The Effect of Intravenous Dexmedetomidine on Postoperative Pain Intensity in Patients undergoing Abdominal Hysterectomy

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Abstract: *Objective*: The control of perioperative pain and its practice can play an important role in short and long term postoperative convalescence. The aim of this study was to evaluate the effect of dexmedetomidine on postoperative pain in patients undergoing abdominal hysterectomy (TAH).

Methods: This double-blind, randomized controlled clinical trial study was conducted on 70 women aged 35-65 years undergoing general anaesthesia for TAH. In dexmedetomidine group, immediately after induction, a bolus dose of dexmedetomidine 1 µg/kg was injected for 15 minutes and then a dose of infusion 0.5 µg/kg until the end of surgery. In the control group, normal saline was injected. Patients were evaluated for pain intensity according to the visual analogue scale (VAS), the amount of analgesic use during 24 hours after surgery and time of administration of the first dose of pethidine.

Results: Although the mean pain intensity at all times in dexmedetomidine group was lower than the control group, there was a significant difference at 4, 8, 16, and 24 hours after surgery ($P < 0.05$). The time of the first request for administration of the first dose of pethidine was greater than the control group, but there was no significant difference in first-time administration of opioid in the two groups ($P > 0.05$). Although the mean dose of pethidine was lower in the dexmedetomidine group, there was no statistically significant difference between the mean values in the two groups ($P > 0.05$).

Conclusion: This study showed the efficacy of dexmedetomidine in reducing post-operative pain and receiving pethidine after surgery.

Keywords: Dexmedetomidine; Abdominal Hysterectomy, Postoperative Pain.

INTRODUCTION

Acute postoperative pain is still a fundamental issue in patients undergoing Total Abdominal Hysterectomy (TAH). One of the undesirable complications of surgery is postoperative pain that may result in serious morbidities such as agitation, hypertension, mood changing, tachycardia [1,2] and delay in wound healing, which can be more dangerous in patients with the underlying diabetes mellitus, hypertension, or coronary heart diseases as it may lead to fatal complications such as myocardial infarction [3]. There is inadequate postoperative analgesia in the half of all surgeries, can lead to chronic postoperative pain [4]. Several methods are available to control and reduce postoperative pain such as administering opioids or nonsteroidal anti-inflammatory drugs (NSAIDs) and patient-controlled analgesia (PCA) as well as low-level laser therapy.

In most cases, inadequate dosage is prescribed to reduce the side effects of these drugs like respiratory depression and therefore, the medication cannot control pain completely [5,6]. Analgesic nephropathy, skin reactions, and peptic ulcers are common side effects of nonsteroidal anti-inflammatory drugs [7] and the research continues to find better alternatives. Alpha-2 adrenergic receptor agonist has several effects such as analgesic effects, inhibitory sympathetic outcomes, anti-anxiety and reduced norepinephrine levels. It also has a positive impact on the supply of myocardial oxygen and cardiovascular oxygen demand and therefore, myocardial protection [3,8]. Alpha-2 agonists have reducing effect on blood pressure and thus reduce bleeding during surgery [9]. One of the major drugs is dexmedetomidine, a specific agonist alpha-2 adrenergic receptors [10,11]. This drug as an adjuvant in general anaesthesia with a central sympathetic effect helps to stabilize the hemodynamic status of the patient and has analgesic effects [12-14], reducing the need for opioids and their complications [15] and improving the quality of recovery [16]. The sedative and analgesic capabilities of dexmedetomidine are unique and cause mild side effects, which makes easy communication between the medical team and the patient in the intensive care unit and need for monitoring [14,17,18]. Considering the beneficial effects and the fewer complications of dexmedetomidine, the aim of this study was to

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determine the analgesic effect of dexmedetomidine on acute postoperative pain in patients undergoing abdominal hysterectomy.

MATERIALS AND METHODS

This double-blind, controlled, randomized clinical trial (IRCT Code: IRCT20190222042805N1) was conducted in 2018-2019 in Imam Khomeini Hospital, Ahvaz, Iran. The study was approved by the Ethical Committee of Jundishapur University of Medical Sciences (Ethical Code: IR.AJUMS.REC.1397.454), and all subjects signed informed consent.

This study was performed on 70 female patients under general anaesthesia for TAH and patients were divided into two groups: dexmedetomidine and control group. Each group included 35 patients. The inclusion criteria included patients aged 35 to 65 years, subjects with body mass index (BMI) between 18 and 40, and American Society of Anesthesiologists [8] classes I and II, and exclusion criteria, including allergy to dexmedetomidine, use of dexmedetomidine in the past week, having illnesses of heart, lung, liver, and kidney, neurological or neuromuscular diseases, having anaemia or bleeding disorders, using alcohol, opioids and antipsychotics, and having diabetes. Patients in the operating room underwent routine monitoring, including 3-lead EKG, capnography, pulse oximetry, non-Invasive blood pressure, and urine output. Two IV lines were established for patients, and all patients underwent anaesthesia with the same drugs, including midazolam 0.3 mg/kg, fentanyl 3 mg/kg, thiopental 5 mg/kg and atracurium 0.5 mg/kg. In addition, immediately after induction, dexmedetomidine group patients received dexmedetomidine (Hospira Company – USA) with a bolus dose of 1 µg/kg in 15 minutes and then the infusion dose 0.5 µg/kg was injected by the end of the surgery. In the control group, the same volume of normal saline was injected within 15 minutes, and then the infusion was injected with the same volume until the end of surgery. During the surgery, in both groups, patients underwent infusion of propofol 50-100 µg/kg/min and remifentanil 0.15 µ/kg/min as maintenance the end of surgery. After surgery, the reversal of neuromuscular blockade occurred with 0.05 mg/kg neostigmine and 0.02 mg/kg atropine. Postoperative pain was quantitatively measured using a visual analogue scale (VAS) and compared at 1, 2, 4, 8, 16 and 24 hours after surgical completion.

Pethidine dose 0.3 mg/kg was administrated at VAS≥3 for the patient. The time of the first request for administration of pethidine and the total opioids used was recorded on the questionnaire. The questionnaire was completed by an anesthesiologist who was not informed about the groups.

To compare the results after collecting statistical findings, SPSS 22 was used. First, for more accurate interpretation of the results, the two groups were matched with the frequency matching method; then, qualitative and frequency variables were compared using a Chi-square test. Also, to compare the quantitative variables based on the normality of the data, independent two-sample t-test or Mann-Whitney or Chi-square were used.

RESULTS

There are match case and control group, and validity data will ensure due to homogeneity of sample characteristic (Table **1**).

Although the mean pain intensity at all times in the dexmedetomidine group was lower than the control group, there was a significant difference at 4, 8, 16, and 24 hours after surgery (P <0.05) (Table **2**).

The time of the first request for administration of the first dose of pethidine in the dexmedetomidine group was higher than the control group, but there was no significant difference between the two groups (P >0.05). Although the mean dose of pethidine was lower

Table 1: Demographic Data, Duration Surgery and Anaesthesia in Two Groups

Variables	Dexmedetomidine	Normal Saline	P-Value
Age (year)	49.64±8.540	51.57±6.116	0.42
Height (cm)	163.67±6.012	165.27±5.902	0.714
Weight (kg)	69.36±10.44	72.95±11.30	0.512
Duration of anaesthesia (mins)	172.51±26.14	181.49±25.08	0.102
Duration of surgery (mins)	141.22±3.61	155.67±2.98	0.215

Table 2: Comparison of Postoperative Pain Intensity at Different Times

Different time points after surgery	Pain scores (measured by VAS)		P-value
	Dexmedetomidine	Normal Salin	
One hour	1.06±0.511	1.07±0.244	0.82
Two hours	2.07±1.048	2.57±1.384	0.302
Four hours	3.97±1.860	4.57±2.064	0.048*
Eight hours	4.45±1.077	5.97±1.375	<0.0001*
16 hours	4.90±2.181	6.85±2.031	<0.0001*
24 hours	4.84±2.217	6.23±2.242	<0.0001*

Data are expressed as mean ± SD. The statistical test used was the t-test.

Table 3: Time of Administration of the First Dose of Opioids in 24 Hours after Surgery in Two Groups

Variable	Dexmedetomidine	Normal Saline	P-value
Time of administration of first dose of pethidine (minutes)	362.82±49.56	343.17±51.61	0.321

Data are expressed as mean ± SD. The statistical test used was the t-test.

Table 4: Comparison of Opioids Consumption in 24 Hours after Surgery in Two Groups

Variable	Dexmedetomidine	Normal Saline	P-value
Total pethidine dose (mg)	62.14±3.21	67.51±5.47	0.451

Data are expressed as mean ± SD. The statistical test used was the t-test.

in the dexmedetomidine group, there was no statistically significant difference between the mean values in the two groups (P >0.05) (Tables **3** and **4**). There were no particular side effects reported in the two groups.

DISCUSSION

This study investigated the effects of dexmedetomidine on the postoperative pain intensity in patients undergoing abdominal hysterectomy.

The current evidence shows there are three major receptor subtypes for dexmedetomidine, including a2A, a2B, and a2C. The roles of the three receptor subtypes are not fully understood, and the studies are ongoing in this regard. Initial findings demonstrated that the a2A and a2C subtypes are predominated in the central nervous system and have been contributed to the sedative, analgesic, and sympatholytic components of the dexmedetomidine action [17,19-21]. The results of the evaluations showed that at 4, 8, 16, and 24 hours after surgery, the pain intensity was significantly lower in the dexmedetomidine group than in the normal saline group (P <0.05), but in other times there were no significant differences in pain intensity in the two groups (P >0.05). In the study conducted by Ge D-J *et al*. in china in 2016 conducted on patients underwent abdominal hysterectomy, patients in the group receiving dexmedetomidine (0.4 µg/kg/h) compared to the normal saline group during the first 24 hours after surgery reported a lower pain score (P< 0.05) [22]. According to the results of the study conducted by Ren *et al*. in China in 2015, who investigated the effect of adding dexmedetomidine to sufentanil on pain relief within 72 hours after surgery, sufentanil (0.02 µg/kg/h) plus dexmedetomidine (0.05 µg/kg/h) showed a significant analgesic effect during the first 72 hours after abdominal hysterectomy (P< 0.05) [23]; so, it was consistent with the results of the present study, which reported an analgesic effect as a result of use of dexmedetomidine. The results of the study conducted by Chen *et al*. in China in 2017, who compared the pain in the group receiving sufentanil and the patients receiving the combination of sufentanil (0.02 µg/kg/h) and dexmedetomidine (0.05 µg/kg/h), showed that the group receiving dexmedetomidine had better sleep quality, more relaxation and less pain at 6, 24 and 48

hours after surgery than the control group (P< 0.05) [24] and were consistent with the results of the present study. The results of the study conducted by Min *et al*. in 2014 in china, who compared pain in the patients receiving tramadol chloride and the patients receiving tramadol chloride and dexmedetomidine, showed that the pain score 24 and 48 hours after abdominal hysterectomy surgery in the group receiving dexmedetomidine was significantly lower than control group and concluded that low doses of dexmedetomidine could improve the analgesic effect of tramadol chloride (P< 0.05) [25].

In the clinical practice, dexmedetomidine administration is currently approved for sedation for up to 24 hours in intubated and mechanically ventilated patients in intensive care units. Dexmedetomidine is an α2-agonist that has been used for pre-medication and as an adjunctive agent to general anaesthesia [26–28]. Intravenous dexmedetomidine reduces the required dose of inhalational anaesthetic agents and the opioid demand during general anaesthesia [29]. Intravenous dexmedetomidine has been reportedly beneficial for extending the duration of spinal anaesthesia, while induces sufficient sedation and with low rates of adverse effects in the patients [30,31]. In the present study, although the mean dose of pethidine consumption was lower in the dexmedetomidine group, there was no statistically significant difference between the two groups. There were also no particular side effects reported in the two groups.

CONCLUSION

The results of this study showed the efficacy of dexmedetomidine in reducing post-operative pain and receiving pethidine after surgery.

ABBREVIATION

VAS = The visual analogue scale

TAH = Total Abdominal Hysterectomy

NSAIDs = Nonsteroidal anti-inflammatory drugs

PCA = Patient-controlled analgesia

BMI = body mass index

DECLARATION

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (Ethics code: IR.AJUMS.REC.1397.454), and all patients provided written informed consent before enrollment.

Consent for Publication

This manuscript has not been published and is not under consideration for publication elsewhere in whole or in part. No conflicts of interest exist in the submission of this manuscript, and the manuscript is approved for publication by all listed authors.

Availability of Data and Material

The data used to support the findings of this study are available from the corresponding author upon request.

Competing Interests

None of the authors has any financial and personal relationships with other people or organizations that could potentially and inappropriately influence this work and its conclusions. Authors declared no competing interest in publishing this paper.

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