Clinical Investigation

Is dexmedetomidine better than propofol and fentanyl combination in minor day care procedures? A prospective randomised double-blind study

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ABSTRACT

Background and Aims: The growing popularity and trend of day care (ambulatory) anaesthesia has led to the development of newer and efficient drug regimen. We decided to evaluate the efficacy of two drug regimens namely dexmedetomidine and propofol with midazolam and fentanyl for moderate sedation characteristics in minor surgical procedures in terms of analgesia, intra-operative sedation, haemodynamic stability and side effects related. **Methods:** Totally, 60 adult American Society of Anaesthesiologists class I-II patients posted for day care surgeries of duration <45 min divided into two groups; Group D, where dexmedetomidine loading dose at 1 μg/kg was administered over 10 min followed by maintenance infusion initiated at 0.6 μg/kg/h and titrated to achieve desired clinical effect with dose ranging from 0.2 to 0.7 μg/kg, Group P, where midazolam at 0.02 mg/kg and fentanyl at 2 μg/kg IV boluses were given followed by propofol infusion. Statistical analysis was done using student *t*-test, analysis of variance and Chi-square analysis. $P < 0.05$ was considered to be significant. **Results:** Degree of sedation (Observer's Assessment of Activity and Sedation Scale ≤3) was comparable in both groups ($P > 0.05$). Rescue analgesia with fentanyl was needed in 30% patients of Group D compared to 17.63% patients of Group P ($P < 0.05$). The level of arousal was faster and better in Group D at 5 min after the procedure ($P < 0.05$). Haemodynamics were stable in Group D as with Group P patients ($P < 0.005$). Dry mouth reported by 16.67% patients. **Conclusion:** Dexmedetomidine can be a useful adjuvant rather than the sole sedative-analgesic agent during minor surgeries and be a valuable alternative to propofol in terms of moderate sedation, haemodynamic stability with minimal transient side effects.

Key words: Day care, dexmedetomidine, fentanyl, moderate sedation, propofol

INTRODUCTION

The growing importance of ambulatory surgery during the past decade has led to the development of efficient anaesthetic techniques in terms of quality and safety of both anaesthesia and recovery. Presently, the most widely used combination for ambulatory anaesthesia is propofol with advantages in terms of rapid, reliable recovery which is being held as primary anaesthetic for the total intravenous (IV) anaesthesia combined with opioids such as remifentanyl, alfentanyl or fentanyl. However, it has very little nociceptive effect; so much so, the agent needs to be combined with an analgesic for surgical procedures. Some of the newer anaesthetic agents have facilitated the attempt. It has recently become evident that complete anaesthesia is possible by employing new, more potent α_2-agonists, such as dexmedetomidine. The Federal Drug Administration has approved the use of dexmedetomidine as a sedative analgesic and/or total anaesthetic in adults and paediatric patients undergoing minimally invasive procedures, with or without the need for tracheal intubation.[1] Mild cognitive impairments with integrated anxiolytic and amnesic effects are generated by α-agonists.[2] In addition, it possesses selective α-adrenoceptor agonism, especially for the

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2_A receptor subtype and reduces opioid requirements without causing significant respiratory depression.[1,3] Dexmedetomidine sedation allows the physician to wake up the patients for easy communication during and just after the procedure.[4] Hence, this study was taken up to evaluate and compare the merits of these two moderate sedation techniques using different agents; dexmedetomidine in one group and propofol and fentanyl in other group for minor day care surgical procedures. We hypothesised that dexmedetomidine as a sole IV anaesthetic agent would be comparable in efficacy to a combination of propofol, midazolam and fentanyl in short surgical procedures associated with mild to moderate pain.

METHODS

A prospective randomised controlled study was conducted in between June 2011 and December 2013 after obtaining the approval of Institutional Ethics Committee and written informed consent from all patients included in the study. A total of 60 patients either sex, having age and body weight ranging in between 20–50 years and 40–75 kg, respectively of American Society of Anaesthesiologists (ASA) physical status I and II scheduled for minor surgical procedures lasting ≤45 min duration such as dilatation-curettage or evacuation, incision and drainage of abscess, carbuncle, cataract, third molar surgery and diagnostic procedures like upper gastrointestinal endoscopy were enrolled in this study after written informed consent. Patients who refused to provide consent, patients with history of any of drug allergy, haemodynamically unstable patients, cardiac patients with history of angina, conduction defects, angioplasty, coronary artery bypass grafting, severely hypertensive patients, septicaemic patients and patients receiving sedation or analgesia were excluded from study.

Every patient was assessed in detail one day prior to surgery. Routine investigations were performed in each case and whenever required, specific tests such as chest X-ray and electrocardiogram (ECG) were asked for. Patients were interviewed for drug history and past history of anaesthesia or related complications. Patients were instructed to undergo overnight fasting before surgery and as a premedication received injection glycopyrrolate 0.2 mg intramuscular (IM) one hour prior shifting to operation theatre (OT). The patients were transferred to preparation room 40 min prior to anaesthesia induction. They were reminded about the procedure and on how to use the visual analogue scale score (VAS). On entering the OT, standard monitoring including non-invasive blood pressure, pulse oximetry and ECG leads were attached to the patient. IV access was established using a 20 gauge cannula and injection Ringer Lactate 500 ml was given during the entire procedure. Based on computer-generated random tables following patients are divided into two groups of 30 patients each: Group D received injection dexmedetomidine loading dose at the rate of 1 μg/kg over 10 min followed by maintenance infusion initiated at rate of 0.6 μg/kg/h and titrated to achieve desired clinical effect with dose ranging from 0.2 to 0.7 μg/kg (Dextomid®, 100 μg/ml, Neon Lab, India, 100 μg or 1 ml added to 100 ml of normal saline and made to a concentration of 1 μg/ml), the infusion was started 15 min before starting the procedure. A volume of 10 ml of normal saline was injected 5 min before starting the procedure. Group P received injection midazolam at 0.02 mg/kg bolus, injection fentanyl at 2 μg/kg bolus, both made up to 10 ml, IV, 5 min prior to surgery. Patients then received propofol at a loading dose of 0.5–1 mg/kg and maintenance at a dose of 1–3 mg/kg/h infusion at the start of the procedure. The amount of normal saline matching the volume of dexmedetomidine infused in Group D was administered to patients in Group P 15 min prior the procedure. The agents used in this study were prepared, labelled and administered by slow IV infusion in the preparation room by an anaesthesiology resident not involved in the study.

The onset time of sedative agent infusion was taken as minute zero and the following parameters were measured and recorded with intervals of 5 min: Observer's Assessment of Activity and Sedation Scale (OAA/S) score: 1 = Not responding to mild prodding or shaking (asleep), 2 = Responds after mild prodding or shaking, 3 = Responds to high tone/repeatedly names, 4 = Lethargic response to name spoken in normal tone, 5 = Responds readily (awake and alert). VAS (patients were asked to self-evaluate their feelings of anxiety with scores of 0–10, with 0 = absent and 10 = very much). Intra-operative vitals and SpO_2 were continuously monitored and recorded at 5 min, 10 min and 15 min, 30 min and 45 min, 60 min intervals. Any incidence of adverse effects such as nausea, vomiting, bradycardia, hypotension, hypoxia and hypertension were recorded. After the completion of the procedure, the patient and the surgeon were asked formally about the satisfaction of anaesthesia and operating conditions.

The total duration of the procedure, IV supplementation required and sedation using OAA/S scale were also recorded. After completion of procedure, patient's vitals were once again recorded and then shifted to recovery room where he/she was kept under close observation for a period of 30 min and then shifted to post-operative ward if found to be fully conscious and oriented with stable vital parameters. The scales used during the study were VAS for pain; OAA/S scale[5] for sedation and modified Aldrete's score[6] for post-operative recovery.

The sedation and analgesic scores were assessed at 5 min regular intervals. Sedation was maintained to meet the OAA/S-score (3–4) criteria. When sedation becomes inadequate (OAA/S score >4), propofol was given as a rescue sedative drug in IV bolus (0.5 mg kg^{-1}) aliquots in either of the groups when required. The pain of the patients was assessed by VAS; when VAS was >4, fentanyl was administered in the dose of 1 μg kg^{-1} IV bolus as rescue analgesic. However, patients who received rescue sedation or analgesia were excluded from this study. Atropine sulphate 0.6 mg for bradycardia (heart rate [HR] <50 bpm) and ephedrine 6 mg incremental doses for hypotension (mean arterial pressure [MAP] <60 mm Hg) were used. If respiratory rates <8 and desaturation at SpO_2 <90% were observed, the depth and rate of respiration were increased with verbal stimuli and oxygen supplementation with a mask.

Data analysis was done using SPSS Version 16.0 (SPSS Inc., Chicago, IL, USA). Power analysis was based on the results of a previous study.[7] Sample size calculation was based on the power of 80% with 5% alpha error and a β-error of 0.2. To detect a difference in VAS of one between groups, a sample size of 30 patients per group was required. Haemodynamics and respiratory data were evaluated using the unpaired *t*-test for intergroup and paired *t*-test for within-group comparisons. Numerical data are reported as means ± standard deviation. Ordinal data are reported as median (interquartile range). Where possible, the doses and infusion rates were standardised to μg/kg or mg/kg and μg/kg/h, respectively. For statistical analysis of the clinical data obtained, the analysis of variance with the *post-hoc* test was applied to compare data within a group and Chi-square and Fisher exact test analysis were done to compare proportions. Categorical data were analysed using Chi-square test. $P < 0.05$ was considered as significant.

RESULTS

Demographic variables [Table 1] in terms of age, body weight, height and gender (male/female) along with their ASA status (class I/II) were comparable in between groups, although there was significantly higher females to male ratio, 56–75 kg weight group and ASA I patients in study population among each group. The mean duration of surgery was 19.83 ± 2.79 and 20.56 ± 3.12 min, respectively in each group.

The pulse rate at 5 min was not significant as compared to pre-operative pulse in Group P patients. However, in Group D there was a drop in pulse rate (HR) by 18.66% by 5 min, but only 4 patients had a pulse rate below 60, which was transient and patient recovered without receiving atropine. Although there was a decrease in HR from baseline similarly in each group found to be non-significant statistically [Figure 1]. Fall in MAP was noted by 10% in Group D and 17.77% of Group P patients that is, found to be statistically significant but none of them required vasopressor ephedrine and responded well to IV fluid boluses [Figure 2].

The OAA/S score was ≥4 that is, all the patients were arousable on command in Group D while score was within 4 invariably in most patients except 5 (16.67%)

Table 1: Demographic characteristics of patients in each group

Parameters	Group D (*n*=30)	Group P (*n*=30)
Age (years) (mean±SD)	38.78±10.24	39.39±12.48
Weight (kg) (mean±SD)	55.02±3.20	53.47±4.68
Height (cm) (mean±SD)	163.44±5.36	162.88±7.40
Gender (male/female)	12/18	13/17
ASA group (I/II)	19/11	20/10

SD – Standard deviation; ASA – American Society of Anaesthesiologists

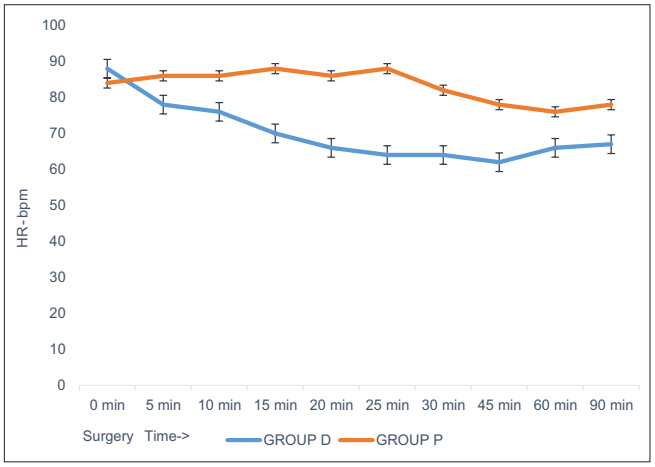

Figure 1: Changes in heart rate in both groups

among Group P who required supplementation with 30 mg of IV propofol for rescue sedation and for the procedure to be completed. In post-operative period by the end of 15 min, all the patients in both the groups were awake and responding to verbal commands ($P > 0.05$) [Figure 3]. In both the groups, VAS score for the post-operative pain was comparable and insignificant ($P > 0.05$) but when compared for intra-operative procedural pain, it was higher in Group D than Group P patients. 30% patients among Group D and 16.67% patients in Group P (those receiving supplement IV propofol) complained of procedural pain and required supplemental fentanyl 50 μg for rescue analgesia intra-operatively [Figure 4]. This difference in both groups on comparison was statistically significant ($P < 0.05$). These patients were excluded from the study as per protocol.

There was no episode of nausea, vomiting in Group D patients while 10.34% patients had nausea and 1 patient had 1 episode of vomiting in recovery period in Group P patients, which was statistically significant ($P < 0.05$). Dry mouth was reported in 5 (16.67%) patients in Group D and 1 (3.3%) patient of the Group P studied ($P < 0.05$). Incidence of bradycardia was noted among 4 patients of dexmedetomidine group as compared to 1 patient of propofol/fentanyl group ($P < 0.05$); hypotension was reported in 10% cases in Group D and 16.67% in Group P but didn't require any pharmacological intervention except IV fluid boluses. The percentage of fall in SpO_2 and respiratory rate (noted in only three patients among Group P) was found statistically insignificant in this study. The post-operative recovery using modified Aldrete's score was in between (9–10) just after and in the initial 5 min of the procedure completion in all Group D patients ($P \leq 0.05$). After 30 min, all the patients of both the groups were having modified Aldrete's score of invariably 10 and were able to shift from post-operative care unit [Figure 5].

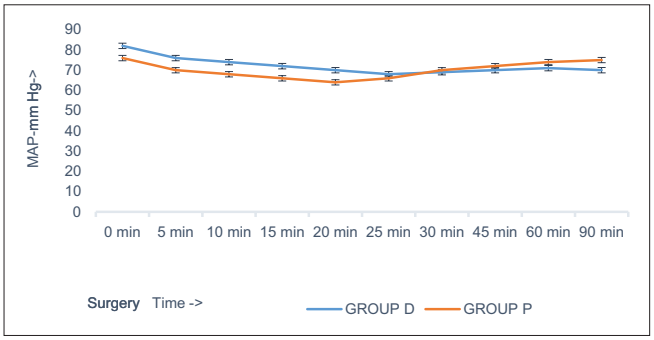

Figure 2: Changes in mean arterial pressure in both groups

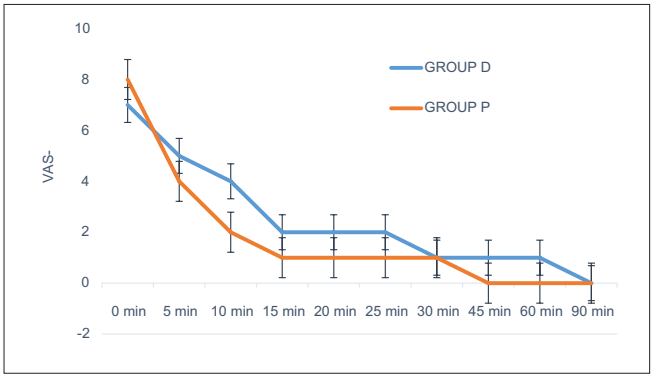

Figure 4: Visual analogue scale comparison between both groups

DISCUSSION

It has recently become evident that satisfactory anaesthesia is made possible by employing the new, more potent α_2-agonists, such as dexmedetomidine.[1] Its unique properties render it suitable for sedation and analgesia during the whole perioperative period.[1,2,4] There is no review in literature available comparing propofol with fentanyl and dexmedetomidine as a sole agent for IV moderate sedation. This paper would help possibly fill this void in knowledge.

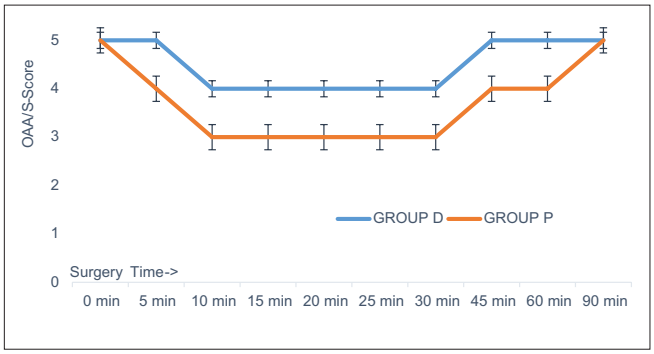

Figure 3: Observer's assessment of activity and sedation score in each group

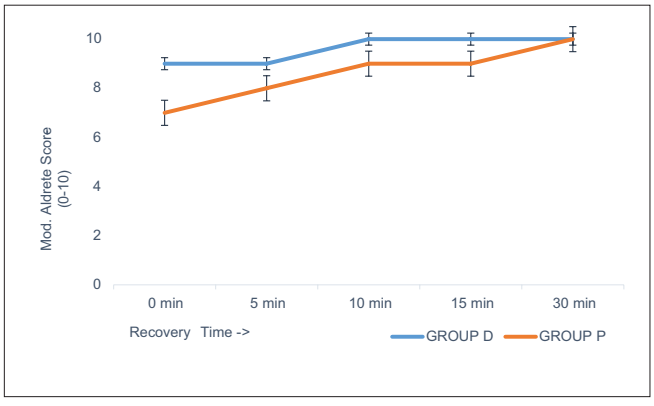

Figure 5: Post-operative recovery (modified Aldrete's score) in each group

In this study, among Group D patients there was a drop in pulse rate (HR < 60/min) by 18.66% at 5 min unlike Group P. The study conducted by Okawa *et al*.[8] showed the mean fall in pulse rate by 7.40%. Another study conducted by Hall *et al*.,[9] showed a decrease in HR between 16% and 18%. There was the comparatively high incidence of fall in MAP in Group P patients. A similar study conducted by Kaygusuz *et al*.,[10] demonstrated comparable fall in MAP between dexmedetomidine and propofol groups while another study conducted by Arain and Ebert[11] showed that intra-operative MAP in both groups was significantly higher than baseline values and in dexmedetomidine group, it was higher than in propofol group, but the need of fluid bolus and vasopressor were similar in both groups. The fall in HR and MAP was attributed to the central sympatholytic activity of dexmedetomidine.[12] The percentage of fall in SpO_2 and respiratory rate were statistically insignificant in both the groups similarly in accordance with studies conducted in past where respiratory endpoints were unchanged in both groups throughout the entire study period.[11,13] Dexmedetomidine is unique in that it does not cause respiratory depression because its effects are not mediated by the γ-amino butyric acid system. However, in contrast, RR of dexmedetomidine group were significantly lower and SpO_2 value higher than those in propofol in a study, where the loading dose of dexmedetomidine was 6 μg/kg/h; quite higher (6 times) than the standard loading dose in this study.[10]

Visual analogue scale values in both the groups for the post-operative pain was comparable and insignificant but when compared for intra-operative procedural pain, it was comparably higher in Group D than Group P patients in contrast to other similar studies[10,11] in which fentanyl 1 μg/kg was given to all patients along with dexmedetomidine. They showed comparable intra-operative pain score and better post-operative scores with use of dexmedetomidine. Analgesic properties have been demonstrated in studies that used dexmedetomidine as the sole analgesic after minor surgery.[7,14] All the patients were arousable on command in Group D, unlike in Group P where patients were found to be deeply sedated after the procedure. Sedation scores fell rapidly initially with propofol but was comparable with dexmedetomidine group intra- and post-operatively.[11] In contrast to other studies,[7,13-16] need of rescue analgesic (in 30% cases) and VAS score was significantly higher in dexmedetomidine group limiting its efficacy as sole agent for combined sedative with analgesic use. There was no episode of nausea, vomiting in Group D, unlike Group P patients. Dry mouth was reported more (16.67%) in patients of Group D as was also seen the study by Eren *et al*.[14] Premedication with injection glycopyrrolate IM could be an additional cause for dry mouth.

Initially, prior atropinisation of patients to decrease the incidence of bradycardia was planned, but looking at the property of dexmedetomidine to produce dry mouth as a side effect we decided to keep the syringe of injection atropine preloaded to be given only as and when required. The incidence of desaturation (SpO_2 <95%) was higher in Group P because of the tendency of propofol to cause apnoea and respiratory (hypoxic ventilatory response) depression when given in IV boluses. We found that in spontaneously breathing patients, the respiratory depressant effect of dexmedetomidine was less significant compared with that observed with propofol. Many trials studied the effect of dexmedetomidine on respiration in spontaneously breathing patients and found that it was not associated with respiratory depression despite profound levels of sedation.[9,11,12,17]

After the procedure, the patients of Group D were conscious, oriented and could be shifed from the post-anaesthesia care unit (PACU) while, in Group P, they required observation in PACU for initial 10 min. After 30 min of surgery or procedure, all the patients of both groups had satisfactory recovery profile including stable haemodynamics and could be shifted. Limitations of this study were the small sample size in each group, lack of control group, and bispectral monitoring not being used for monitoring the depth of anaesthesia during the procedure. The administration of drugs at different rate and time in each group and the white colour of the propofol infusion could have also lead to bias in the study.

CONCLUSION

Dexmedetomidine can be a useful adjuvant during minor surgeries with advantages of minimal to mild pain. It can be an alternative to propofol in terms of moderate sedation, haemodynamic stability, minimal and transient side effects but not as a sole sedative-analgesic agent. It can be opioid sparing in a multimodal analgesia technique for surgeries associated with mild to moderate pain or procedures of small duration.

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