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COMPARISON OF INTRAVENOUS DEXMEDETOMIDINE AND PARACETAMOL FOR POSTOPERATIVE ANALGESIA IN ABDOMINAL HYSTERECTOMY UNDER GENERAL ANAESTHESIA

Anaesthesiology

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ABSTRACT

Background: Hysterectomy is associated with moderate to severe postoperative pain. Adequate perioperative analgesia may lead to better postoperative pain management. Different pharmacological agents such as NSAID, paracetamol, α2 adrenoreceptor agonist etc have been used to provide postoperative analgesia.

Methods: A randomised double blind interventional study was done on 100 ASA I/II patients between 20 and 60 years of age,undergoing elective abdominal hysterectomy under general anaesthesia and randomly divided into two groups. ASA III/IV patients, patients with H/O chronic illnesses, patients on previous opioid or α2 agonist treatment, and patients with coagulopathies or with difficult airway were excluded. Group A received IV dexmedetomidine in a dose of 1 µg/kg as a loading dose over 15 min prior to skin closure followed by 0.5 µg/kg per hour. Group B received IV paracetamol 15 mg/kg over 15 min just prior to skin closure and repeated after 6 hours. The patients were monitored for VAS score and hemodynamic parameters after extubation till 24hours. The rescue analgesics requirements were met with inj. tramadol (100 mg)IV when VAS score was recorded ≥ 3 and the time interval till requirement of first dose of rescue analgesia was recorded.

Results: In Group A 48% required rescue analgesia as compared to 20% in Group B. Mean time (hrs) to first analgesia request was longer in Group B as compared to Group A (3.32 ± 4.96 for A vs 6.42 ± 9.54 for B ; P=0.01). Total postoperative tramadol consumption was also significantly lower in Group B as compared to Group A (0.9±1.38 for A vs 0.46±0.705 for B ; P=0.04). There was no significant difference in side effects between the two groups at different time intervals (p value>0.05).

Conclusion: We conclude that paracetamol is associated with superior level of post operative analgesia as compared to Dexmedetomidine in surgical procedures of short duration and should form a part of multimodal analgesia.

KEYWORDS

Dexmedetomidine, Paracetamol, Abdominal Hysterectomy, Postoperative Analgesia

INTRODUCTION

Hysterectomy is one of the most common major surgical procedures performed in women between age of 25 and 50 years after caesarean section, and is associated with moderate to severe postoperative pain.[1,2] The laparoscopic approach is increasingly used, as it is associated with reduced postoperative pain and morbidity, as well as earlier recovery and a shorter hospital stay when compared with open hysterectomy.[3] However, pain may still be quite severe, particularly in the early postoperative period.[4] Epidural analgesia may be considered by some to be gold standard for pain management after abdominal surgeries.[5] Literature assessing non-opioid pain therapy for patients undergoing vaginal and laparoscopic hysterectomy has been recently evaluated.[6]

Proper pain control is essential for optimizing clinical outcomes and earlier ambulation after surgery. Multimodal analgesia management is utilized for pain observed in the postoperative period. Traditional pain management with opioids increases the incidence of side effects such as postoperative nausea and vomiting, constipation, urinary retention, and excessive sedation resulting in respiratory depression.[7] Paracetamol and dexmedetomidine are both effective component in respect of multimodal analgesia in combination with opioids. Paracetamol has both analgesic and antipyretic effects similar to aspirin and it is devoid of many side-effects of non-steroidal anti-inflammatory drugs, such as GI ulceration, impaired platelet function, and adverse cardio-renal effects.[8] Dexmedetomidine is a new generation highly selective α2 adrenoreceptor agonist, that dose-dependently reduces blood pressure and heart rate and has a sedative and analgesic effect without activation of α1 receptors. It also induces a centrally mediated reduction of sympathetic nervous system activity thereby decreasing the hemodynamic and plasma catecholamine response to stressful events of surgery.

Although IV paracetamol and IV dexmedetomidine have individually been studied to see their efficacy in reducing postoperative narcotic requirement and other side effects after abdominal hysterectomy, only few studies have compared them with each other for the same purpose. Thus, the present prospective randomized study attempts at comparing the effects of IV dexmedetomidine and paracetamol on postoperative pain after abdominal hysterectomy under general anaesthesia.

MATERIALS AND METHODS

The study was conducted in the Department of Anaesthesiology in collaboration with the Department of Obstetrics and Gynaecology at SMS Medical College and the attached hospital Mahila Chikitsalaya in Jaipur, Rajasthan after obtaining permission from institutional ethics committee, review board, and the written informed consent from the patients. The study was a hospital-based double-blinded randomized interventional study conducted over a period of 4 months and included 100 eligible abdominal hysterectomy candidates in total. The patients were between 20-60 years of age, belonged to ASA I/II, and were undergoing elective abdominal hysterectomy under general anaesthesia. The patients weighed between 40-60 kg. The patients were randomly allocated to two groups (A and B) using a computerised random number table. In order to eliminate the subject and the observer bias, the anaesthetist who measured the study variable was different from the anaesthetist who gave the analgesic agent. Both the agents were transparent solutions and looked the same. Hence, neither the doctor nor the participant was aware of group allocation and the drugs received. The following patients were excluded: (a) patients with H/O chronic illnesses like hypertension, diabetes mellitus, respiratory disease, epilepsy, cardiac disease, (b) patients on previous opioid or α2 agonist treatment, (c) patients who were unwilling to participate, and (d) patients with coagulopathies or with difficult airway.

For the study, the patients were premedicated with injection ranitidine 50 mg, inj. metoclopromide 10 mg, inj. glycopyrrolate 0.02 mg, inj. midazolam 1 mg, and inj. tramadol 100 mg. The anaesthesia was induced with inj. propofol 2 mg/kg and inj. succinyl choline 2 mg/kg, and tracheal intubation was done. The anaesthesia was maintained with 0.2-2% isoflurane and N_2O:O_2 (60%-40%). Inj. atracurium with a loading dose of 0.5 mg/kg and a maintenance dose of 0.1 mg/kg was given. Intraoperative monitoring included SBP, DBP, MAP, SpO_2, ECG, $ETCO_2$ and end tidal isoflurane concentration. The $ETCO_2$ was maintained between 30-35 mm of Hg. The BP and heart rate were

maintained between 80-120 % of preoperative value by altering the concentration of isoflurane. At the end of surgery, before skin closure, the study drug, i.e. paracetamol or dexmedetomidine, was given intravenously over 15 min. The residual muscle relaxation was reversed with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.01 mg/kg IV.

The study drug was prepared beforehand by an assistant and its identity was unknown to the anaesthetic. The total volume of the study drug was 100 ml in both the groups. Group A received intravenous dexmedetomidine in a dose of 1 µg/kg as a loading dose over 15 min prior to skin closure followed by 0.5 µg/kg per hour till 4 hours in a drip of normal saline, 500 ml managed with drops per minute and repeated a plain normal saline 100 ml drip after 6 hours. Group A received intravenous paracetamol 15 mg/kg over 15 min just prior to skin closure followed by a plain drip of normal saline for 4 hours and repeated after 6 hours. After the surgery, the patients were shifted to post anaesthesia recovery room where the base line analgesia (on a 10-point VAS score) and the vital parameters (heart rate, oxygen saturation, SBP, and DBP) were monitored at extubating and until 24 hours afterwards – at every 2 hours for the first 12 hours, then every 4 hours for the next 12 hours. The rescue analgesics requirements were met with intravascular inj. of tramadol (100 mg) when VAS score was recorded ≥ 3.

The statistical analysis was done as follows: The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of means and standard deviations. The unpaired t test (for quantitative data to compare two independent data) was used for quantitative data comparison of all clinical indicators. Level of significance was set at P≤0.05.

RESULTS AND STATISTICAL ANALYSIS

Table 1 shows the mean value, the standard deviation, and the P value for the key demographic details of the patients. Additionally, the P values for the hemodynamic parameters at baseline were 0.26 (SBP), 0.93 (DBP), 0.39 (MAP), 0.26 (HR), and 0.25 (SpO_2). From these values, it may be concluded that all the patients were comparable with respect to the demographic details and the hemodynamic parameters.

Table 1: Patient Demographic Details

Parameter	Mean ± SD		P value
	Group D	Group P	
Age (years)	44.1 ± 8.17	42.7 ± 7.97	0.38
Body weight (kg)	52.6 ± 7.30	53.3 ± 8.31	0.65
ASA I/II (%)	84/16	78/22	0.47

Table 2: VAS Score Comparison

Interval	Group	Mean	P value
At extubation	A	51.00	0.31
	B	50.00	
2 hours	A	51.50	0.15
	B	49.50	
4 hours	A	48.80	0.35
	B	52.20	
6 hours	A	48.36	0.39
	B	52.64	
8 hours	A	55.15	0.07
	B	45.85	
10 hours	A	56.85	0.01
	B	44.15	
12 hours	A	57.08	0.006
	B	43.92	
16 hours	A	56.45	0.02
	B	44.55	
20 hours	A	55.34	0.05
	B	45.66	
24 hours	A	54.46	0.08
	B	46.54	

Table 2 shows the comparison of VAS scores between the two groups at the various intervals. The VAS scores up to 8 hours after extubating are almost same among both the groups while at 10 hours, 12 hours, 16 hours, and 20 hours, the scores were lower for group B which showed statistically significant results. In Group A, 48 % patients required rescue analgesia in 24 hours whereas in group B, only 20 % patients required rescue analgesia in 24 hours. The mean time to first analgesia request was longer in Group B than in Group A (6.42 ± 9.54 for B vs 3.32 ± 4.96 hours for A; P < 0.001). Total analgesic in 24 hours was more in Group A than Group B which showed statistically significant results. Figure 1 shows the group wise number of patients exhibiting various side effects. It may be observed that there was no significant difference in side effects between the two groups at different time intervals (P > 0.05) but more patients in Group B than Group A did not show any side effects, and no patient in Group B showed hypotension and bradycardia.

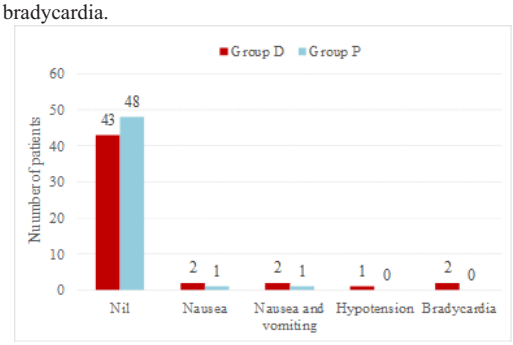

Figure 1: Group-wise Number Of Patients With Various Symptoms

DISCUSSION

Hysterectomy, the surgical removal of uterus, was chosen for this study because it is the second most frequently performed non-obstetric surgery after caesarean section in many parts of the world.[9] The pain after abdominal hysterectomy may include the pain at the incision site, the pain from the visceral structures, and the dynamic pain due to coughing and mobilization. Some of these components may be felt more than others at different times of post-operative period.[10] As the surgery chosen was abdominal hysterectomy, only female patients were included in the study. So, both the groups were comparable with regards to age and gender distribution. This has helped us to judge the clinical significance of our study as the distribution, metabolism, excretion, and action of drug are undoubtedly varied in different age groups.

The results on age, body weight, and ASA grading were statistically comparable for both the groups in this study, similar to study done by Sarkar M et. al.[11] Therefore, clinically insignificant variation in demographic parameters helped to alleviate the confounding factors. Additionally, the mean baseline hemodynamic variables were also comparable between both groups. We also did not encounter any difference between two groups and the mean arterial pressure and SpO_2 were within acceptable limits throughout the study period. The hemodynamic parameters remained stable in both the dexmedetomidine and paracetamol groups and did not show any comparative difference when results were analysed statistically. The same has been observed by Sharma R et al[12] in their literature and in the literature[13,14] on intracranial surgery when dexmedetomidine infusion without a preceding bolus was administered as compared to control group.

The lowest mean SBP and DBP rate was significantly lower in Group A than in Group B at extubation time and after 2 hours till the end of the study periods which was significant. We observed that in Group B patients, the SBP and DBP values increased from baseline immediately following extubation. But in Group A, there was no rise in SBP and DBP, instead the BP fell below the baseline following the start of dexmedetomidine infusion. But after that from 4 hours from extubation to 24 hours, both SBP and DBP changes were non-significant in both the groups. This change can be due to sympathetic response to extubation which is not curbed by paracetamol.

We also observed that in patients in the Group B, the MAP increased from baseline immediately after extubation but remained near the baseline values. In Group A, there was sudden fall in MAP 2 hours after extubation and it rose continuously after extubation till 24 hours and remained almost near to baseline. This is similar to what has been reported in study done by Swaika S et al.[15]

The lowest mean heart rate was significantly lower in Group A as compared with the Group B at extubation time and after 2 hours. There

was significant rise in heart rate in paracetamol group from baseline to immediately after following extubation to till the study period too and remained higher than Group A but normal at end of 24 hours. In Group A, there was no rise in heart rate, instead, the heart rate fell below the baseline following the initiation of dexmedetomidine infusion and it remained near at baseline thereafter. The mean heart rate was lower in Group A as compared with Group B, but showed statistically non-significant results which may be due to sympatholytic action of dexmedetomidine. In our study, Group A showed statistically non-significant variation in HR and MAP with Group P after 2 hours of extubation.

Sarkar M et.al[11] showed mean time at which the first dose of rescue analgesia administered in group paracetamol was much longer as compared to group dexmedetomidine (134.42 ± 12.67 vs 82.76 ± 9.38 min; P=0.001).The time interval between the stoppage of anaesthetic agents to response of eye opening to verbal command was significantly prolonged in dexmedetomidine group because of the inherent sedative properties of dexmedetomidine via central actions in the locus ceruleus and in the dorsal horn of the spinal cord.

Dholakia C et. Al[16] did a retrospective study in which they concluded that dexmedetomidine provides postoperative analgesia compared to control group.

Based on the VAS score, our results indicate that dexmedetomidine provides a modest analgesic effect in early postoperative period, but the beneficial effect would appear to diminish because rescue analgesia requirement was more in Group A. On the other hand, paracetamol consistently showed less VAS score without requiring frequent rescue analgesia. Moreover, the 24 hours mean requirement of tramadol were less in Group B. Paracetamol was found to be effective in providing postoperative analgesia in the present study.

Limitations

The main limitation of our study is that it required more systemic reviews of high-quality randomized control trials (RCTs) to be conducted regarding the use of IV dexmedetomidine as an opioid-sparing agent in case of abdominal hysterectomy to provide us with level I evidence for evidence-based study. Several studies tried to investigate the postoperative analgesic effect of PCM compared with normal saline, in contrast to our study that compared dexmedetomidine, but required need for further multicentric RCTs to confirm the finding of our study so that dexmedetomidine can become an adjuvant of choice for postoperative analgesia. More studies are needed to establish the safe dose and timing of dexmedetomidine administration, especially in patients having hepatic and renal failure as well as in paediatric age group.

Conclusion

Paracetamol significantly reduced the intensity of postoperative pain and prolonged the duration of analgesia with significant advantage of good to excellent patient satisfaction as compared with dexmedetomidine. Paracetamol consistently showed less VAS score without requiring frequent rescue analgesia. Therefore, it may be concluded that paracetamol is associated with superior level of postoperative analgesia than dexmedetomidine in surgical procedures of short duration and should form a part of multimodal analgesia.

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