Original Article

Discharge readiness after minor gynaecological surgeries comparing dexmedetomidine and ketamine premedication in bispectral index (BIS) guided propofol-based anaesthesia

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ABSTRACT

Background and Aims: Dexmedetomidine and ketamine are commonly used pre-medicants to propofol. Previous literature shows a delay in recovery with their use without any clarity on discharge. This study was planned to find out whether adding these premedicants to Bispectral index (BIS) guided propofol anaesthesia led to delayed discharge in minor gynaecological surgeries. **Methods:** Totally, 120 adult females belonging to American Society of Anesthesiologists (ASA) physical status I and II undergoing minor gynaecological surgeries under general anaesthesia were randomly allocated to receive 1 μg/kg dexmedetomidine (Group D), 0.5 mg/kg ketamine (Group K) and normal saline (Group P) as premedication. Propofol 1% was used for induction and maintenance of anaesthesia keeping BIS between 55 and 70. After the procedure, patients were assessed primarily for discharge readiness using Modified Post Anaesthesia Discharge Scoring System (MPADSS).The secondary outcomes were Modified Aldrete Score (MAS), total dose of propofol used and haemodynamics. **Results:** The percentage of patients ready for discharge were 22.5%, 30% and 15%at 1 hour in group D, K and P, respectively (p = 0.275). Median MAS was 5, 4 and 6 respectively for group D, K and P immediately post-surgery (p = 0.000). The mean dose of propofol used was 69.75 ± 12.56 mg in group D and 135.25 ± 9.2 mg in group *P* (p = 0.001). There were significant haemodynamic variations in group D (16.4% fall in heart rate at 5 minutes and 24.18% fall in mean arterial pressure at 15 minutes). **Conclusion:** Premedication with dexmedetomidine and ketamine in propofol anaesthesia does not delay discharge. However, stable haemodynamics and good analgesia with ketamine make it a better option.

Key words: Dexmedetomidine, discharge readiness, ketamine, minor gynaecological surgery

INTRODUCTION

Minor gynaecological surgeries for diagnostic and therapeutic purposes are being extensively done these days on a day care basis. Patients going home on the same day after surgery while decreasing the burden on healthcare system, increase the physician's responsibility in ensuring patient's safety and readiness for discharge. Anaesthesia techniques are being modified on day to day and place to place basis as per the availability of drugs and type of procedure.

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Propofol has undoubtly emerged as the most suitable drug for ambulatory anaesthesia. Its combination with shorter acting opioids is the most commonly used regime nowadays as it offers rapid onset and quicker offset leading to early discharge.[1-3] Since availability of opioids is a big issue in a country like India, switching to other options like sedatives or anxiolytics is a kind of necessity. Dexmedetomidine and ketamine, both possess sedative as well as analgesic properties and have been used successfully alongwith propofol to decrease its dose while improving the haemodynamic profile.[4,5] Although, some previous studies suggest a delayed recovery with the use of these two drugs along with propofol,[6-11] there has been no study till date clearly mentioning any delay in discharge with this combination.

We have tried to fill this gap by studying both recovery and discharge readiness based on validated criterias in patients undergoing minor gynaecological surgeries, using dexmedetomidine or ketamine as pre-medicants to propofol. Because the success of a good ambulatory anaesthetic technique rests on safe discharge of the patient, our aim was to study the percentage of patients ready for discharge in each group at one hour post-surgery based on Modified Post Anaesthesia Discharge Scoring System (MPADSS) [Table 1].

Table 1: Modified Post Anaesthesia Discharge Scoring System(MPADSS) used in the study (Total score+12. Patient achieving score≥ 9 with no parameter scoring 0 were considered ready for discharge)

Vital signs (blood pressure, pulse, heart rate)
0≥40% of preoperative value
1=20-40% of preoperative value
2≤20% of preoperative value
Ambulation
0=Difficult/Impossible
1=Toddle
2=Steady
Post-operative nausea/Vomiting (PONV)
0=Severe
1=Moderate
2=Minimal
Pain
0=Severe
1=Moderate
2=Minimal
Surgical Bleeding
0=Severe
1=Moderate
2=Minimal/Absent
Voiding
0=Retention
1=Difficult
2=Normal

METHODS

After approval from institutional ethics committee, study was designed as prospective, randomised, placebo controlled and conducted from April 2019 to March 2020 in the gynaecology operation theatre. Females aged 18-60 years, belonging to American Society of Anesthesiologists (ASA) physical status I–II, posted for minor gynaecological procedures of less than 30 minutes duration were enrolled in the study. The exclusion criteria were patients on alpha adrenergic receptor blocker, known hypersensitivity to study drugs, egg allergies, compromised cardiac, renal or hepatic disease, neurological disease with motor/sensory deficit and pregnancy. A written informed consent was taken from all participants. Randomisation was done using computer generated random number table and the groups thus assigned were sealed in an envelope. The study drug was prepared by an independent personnel after taking out the slip and handed over to investigator.

On arrival to the operation theatre, non-invasive blood pressure and pulse oximeter (SpO_2), electrocardiogram and BIS monitoring was started. The baseline vitals – Heart Rate (HR), mean arterial pressure (MAP), respiratory rate (RR), oxygen saturation (SpO_2), and BIS value were recorded. After securing venous access, injection glycopyrrolate 0.02 mg/kg and tramadol 2mg/kg were given intravenously and infusion ringer lactate started. The study drug was administered intravenously to the patient slowly over 10 minutes.

Group D: Received dexmedetomidine 1 µg/kg in normal saline made to a total volume of 10 mL.

Group K: Received ketamine 0.5mg/kg in normal saline made to a total volume of 10 mL.

Group P: Received normal saline 10 mL.

Induction was started with injection propofol 1% given in variable boluses to achieve BIS between 55 and 70 and airway maintained on anatomical face mask with Bains circuit. This value was chosen to standardise the depth of anaesthesia between moderate sedation and general anaesthesia.[12] If BIS value became >70, a further incremental dose of 10-20 mg propofol was given. The total dose of propofol used during procedure was calculated at the end. Haemodynamics were recorded every five minutes till end of procedure. When the patients achieved BIS score >90 and started obeying commands, they were shifted to post anaesthesia care unit (PACU).

The recovery was assessed in PACU using Modified Aldrete Score (MAS) immediately at arrival, at 15 and 30 minutes [Table 2]. Vitals were recorded every 5 minutes for first 30 minutes and then at 60, 90 and 120 minutes. Discharge readiness was assessed based on MPADSS using six parameters [Table 1]. Patients achieving MPADSS ≥9 out of 12 with no parameter scoring 0 were considered ready to be discharged home with an adult escort. This percentage in each group at 1 hour was taken as primary outcome of the study and additionally recorded at one and a half and two hours. Secondary outcomes included total dose of propofol used, recovery based on MAS, intra and postoperative haemodynamics, any incidence of bradycardia or hypotension requiring intervention or any other complication.

Bradycardia, defined as HR <60 beats/minute was treated with injection atropine (10 µg/kg) i/v. Hypotension (reduction in MAP >20% from baseline) was managed by giving injection mephenteramine (0.1 mg/kg) i/v. Episodes of sustained apnoea (loss of spontaneous respiratory effort >20 seconds) leading to SpO2 <90% were managed by assisted ventilation on Bains circuit. In PACU, any complication like nausea, vomiting, hallucinations, etc. were noted and managed accordingly. If required, injection diclofenac 75 mg was used as rescue analgesic for post-operative pain.

Sample size calculation was done on the basis of discharge readiness in a pilot study conducted on 14 subjects. The prevalence of drug effectivity was observed to be 14.2%. Epi Info™ software was used with acceptable margin alpha error of 5% and beta error 80%. Eighty patients were divided into two equal groups and 40 patients enroled in control group.

Statistical calculations were done using Statistical Package for Social Sciences(SPSS) 20.0 software (SPSS Inc. Chicago, Illinois, USA) and Microsoft Excel 2011 (Microsoft Corporation, Redmond, Washington, USA). The results were tabulated in the form of mean ± standard deviation (SD). For categorical data, Chi square test was applied. For parametric data, Analysis of Variance (ANOVA) with Post Hoc Tukey test was applied to find the significance. The level of significance was determined as its '*p*' value with $P < 0.05$ as significant and $P < 0.001$ as highly significant.

RESULTS

One hundred and sixty-two patients posted for minor gynaecological surgery were screened on the basis of inclusion criteria. Out of 132 patients who gave consent for surgery, three patients got excluded before randomisation as shown in Figure 1. At the end for non-inferiority trial, data from 40 patients in each group was analysed. The three groups were comparable in their basic demographic characteristics, ASA status, mean duration of surgery and vitals [Table 3].

The percentage of patients ready for discharge were 22.5% in group D, 30% in group K and 15% in group *P* at 1 hour post-surgery (p = 0.275). At one and a

Table 2: Modified Aldrete Score (MAS) Scale (used in the study)

Oxygenation	
SpO2>92% on room air	2
SpO2>90% on oxygen	1
SpO2<90% on oxygen	0
Respiration	
Breathes deeply and coughs freely	2
Dyspnoeic, shallow or limited breathing	1
Apnoea	0
Circulation	
Blood pressure±20 mmHg of normal	2
Blood pressure±20-50 mmHg of normal	1
Blood pressure more than±50 mmHg of normal	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responsive	0
Activity	
Moves all extremities	2
Moves two extremities	1
No movement	0

SpO2: Peripheral oxygen saturation

Table 3: Patient Demographics, procedure duration, baseline vitals and total propofol used during the procedure

Variables	Group D	Group K	Group P	*P*
Age (years)	39.13±8.38	38.3±7.72	37.98±9.96	0.832
Weight (kg)	56.6±5.04	56.5±4.53	56.58±6.5	0.996
Duration (min)	27.23±2.04	27.78±2.13	27.13±1.9	0.307
ASA I (*n*)	32	35	36	
ASA II(*n*)	8	5	4	
HR (min) (Baseline)	76.4±8.87	73.43±6.33	72.1±5.66	0.024
Mean arterial pressure (mm Hg) (Baseline)	93.23±6.77	95.05±4.49	92.85±6.92	0.236
BIS (score) (Baseline)	96.38±1.05	96.45±1.41	96.3±1.44	0.878
Total dose of Propofol given (mg)	69.75±12.56	76.88±4.63	135.25±9.2	0.001

Values expressed as mean±Standard deviation or number (*n*). ASA: American Society of Anesthesiologists grade; HR: Heart rate; MAP: Mean arterial pressure; BIS: Bispectral index

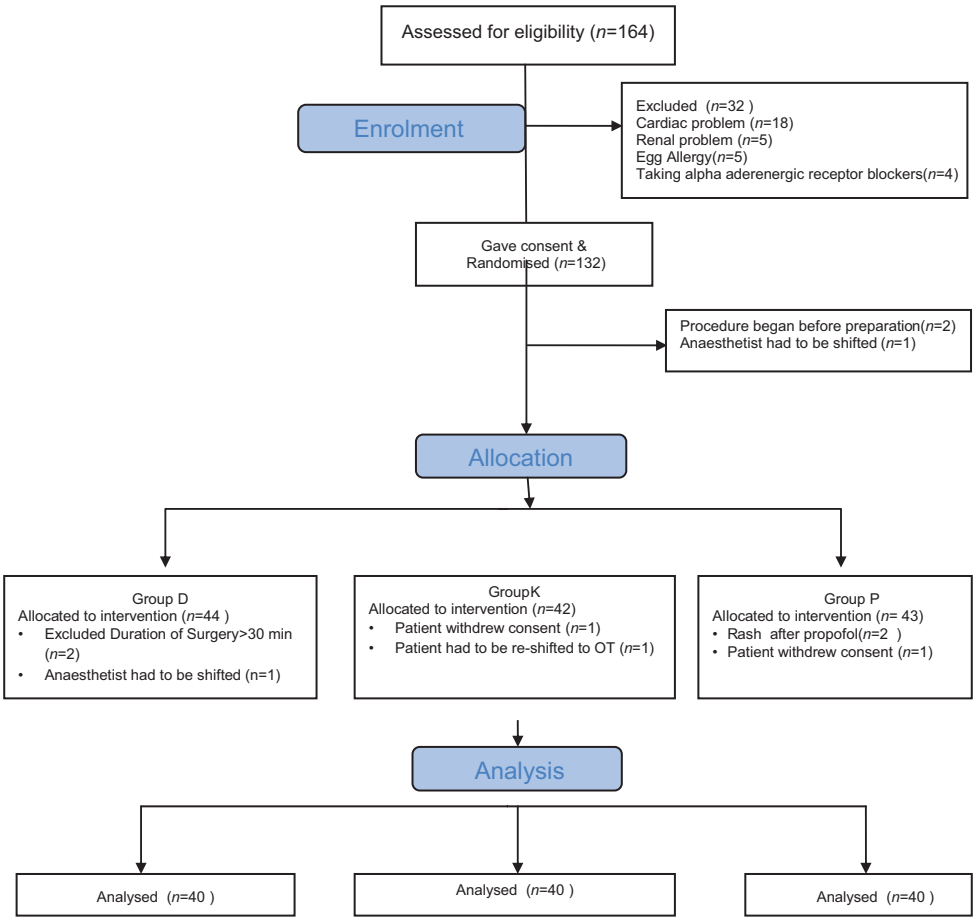

Figure 1: Flow Chart of patient participation

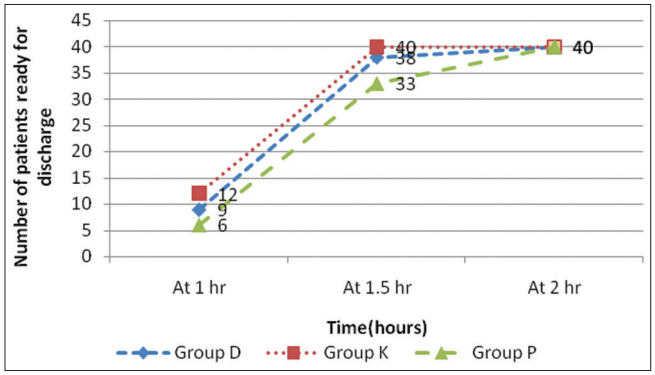

Figure 2: Number of patients ready for discharge at 1, 1.5 and 2 hours according to MPADSS. *P* value was >0.05 (non-significant) among all three groups at one hour. At 1.5 hours it was significant only between group K and *P* (p = 0.041)

half hour, these values were 95%, 100% and 82.5%, respectively in group D, K and P, difference being significant between group K and *P* (p = 0.041). All patients in all the groups achieved MPADSS >10 at 2 hours post-surgery [Figure 2]. Group K showed stable haemodynamics and better ambulation which resulted in overall higher scores on MPADSS in these patients.

The median MAS recorded immediately and at 15 minutes was significantly different in all the groups with highest value recorded in group *P* and lowest in group K (p = 0.000). However at 30 minutes, the median MAS in group K was 10 comparable clinically to 9 in the other two groups [Table 4].

The maximum fall in HR was recorded in group D (16.4% fall from the baseline) at five minutes after giving the premedication and this fall continued throughout the duration of the study, requiring injection atropine in two patients. The MAP remained stable intraoperatively in this group but there was a highly significant fall (24.18%) at 15 minutes, postoperatively. In group K and P, both HR and MAP remained stable when compared to baseline with statistically insignificant changes (p = 0.000). No episode of tachycardia was noted in either of the three groups throughout the duration of the study. There was one patient in group K who had excessive bleeding leading to hypotension and re-exploration but was later excluded from the study before analysis [Figure 3].

Table 4: MAS values recorded in all the groups at various time intervals

	Group D	Group K	Group P	D vs K	K vs P	D vs P
MAS immediately	5	4	6	0.000	0.000	0.000
MAS at 15 min	8	7	9	0.000	0.000	0.000
MAS at 30 min	9	10	9	0.001	1.000	0.001

MAS: Modified Aldrete Score

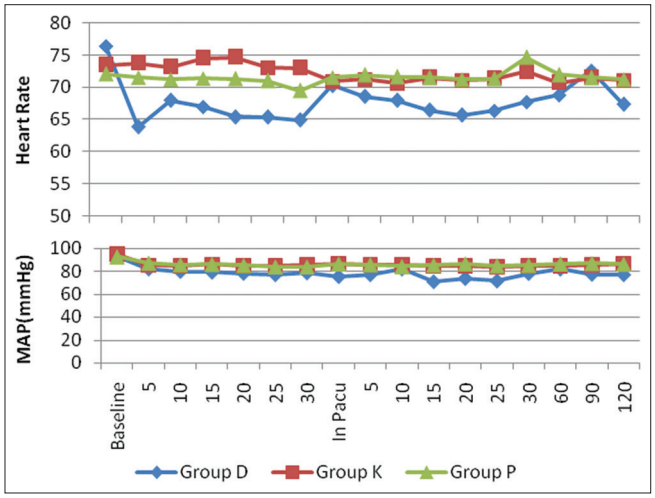

Figure 3: Comparison of Perioperative Heart Rate (HR) and Mean Arterial Pressure (MAP) among three groups:Maximum fall in heart rate seen in group D that is, 16.4% from baseline at 5 mins.Maximum fall in MAP seen in group D that is, 24.18% from baseline at 15 mins, post-operatively

Mean dose of propofol used was lowest in group D that is, 69.75 ± 12.56 mg and highest in group *P* (135.25 ± 9.2 mg) [Table 3]. This difference was highly significant among all the groups (p = 0.001).

A total of 17 patients complained of nausea and vomiting in PACU (3 in group D, 5 in group K and 9 in group P) and were managed by giving injection ondansetron 4 mg IV. There was no incidence of urinary retention. Minor hallucinations were noted in 2 patients of group K while in PACU, but it was not significant clinically and no intervention was done.

DISCUSSION

In this study we demonstrated that addition of dexmedetomidine 1 μg/kg or ketamine 0.5 mg/kg as pre-medicants to propofol in patients undergoing minor gynaecological day care surgeries, does not delay discharge compared to propofol only anaesthesia. Instead, the percentage of patients ready for discharge were significantly more with ketamine premedication compared to control at 90 minutes. Our results could not be compared to previous publications as discharge readiness based on validated discharge criteria has not been studied separately from recovery. Edokpolo *et al*.compared dexmedetomidine premedication to placebo in propofol-based anaesthesia and found that addition of dexmedetomidine delayed discharge in patients undergoing colonoscopy.[13] On the contrary, few authors have reported early discharge with dexmedetomidine, but the discharge criteria used were different from our study.[4,14]

Recovery from anaesthesia has been divided into three stages –early, intermediate and late. Early or phase 1 recovery is return of patient's protective reflexes and motor functions, which can be assessed on the operation table or in PACU. Intermediate recovery or discharge readiness is when the patient is coordinated, ambulating and ready to go home, assessed in PACU. Late recovery is complete psychological recovery from anaesthesia that may take days. We assessed both early recovery and discharge readiness using different criteria and found delayed recovery without any delay in discharge. Dexmedetomidine produces its sedative, analgesic and sympatholytic effects by suppressing the neuronal firing in the locus ceruleus. Being highly protein bound, its elimination half life is 2.1-3.1 hours after an intravenous loading dose that could be the reason for lower MAS recorded in this group. Previous studies using dexmedetomidine in dose range varying from 0.3 μg/kg to 1 μg/kg also reported delay in phase 1 recovery.[6,8,11] Ketamine too has shown delayed phase 1 recovery compared to propofol alone when used at subanaesthetic doses during induction.[5,9] Comparing the two premedicants, we found that dexmedetomidine premedication lead to faster recovery of consciousness, similar to the findings of Tiwari K *et al*.[15] This could be due to the inherent effects of ketamine on central nervous system as most patients scored less on the consciousness parameter in this group.

Intermediate recovery means that patient can be discharged home with an adult escort. Post Anaesthesia Discharge Scoring System (PADS) is an extensively used criteria for assessing discharge readiness for the last two decades. However, due to its low sensitivity for the surgical procedures a few modifications were done.[16] Because our study group included pelvic surgeries where urinary retention could be a cause for delayed discharge, we added a sixth criteria that is, voiding to our scoring system. Out of 40 patients analysed in each group, 12, 9 and 6 patients were ready for discharge at one hour in ketamine, dexmedetomidine and normal saline group, respectively. Although the difference was statistically insignificant, clinically the patients who received

ketamine premedication experienced least pain, had stable haemodynamics and better ambulation. At one and a half hour, all 40 patients receiving ketamine premedication were ready for discharge whereas in the propofol group this number was 33. It is worth highlighting that ketamine group although scored least while assessing phase 1 recovery, had foremost phase 2 recovery emphasising that its analgesic effects outlast hypnotic and psychomimetic effects.[17]

Dexmedetomidine significantly decreased the total dose of propofol resulting in nearly 50% reduction compared to placebo. The relatively lesser propofol sparing effect with ketamine premedication explains its dissociative anaesthesia properties resulting in a persistently elevated BIS index thus requiring frequent top-ups of propofol.[18] Numerous studies have verified the propofol-sparing effect of dexmedetomidine as well as ketamine and our findings are consistent with their observations with BIS monitoring providing objective assessment of the level of sedation.[4,5,13,19,20]

Propofol is known to decrease the sympathetic activity, but due to its inhibitory effect on baroreflexes, it can have a variable effect on HR. Dexmedetomidine, being ά2-AR agonist, is also known to cause bradycardia through vagomimetic action. When both the drugs are combined, a larger decrease in HR has been reported, but the effect on MAP is variable.[13,21] Our study showed an early decrease in HR (at five minutes) continuing till end of study. There was also a significant drop in MAP postoperatively that could be due to the $\acute{\alpha}_2$ mediated presynaptic inhibition in release of catecholamines and increased vagal activity. On the contrary, the sympathetic stimulant effect of ketamine actually counter balanced the inhibitory effect of propofol on sympathetic nervous system leading to a stable haemodynamic profile.

While assessing MPADSS, we also made some interesting observations. There was a lesser incidence of postoperative nausea and vomiting (PONV) in patients who had received either dexmedetomidine or ketamine premedication. This fact is supported by a meta-analysis done by Zhong *et al.*who concluded that dexmedetomidine premedication helped in attenuating PONV, post-operative shivering and pain.[22] Ketamine too is known to possess antiemetic properties at lower doses as reported in previous studies due to its beneficial effects on the relief of pain.[23,24] So, the superior effects of these drugs on amelioration of PONV and pain can't be ignored. Though dexmedetomidine is easily available, the enlistment of ketamine in Schedule X does involve some regulatory restraints. However, considering it's minimal pre-medicant dose, its multidose vial, once procured can serve many patients, hence reducing the financial burden on the hospital as well as the patient.

There were a few limitations in our study. Various authors have used clinical evaluation of sedation using different subjective assessment scales like Observer Assessment of Alertness/Sedation (OAAS), Richmond Agitation Sedation Scale, etc. We instead used BIS monitor to maintain and assess the anaesthetic depth which is only objective assessment. Combining both the systems could have given a better assessment of sedation and depth. Second, we evaluated the effects of only single doses of dexmedetomidine and ketamine. Premedication with different doses can have different effects on all the parameters that need to be studied with more future research.

In conclusion, administering dexmedetomidine 1 μg/kg and ketamine 0.5 mg/kg as pre-medicants to propofol based anaesthesia in minor gynaecological surgeries of less than 30 minutes duration does not delay discharge. Ketamine premedication provides better haemodynamic stability both intraoperatively and post-operatively and leads to better ambulation, giving it an edge over dexmedetomidine.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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