.

DISCUSSION

In our study, we used BIS for evaluating depth of anaesthesia and sedation. There was a statistically significant decrease in the induction dose of propofol in the D-P group when compared to the F-P group was observed. This may be due to the hypnotic effect of dexmedetomidine which is induced by hyperpolarisation of noradrenergic *locus coeruleus* neurons as opposed to GABA agonism by propofol. Similar results were obtained in another study[12] where effect of dexmedetomidine versus normal saline on intraoperative haemodynamics and propofol requirement in patients undergoing laparoscopic cholecystectomy was studied. Our study differs from the above study in that the normal saline was replaced with fentanyl 2 μg/kg which was given 10 min before induction.

In another study,[13] the effect of dexmedetomidine infusion on propofol requirement during the maintenance of anaesthesia was studied. The authors[13] reported a decrement in mean requirement of propofol in the dexmedetomidine group by 58% lesser than the requirement in the placebo group. There was no significant difference between the two groups with respect to intraoperative haemodynamics. This may be due to the lesser dose of dexmedetomidine used during the maintenance dose (0.2 μg/kg/h).[13] In our study, we used dexmedetomidine 0.5 μg/kg/h, so there was a fall in HR with stable SBP, mean arterial blood pressure (MABP) and DBP. The relatively higher dose manifested as a bradycardic response.

In a study,[14] the effects of dexmedetomidine in attenuating the pressor response of laryngoscopy and intubation and perioperative haemodynamic stability were studied. The authors[14] also substantiated our findings in that there was a decrease in HR in the dexmedetomidine group from the baseline at all time points till extubation. The authors[14] had opined that dexmedetomidine decreases plasma epinephrine and norepinephrine levels peri-operatively also. If they decreased the haemodynamic response to surgical stress there by providing haemodynamic stability intra-surgery. In our study, we also observed a decrease in HR in dexmedetomidine group of patients at all time points.

A study[6] was done to assess the ability of intraoperative infusion of dexmedetomidine in providing effective

post-operative analgesia in patients undergoing total abdominal hysterectomy. They found that an intraoperative loading dose of dexmedetomidine 1 μg/kg followed by infusion at the rate of 0.5 μg/kg/h provided adequate analgesia for at least 48 h after surgery which was reflected by a significant reduction in patient-controlled analgesia morphine requirement in the dexmedetomidine group.[6] In our study also, there was a significant delay in time to first analgesic request post-extubation in the dexmedetomidine group. One explanation for prolonged postoperative analgesia with dexmedetomidine is probably due to anxiolytic and thymoanaleptic property of alpha-2 agonists which act on the emotional component of postoperative pain. Just like us, they also did not observe clinically important sedation in any patient who received intra-operative dexmedetomidine at the rate of 0.5 μg/kg/h. There was also a significant decrement in the intra-operative fentanyl consumption by the dexmedetomidine group when compared to placebo group.[6] In our study also, we observed a similar dose decrement of intraoperative fentanyl in the dexmedetomidine group.

Propofol–dexmedetomidine provides better haemodynamic stability, lesser intraoperative propofol and fentanyl requirement, early cognitive recovery and longer postoperative analgesia compared to propofol–fentanyl combination. There were a few limitations in our study include smaller sample size, we does not taken into account of first 24 h analgesic requirement postoperatively, we did not in particular examined the post-intubation increase in haemodynamic parameters which was a mistake in hind-sake and the administration of muscle relaxants was in the form of time-bound boluses and not guided by neuromuscular monitoring.

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Nil.

Conflicts of interest

Natham Hemanth is an Associate Editor of Journal of Clinical and Scientific Research. The other authors are faculty members/research scholars of Sri Venkateswara Institute of Medical sciences, Tirupati, of which Journal of Clinical and Scientific Research is the official Publication. The article was subject to the journal's standard procedures, with peer review handled independently of these faculty and their research groups.

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