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Analgesic Effects of Dexmedetomidine and Remifentanil in Patients with Herniated Disc

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Abstract--

Introduction: *The purpose of this study was to compare analgesic effects of dexmedetomidine with those of remifentanil in patients undergoing herniated disc surgery.*

Material and Methods: *In this double-blind clinical trial study, 96 patients who were candidates for herniated disc surgery were enrolled. Patients were randomly divided into three groups with epidural block. In all three groups, leg and back pain were recorded within 2, 6, 12 and 24 hours after surgery. Patient sedation was recorded by* Ramsay sedation *score within 2, 6, 12 and 24 hours postoperatively. Data were analyzed by SPSS 20 software.*

Results: *Foot pain and low back pain were lower in the dexmedetomidine-apotel group within 2 to 24 hours after surgery (p <0.05). There was a statistically significant difference between the three groups in terms of sedation within 2 to 24 hours after surgery (p <0.05). Furthermore, sedation was found to be higher in the apotel-normal saline group than the other two groups, 2 to 6 hours after surgery. But no signoficant difference was observed between the dexmedetomidine-apotel and remifentanil-apotel groups (p <0.05).*

Conclusion: *Dexmedetomidine-apotel was capable of reducing back and leg pain in postoperative period, but there is no difference between dexmedetomidine-apotel and remifentanil-apotel in sedation.*

Key words--*Apotel, Dexmedetomidine, Remifentanil, Pain Reduction, Herniated Disc*.

I. INTRODUCTION

Herniated disc is a problem that human beings have been involved in. About two-thirds of adults suffer from back pain throughout their lives, the most common time of disease is described to be the 4th and 5th decades of life. In lumbar herniated disc, a portion of the nucleus pushes the spinal canal through a crack in the annulus, which can cause damage to the nerve, resulting in pain, numbness, and weakness in the lumbar spine and legs. Lumbar radiculopathy is also a disease of the lumbar spinal nerve root that is caused by pressure on the nerve. This disease is related to intervertebral disc movement, injuries and spinal cord diseases etc. Its features include pain, paresthesia, numbness, weakness, reflex change, and loss of sensation. Pain and paresthesia spread to the affected lumbar spinal nerve root (1, 2). Prevention of deaths and complications after surgery is considered as the fifth vital sign (3, 4). Postoperative pain can significantly alter body metabolism in susceptible individuals by causing adverse effects and affecting various mechanisms. It can cause hypertension, cardiac ischemia, respiratory, gastrointestinal and renal

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problems, as well as increased mortality. Pain increases hospital stay and medical costs by delaying patient movement and walking.

Today, the use of opioid analgesics is one of the mainstays of treatment (5-7). Today, acetaminophen (Apotel) is one of the most commonly used medications in the operating room and in most parts of the patient's pain control units. It is an antinociceptive and antipyretic drug that ampoule contains 1 g Paracetamol (1g/6.7ml). Its mechanisms of action include inhibition of prostaglandin secretion in the CNS, reduction of peripheral inflammatory effects, and reduction of the fever by effecting the central control of body temperature in the hypothalamus. The drug is used to temporarily relieve mild to moderate pain, especially after surgery. In addition, it is commonly applied to rapidly relieve fever and emergency hyperthermia (8,9). Dexmedetomidine is considered as a selective alpha *2*-adrenoceptor agonist that its infusion is associated with reduced heart rate, reduced systemic vascular resistance, and reduction of blood pressure. This drug has helped to stabilize the patient's hemodynamic status and has a strong anesthetic and analgesic effect, reducing the need for opioids and their complications, furthermore, it was effective in reducing stress response and improving recovery quality (10,11). The antinociceptive effects of dexmedetomidine appear to be due to activation of α_2-adrenoceptor in the dorsal horn of the spinal cord and inhibitory effect on the release of substance P (12).

Remifentanil is a novel short-acting μ-opioid agonist with a clinical potency and metabolized by blood and tissue esterases due to its unique chemical structure (an alpha-amino acid ester), indicating a rapid metabolism without involvement of the liver (13). Remifentanil results in faster awakening and shorter recovery time in comparison with other opiates of the same group (alfentanil, sufentanil and fentanyl) (14), thus providing potential neurological evaluation within 10-30 minutes.

Due to the fact that no comparative study has compared the antinociceptive effect of dexmedetomidine-apotel and remifentanil- apotel, the current study aimed to compare the effect of dexmedetomidine- apotel and remifentanil- apotel on pain relief in patients with herniated disc.

II. MATERIAL AND METHODS

In this double-blind, placebo-controlled clinical trial, 96 patients who were candidates for herniated disc were enrolled. After obtaining written informed consent, the patients were enrolled based on inclusion and exclusion criteria. Inclusion criteria included; both sexes, American Society of Anesthesiologists Classification (ASA Class) I and II, herniated disc candidate, insensitivity to the drugs used.

Exclusion criteria were: dissatisfaction, drug side effects, drug addiction or abuse of psychiatric medications. Patients were randomly divided into three groups with epidural block. The groups were as follows:

Dexmedetomidine and Apotel group: Acetaminophen (2 g) and dexmedetomidine (0.15 μg / kg body weight) at 100 ml normal saline were given via a syringe infusion pump at an infusion rate of 4 ml/hour.

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Remifentanil and apotel group: Remifentanil (0.5 µg/kg) and acetaminophen (2 g/h) at 100 ml normal saline were given via a syringe infusion pump at an infusion rate of 4 ml/hour. Placebo group: Acetaminophen (2 g/h at 100 ml normal saline) was pumped at an infusion rate of 4 ml/hour.

Patient status was evaluated in all three groups at the time of recovery and at 2, 6, 12 and 24 hours after surgery. Pain score was recorded according to the Visual Analogue Scale (VAS; 0-10) by a physician assistant neurosurgery. Patient sedation was recorded by Ramsay Sedation Scale at 2, 6, 12 and 24 hours postoperatively. If the patient's pain was greater than 3 during this period, 25 mg of intravenous pethidine was injected. Bradycardia and hypotension were considered as > 20% decrease in heart rate/minute and decreased mean arterial pressure (MAP) over 20%, respectively.

In the event of bradycardia and hypotension, atropine (0.02 mg/kg) and ephedrine (0.1 mg/kg) were administered intravenously, respectively. In order to succeed with double-blinding, study, the data were measured by a resident who was unaware of the groupings .Drugs were prepared in each group by the anesthesiologist or anesthesiologist. Patients were also unaware of the group in which they were assigned.

Data were analyzed by SPSS 20 software. Descriptive statistics, ANOVA, and chi-square tests were used to analyze the parametric and nonparametric data.

III. RESULTS

The purpose of this study was to compare the effects of dexmedetomidine and remifentanil on pain relief in herniated disc. In this double-blind, placebo-controlled clinical trial, 96 patients who were candidates for surgery in Vali-e-Asr Hospital in Arak were randomly divided into three groups.

Age, sex, BMI and duration of surgery were not found to be statistically significant among groups ($p < 0.05$).

Table 1. Comparison of mean and standard deviation of leg pain in three groups

Group / **Leg pain**	**Dexmedetomidine - Apotel Mean ±SD**	**Remifentanil - Apotel Mean ±SD**	**Normal salin-Apotel SD±Mean**	**pvalue**
Preoperation	8.35±1.190	8.31±1.46	7.96±1.513	0.273
Recovery	4.43±1.644	4.75±1.344	4.59±1.340	0.691
2h after surgery	7.71±2.260	5.71±2.344	7.71±2.260	0.0001
6h after surgery	2.15±1.483	3.68±1.468	5.37±1.718	0.0001
12h after surgery	1.31±1.533	2.12±1.288	3.40±1.478	0.0001
24h after surgery	0.812±0.965	1.00±1.135	5.336±3.09	0.009

According to the results, there was a statistically significant difference between the three groups in terms of leg pain within 2 to 24 hours after surgery ($p < 0.05$). Leg pain was less in the dexmedetomidine-apotel group than the other two groups. In the Apotel-normal saline group, leg pain was greater than the other two groups within 2 to

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24 hours after surgery. There was a statistically significant difference between two groups (dexmedetomidine-apotel and remifentanil-apotel groups) within 2 to 12 hours after surgery (p <0.05). Leg pain was less in the dexmedetomidine-apotel group as compared to the remifentanil-apotel group.

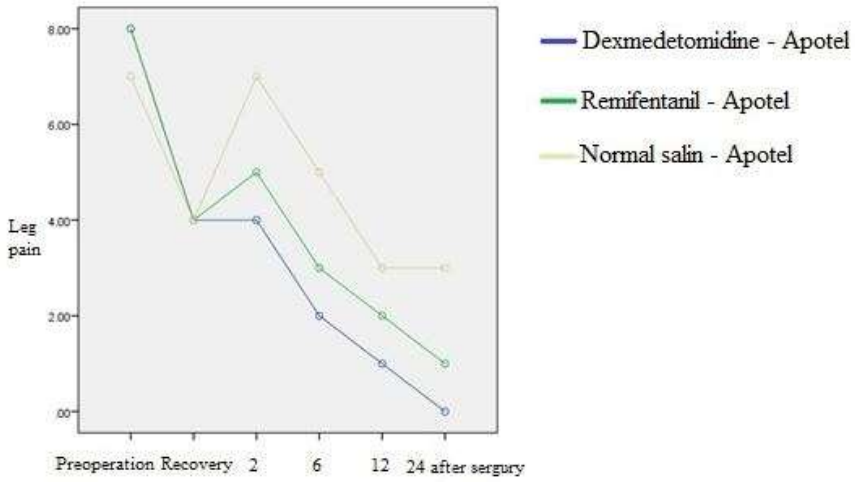

Figure 1. Comparison of leg pain in three groups

Table 2. Comparison of mean and standard deviation of back pain in the three groups

Group **Back pain**	**Dexmedetomidine - Apotel Mean ±SD**	**Remifentanil - Apotel Mean ±SD**	**Normal salin-Apotel SD±Mean**	**pvalue**
Preoperation	6.125±1.946	5.68±2.235	6.250±1.722	0.493
Recovery	2.875±2.196	2.906±1.672	3.781±1.698	0.095
2h after surgery	1.937±1.389	2.750±1.391	3.781±1.698	0.0001
6h after surgery	1.125±1.070	1.843±1.416	2.687±1.281	0.0001
12h after surgery	0.812±0.780	1.781±1.361	2.406±1.316	0.0001
24h after surgery	0.656±0.653	1.00±0.803	2.187±1.387	0.0001

There was a statistically significant difference in back pain within 2 to 24 hours after surgery (p <0.05). Back pain was lower in the dexmedetomidine-apotel group than the other two groups.

In the Apotel-Normal Saline group, back pain was greater than the other two groups within 2 to 24 hours after surgery. A statistically significant difference was found between two groups (dexmedetomidine-apothel and remifentanyl-apothel) within 2 to 12 hours after surgery (p <0.05). Low back pain was less in the dexmedetomidine-apotel group than in the remifentanil-apotel group.

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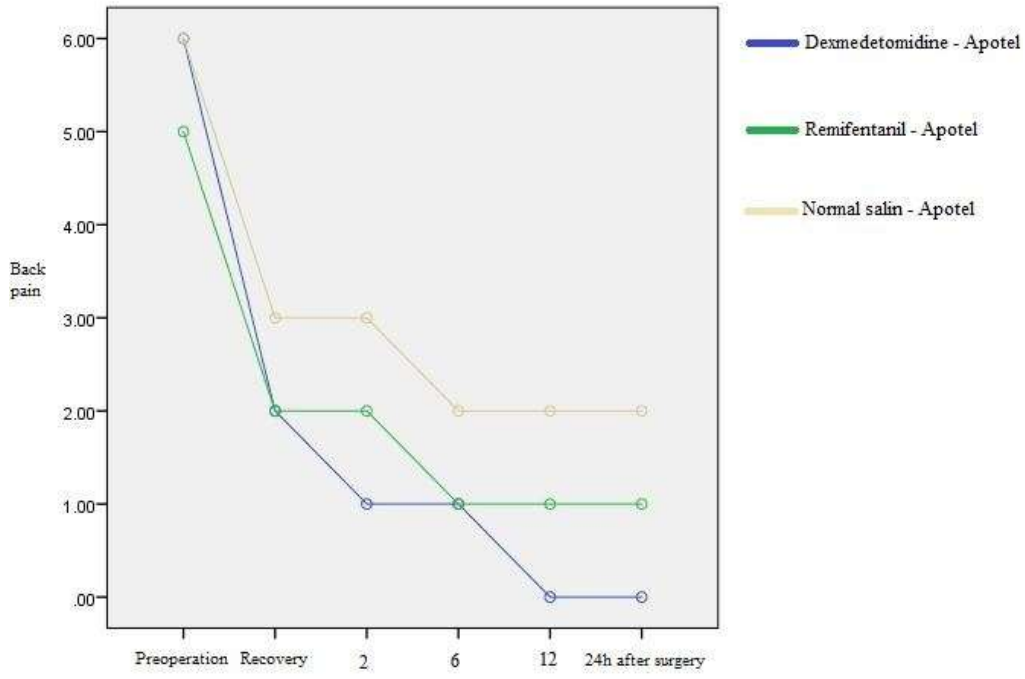

Figure 2. Comparison of back pain in three groups

Table 3. The mean of Ramsay score and its standard deviation in the three groups

Group / Ramsay score	Dexmedetomidine - Apotel Mean ±SD	Remifentanil - Apotel Mean ±SD	Normal salin-Apotel SD±Mean	pvalue
Recovery	3.031±0.822	2.781±0.750	2.843±0.846	0.439
2h after surgery	2.312±0.470	2.218±0.420	1.562±0.504	0.0001
6h after surgery	1.968±0.400	1.875±0.336	1.562±0.504	0.001
12h after surgery	1.593±0.498	1.656±0.482	1.312±0.470	0.013
24h after surgery	1.562±0.504	1.656±0.482	1.489±0.502	0.003

There was a statistically significant difference between the three groups in terms of sedation within 2 to 24 hours after surgery ($p < 0.05$). Sedation in the dexmedetomidine-apotel group was less than the other two groups. In the Apotel-normal saline group, sedation was found to be higher than the other two groups within 2 to 6 hours after surgery. No statistically significant difference was found between the two groups of dexmedetomidine-apothel and remifentanil- apotel at all times ($p < 0.05$).

IV. DISCUSSION

The purpose of this study was to compare the effects of dexmedetomidine and remifentanil on pain relief in herniated disc. In this double-blind, placebo-controlled clinical trial, 96 patients who were candidates for surgery in

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Vali-e-Asr Hospital in Arak were randomly divided into three groups including dexmedetomidine-apotel, remifentanil-apotel and placebo (normal saline-apotel).

There was no statistically significant difference between the three groups in terms of age, gender and BMI ($p < 0.05$). Leg pain was found to be less in the dexmedetomidine-apotel group 2 to 12 hours after surgery when compared with the other two groups ($p < 0.05$). In the apotel-normal saline group, the leg pain was higher than the other two groups. The back pain was lower in the dexmedetomidine-apotel group 2 to 24 hours after surgery ($p < 0.05$).

In the apotel -normal saline group, back pain was revealed to be greater than the other two groups. Low back pain was found to be less in dexmedetomidine-apotel group within 2 to 24 hours after surgery when compared with remifentanil-apotel group, but no significant difference was observed between the two groups within 24 hours after surgery ($p < 0.05$). There was a statistically significant difference between the three groups in terms of sedation within 2 to 24 hours after surgery ($p < 0.05$). In the apotel-normal saline group, sedation was also found to be greater than the other two groups within 2 to 6 hours after surgery, however, no significant difference was found between dexmedetomidine-apothel and remifentanil-apothel groups ($p > 0.05$).

Overall, it can be concluded that dexmedetomidine-apotel was capable of reducing post-operative back and leg pain, but there is no difference between dexmedetomidine-apotel and remifentanil-apotel sedation.

Dexmedetomidine, an imidazole derivative, is defined to be a pure S-enantiomer of the racemic α_2-agonist medetomidine. Dexmedetomidine is soluble in water. The sedative effect of dexmedetomidine has a different quality than other intravenous anesthetic drugs, which is more similar to physiological sleep mode through activation of endogenous sleep pathways. Postoperative patients may experience not only dexmedetomidine-induced sedationm but also experience analgesic effects without decreased respiratory rate. Dexmedetomidine was capable of reducing intraoperative opioid use and improving pain scores, but no analgesic benefit has been shown in all settings (15). Stimulation of α_2 adrenergic receptors may improve postoperative pain, which dexmedetomidine belongs to this drug class (16).

Anderson et al. reported that dexmedetomidine had more analgesia at postoperative time and longer duration of sensory and motor block with minimal complications (17). Kamali et al. conducted a study in 2018 to compare the efficacy of apotel-remifentanil in postoperative pain control among women undergoing non-emergency cesarean section.

They suggested that remifentanil could have a better effect on pain management immediately after surgery (18). Their results were consistent with our study, where remifentanil-apotel had better pain management than normal saline-apotel in the current study, and dexmedetomidine-apotel had better efficacy than remifentanil in pain management. A study aimed to compare sedation of exmedetomidine-fentanyl and midazolam-fentanylin in patients undergoing awake lumbar disc surgery, where exmedetomidine-fentanyl or midazolam-fentanylin combination was found to show good sedation due to decreased consumption of opioid analgesics in both groups (19). The results of

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our study were not in line with those of Peng et al. In our study, dexmedetomidine-apotel had a better effect, which may be due to differences in the various drugs used along with dexmedetomidine.

In 2007, Balki et al performed a study to evaluate the efficacy of remifentanil for labour analgesia. Twenty patients entered the study. Both groups received remifentanil (0.025 $\mu g \cdot kg^{-1} \cdot min$) and PCA bolus of 0.25 $\mu g \cdot kg^{-1}$. In the second group, the dose of remifentanil increased from 0.025 to 0.05, 0.075 and 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$. In the first group, the side effects were less and the pain control was better (20). Their results were in line with our stud, where remifentanil-apotel exhibited better pain management than normal saline-apotel and dexmedetomidine-apotel demonstrated better pain management than remifentanil. Alhashemi and Kaki conducted a study aimed at evaluating analgesic effects of dexmedetomidine/morphine on patient-controlled analgesia (PCA), where dexmedetomidine in combination with morphine PCA revealed better analgesic effects (21). Their results were consistent with our study, where our findings demonstrated that remifentanil-apotel had better pain management as compared to normal saline-apotel, and dexmedetomidine-apotel had better pain management than remifentanil.

V. CONCLUSION

Overall, dexmedetomidine-apotel was capable of reducing post-operative back and leg pain, but there is no difference between dexmedetomidine-apotel and remifentanil-apotel groups in sedation.

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