Research Article

Comparative Study Betweeen Dexmedetomidine and Remifentanyl for Efficient Pain and Ponv Management in Propofol Based Total Intravenous Anesthesia after Laparoscopic Gynaecological Surgeries

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ABSTRACT

Postoperative nausea and vomiting is a common and distressing complication following anaesthesia and surgery. Serotonin 5 hydroxytryptamine type 3 (5HT) receptor antagonists, because of their good efficacy and minimal side effects are used widely as one of the first line therapeutic agent for the prevention of PONV. Total intravenous anaesthesia (TIVA) methods are well tolerated and are associated with less postoperative nausea, vomiting than inhalational anaesthesia with no residual paralysis. Dexmedetomidine is a potent and highly selective alpha2 adrenoreceptor agonist which is presently being used as an adjunct for propofol based TIVA. The present study has been undertaken to compare the effects of Dexmedetomidine and remifentanyl on pain intensity, postoperative nausea and vomiting as well as the analgesic requirement after post anaesthesia care unit discharge in patients undergoing laparoscopic gynaecological surgeries. We found that Dexmedetomidine used as an adjunct in propofol based TIVA as compared to remifentanyl has a superior efficacy in alleviating pain as well as managing postoperative pain for 48 hours following laparoscopic gynaecological surgeries. It also reduced the requirement for rescue analgesics and postoperative nausea and vomiting (PONV). Therefore Dexmedetomidine may now be a better alternative to remifentanyl when used as an adjunct in propofol based TIVA.

Keywords: Remifentanyl, Dexmedetomidine, total intravenous anaesthesia, post-operative nausea and vomiting.

INTRODUCTION

The introduction of Dexmedetomidine has made a revolution in the field of anaesthesia because of its varied applications. Dexmedetomidine is a selective alpha-2 adrenergic receptor agonist used for sedation and analgesia. It is also used as an adjunct in anaesthesia to reduce anaesthetic requirements in procedures requiring total intravenous anaesthesia (TIVA).[1] As compared to clonidine Dexmedetomidine has a shorter duration of action (plasma half-life ~2.3 hours) and anaesthetic and analgesic sparing effect which have led to its usage as an adjuvant in general anaesthesia.[2] For this reason, Dexmedetomidine is now days used as an adjuvant for propofol-based TIVA.[3,4] Remifentanyl is a standard adjuvant for propofol-based TIVA, which has a rapid onset and ultra-short duration of action. Remifentanyl provides rapid recovery from anaesthesia, but its long-term infusion may cause opioid-induced hyperalgesia (OIH)[5,6].

In a randomized, placebo controlled double blind trial in 24 ASA 1 patients, Dexmedetomidine 0.6mcg/kg or saline was given IV 10 min. before induction of anaesthesia. Dexmedetomidine attenuated the hemodynamic response to laryngoscopy and tracheal intubation and also reduced the dose requirements of other agents.[7]

In this study we compared the effects of remifentanyl and Dexmedetomidine on pain intensity, analgesic requirements, and postoperative nausea and vomiting (PONV) after discharge from the PACU in those patients who are undergoing laparoscopic gynaecological surgeries.

METHODS

In the present study a total of 160 patients undergoing laparoscopic gynaecological surgeries like total laparoscopic hysterectomy, laparoscopic radical hysterectomy, laparoscopic myomectomies under general anaesthesia were enrolled during the study period from January 2013 to October 2015. The exclusion criteria included Patients with coronary artery or ischemic disease, patients with pre-existing severe bradycardia i.e. Advance heart block, and patients with severe ventricular dysfunction. A total of 160 women were randomly selected for the prospective study and were divided into two groups of 80 each. Group I: Remifentanyl was administered along with TIVA. Group II: Dexmedemitidine was administered along with TIVA. On the day of surgery, in the operation theatre, an 18-gauge venous cannula was inserted to administer Ringer's lactated solution. Five lead ECG was applied to the patient along with pulse oximeter. Blood pressure monitoring was done by non-invasive blood pressure monitor. Intravenous glycopyrrolate 0.4 mg was administered before induction of anaesthesia. In group 1, before induction of anaesthesia Remifentanyl was administered at a dosage of 0.01 μg/kg/min continuously using target-controlled infusion (TCI whereas 0.01 μg/kg/min of Dexmedetomidine was administered continuously using a syringe pump in Dexmedetomidine group. Propofol was

manually administered at the rate of 1 mg/kg followed immediately by an infusion of 10 mg/kg/hr. for 10 min, 8 mg/kg/hr. for the next 10 min and thereafter 6 mg/kg/hr. After 10 min. of administration of the study drug, when the patients were fully sedated 1 mg/kg of vercuronium was administered and the trachea was intubated with an approximately sized endotracheal tube after manual ventilation for 1 minute. Anaesthesia was maintained using propofol at 3–12 mg/kg/h with remifentanyl at 0.05µg/kg/min in group 1 or Dexmedetomidine at 0.05 µg/kg/min in group 2 using infusion pump. The end-tidal CO_2 in both groups was maintained at 30–40 mmHg. Remifentanyl was discontinued on completion of surgery in group 1, whereas Dexmedetomidine was ceased 15 to 20 minutes before completion of the surgery in group 2, taking into consideration their respective half-times. Propofol was terminated upon the completion of the surgery. On completion of surgery, 0.3 mg of ondansetron was administered for PONV, while 0.2 mg/kg of neostigmine and 0.008 mg/kg of glycopyrrolate were administered to reverse muscle relaxation. The patient was extubated after spontaneous ventilation was adequate. The patients were then transferred to the PACU.

In the PACU patient controlled analgesia was given. PCA consisted of 2 mg of morphine in a bolus dose dissolved in 100 ml of normal saline and was administered using an infusion pump, at a background rate of 1 ml/h with a lockout interval of 10 minutes. In the PACU and general ward, 1 µg/kg of fentanyl and 50 mg of tramadol were intravenously administered, respectively, as rescue analgesics. A registered nurse in the ward was assigned to assess the following, vital signs, pain sedation and rate and quality of respiration hourly for 24 hours postoperative and then 2 hourly for the next 24 hours. At consistent intervals the nurse was given orders to determine the patient's response to the ordered pain management approach. Assessment results were documented in the patient's chart.

A statistical analysis was performed using SPSS software. Chi-squared or Fisher's exact tests were performed to compare categorical data between the two groups. A value of $P < 0.05$ was considered to indicate statistical significance.

RESULTS

A total of 160 patients were enrolled. There was no significant difference in demographic characteristics between the two groups (Table 1, Table 2).

It was observed that the VAS score in group 1 was significantly higher than in group 2 at immediate and late postoperative period. (Figure 1 whereas in group 2 there was a statistically significant lower PCA requirement at every point of time after surgery but except before discharge from the PACU. (Figure 1. Patients in group 1 displayed more PONV until 24 hours post-surgery. Patients in Remifentanyl group required more analgesics at every point of time after surgery and displayed more PONV until 24 hours post-surgery (p <0.05, Table 1. The PACU stay duration was not significantly different between the two groups (Table 3, Table 4).
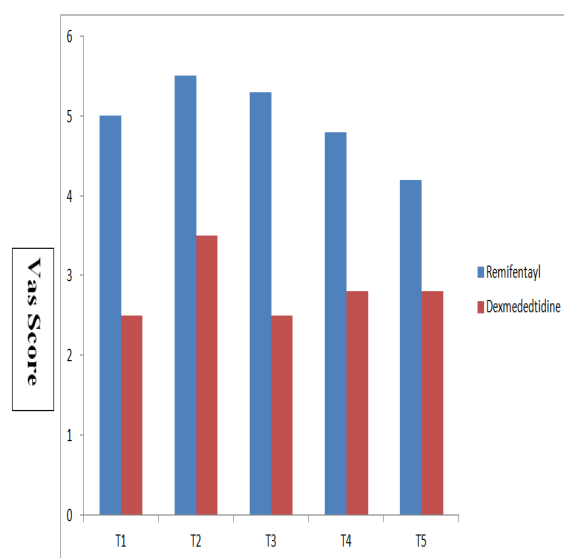
Figure 1: Comparison of postoperative VAS scores between the groups. VAS = visual analog scale; T1 = before PACU discharge; T2 = 2 hours after surgery; T3 = 8 hours after surgery; T4 = 24 hours after surgery; T5 = 48 hours after surgery. *$P < 0.05$.

Table 1

Demographic profile	Remifentanil group	Dexmedetomidine group
No of Patients	80	80
Age mean±SD	45±3.22	41±2.58
Weight (kg)	53±4.1	53±1.85
Height	157±6.528	158 ± 2.5
Hypertension	16(20%)	14(17.5%)
Diabetes mellitus	14(17.5)	17(21.25)
Preoperative VAS	3.72±2.13	4.1± 0.12

Table 2: Intraoperative and recovery data

Intraoperative and recovery data	Remifetnanil group	Dexmedetomidine group	P-value
Duration of surgery (min)	121.1 ± 23.2	137.2 ± 23.9	0.451
Duration of anesthesia (min)	180.3 ± 26.3	184.3 ± 21.6	0.256
Propofol used (mg/kg/h)	7.2 ± 1.2	7.8 ± 1.2	0.784
Remifentanil used (µg/kg/min)	0.10 ± 0.03	0.11±1.5	0.452
Dexmedetomidine used (µg/kg/min)	0.06 ± 1.27	0.01 ± 0.01	0.594
Time of eye opening (min)	6.9 ± 5.5	21.3 ± 4.9	0.256
Time of first verbal command response (min)	12.8 ± 9.3	23.2 ± 6.8	0.15
Incidence of rescue analgesics requirement, n (%)	16 (88.9)	12 (63.2)	0.018
Time of rescue analgesics requirement (min)	29.9 ± 11.6	13.0 ± 10.2	0.011
Incidence of PONV, n (%)	25 (31.28)	11 (13.75)	0.003
Duration of PACU stay (min)	79.2 ± 18.5	76.6 ± 13.5	0.785

Table 3: Incidence of rescue analgesics

Incidence of rescue analgesic requirement	Remifentanil group	Dexmedetomidine group	P-value
Postoperative 2 h (%)	19(23.75)	3(3.75)	0.046
Postoperative 8 h (%)	24(30)	14(17.5)	0.038
Postoperative 24 h (%)	9(11.25)	9(11.25)	0.045
Postoperative 48 h (%)	15(18.75)	3(3.75)	0.038

Table 4: Incidence of PONV

Incidence of PONV (n)	Remifentanil group(80)	Dexmedetomidine group(80)	P-value
Postoperative 2 h (%)	29(36.25)	3(3.75)	0.008
Postoperative 8 h (%)	36(45)	11(13.75)	0.029
Postoperative 24 h (%)	21(26.25)	2(2.5)	0.008
Postoperative 48 h (%)	11(13.75)	2(2.25)	0.23

DISCUSSION

Dexmedetomidine was initially approved by FDA for short term sedation in critical care. It has a unique pharmacodynamic profile which renders it suitable for perioperative care during administration of anaesthesia. This study demonstrates the superior pain control efficacy of dexmedetomidine as compared to remifentanil for the first 48 hours following laparoscopic gynaecological surgeries. It also lowers the VAS score and reduces the PCA requirement. As compared to remifentanil dexmedetomidine also reduced the analgesic requirement and PONV incidence. Our findings were similar to the findings of a study done by Hwang.[8] Immediate postoperative pain is mainly acute physiological pain; whereas late postoperative pain may progress to pathological pain. Pathologic pain differs from physiologic pain in that it is excessive in intensity and spread and can be activated by low-intensity stimuli and hyperpathia.[9] Several studies have demonstrated that dexmedetomidine had superior efficacy compared to

fentanyl and remifentanil in pain management during a PACU stay.[10-12] These authors have showed the efficacy of dexmedetomidine in alleviating postoperative pain was focused on the immediate postoperative period in the PACU. Unlike these reports, our study demonstrates that dexmedetomidine is effective for an extended period after surgery, and therefore may improve the postoperative outcome. Hwang[8] in their study demonstrated that dexmedetomidine is effective for an extended period after surgery. Hwang[8] attributed this result to the nociceptive cascade. When nociceptors are sensitized, the threshold for activation is decreased, discharge rate with activation is increased, and rate of basal discharge is increased, resulting in easier response of nociceptors to incoming stimuli.[13] Dexmedetomidine, with its longer action duration compared to remifentanil, may have reduced the "no pain control period" interval and the time from discontinuation of the adjuvant in propofol-based TIVA to PCA initiation, thereby increasing the stimulus threshold and resulting in a reduced VAS

score and PCA requirement.[8] Numerous studies have suggested that remifentanyl when given introperatively may paradoxically enhance postoperative pain and hence the opioid analgesic requirement, and this may occur after 60–90 minutes of infusion.[14] A recent study by Lee[6] demonstrated that intraoperative high-dose remifentanyl decreased the mechanical hyperalgesia threshold and enhanced the pain intensity. It also reduced the time to the first postoperative analgesic requirement, and increased patient morphine consumption, indicating OIH, which was alleviated efficiently using a Dexmedetomidine infusion. In the present study, we infused remifentanyl at the rate of 0.1 ± 0.03 µg/kg/min over three hours which is sufficient to induce OIH. A higher VAS score and greater PCA requirement imply OIH. The present findings were not influenced by the longer duration of Dexmedetomidine compared to remifentanyl. The superior efficacy of pain control beyond the known duration of Dexmedetomidine (i.e., until 48 hours after surgery) in combination with similar recovery time in PACU suggest that the alleviated postoperative pain over a longer period during recovery might have been influenced by affective-emotional effect of Dexmedetomidine rather than the analgesic effect of Dexmedetomidine on mechanical stimuli after surgery.[8] Another reason for the superior postoperative pain control efficacy of Dexmedetomidine compared to remifentanyl may be related to opioid-induced hyperalgesia (OIH). OIH is characterized by a paradoxical increase in pain intensity or sensitivity in patients receiving opioids at high doses or for an extended duration.[15]

Postoperative nausea and vomiting (PONV) is a frequent complication in postoperative period. Vomiting can stress wounds, cause electrolyte imbalance and bleeding.[16] Moreover the risks of PONV may also vary with preanaesthetic medication, anesthetic techniques, postoperative pain management.[17] Perioperative opioid use is a major factor in PONV. Apart from that pain itself is an important risk factor for PONV. A meta-analysis demonstrated that the intravenous infusion of dexmedetomidine may reduce the incidence of PONV, compared with placebo and opioids, rather than sedatives, which is due to the reduced consumption of intraoperative opioids probably.[18] Our study also demonstrated that, dexmedetomidine reduced PONV for 48 hours after surgery, in agreement with a previous study.[6] PONV may have been induced by more intense pain which increased the opiod analgesic requirement, which in turn aggravated PONV. The greater PCA required may be a contributory factor for the increased PONV incidence in the Remifentanyl group. Therefore Dexmedetomidine shows superiority to Remifentanyl when used as an adjuvant in propofol based TIVA in reducing postoperative nausea and vomiting. This beneficial antiemetic effect may be explained by direct antiemetic properties of α_2 agonists, although the biologic basis remains obscure.[18] Finally, consumption of intraoperative opioids, which increases the risk of PONV, may be reduced through the use of dexmedetomidine.

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