Original Article

Comparison of the effect of apotel and pregabalin on postoperative pain among patients undergoing lower limb orthopedic surgeries

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Abstract

Introduction: Proper control of postoperative pain is one of the major challenges after surgery. Such pains result in physical complications, increased metabolism, exacerbations of underlying diseases, and increased blood pressure. The aim of the present study was to compare the effect of apotel and pregabalin on postoperative pain among patients undergoing lower limb surgery. **Materials and Methods:** This study is a double-blind randomized clinical trial. About 75 patients undergoing lower limb orthopedic surgeries in Valiasr Hospital in Arak, Iran, were enrolled in the study. Patients were divided into three groups as follow: The first group received a 150-mg pregabalin capsule 2 h before the surgery. The placebo group received capsule that was replaced by starch. Furthermore, other group received 1 g of apotel in 200 mL of normal saline, 20 min before surgery. Pain at 2, 4, 12, and 24 h after surgery was recorded based on visual analogue scale. The amount of opioid use was recorded in the first 24 h in milligrams. Patient sedation was recorded by Ramsey Sedation Scale at 2, 6, 12, and 24 h after surgery. Finally, the data were analyzed using SPSS-20. **Results:** Pain in the apotel group was found to be lower when comparing with other group in 2, 4, 12, and 24 h after surgery ($P = 0.0001$). Ramsey score was found to be more in the pregabalin group at 2.6, 12, and 24 h after surgery ($P < 0.05$). In addition, the lowest opioid use was in the apotel group ($P = 0.0001$). **Conclusion:** Our findings revealed that apotel had a better effect on pain management, whereas pregabalin exhibited better effect on the sedation of patients.

Keywords: Apotel, orthopedics, pain, pregabalin

Introduction

Acute postoperative pain is a known problem that most patients suffer from, but chronic postoperative pain is a less complicated problem. About 10%–65% of the patients may have chronic pain, whereas 2%–10% of them will experience severe pain.[1] The proper control of acute postoperative pain remains one of the major challenges after surgery. Such pain causes physical complications, increased body metabolism, exacerbations of underlying diseases, and increased blood pressure, resulting in an increase in hospital stay, increased patient costs, dissatisfaction, and lack of patient collaboration as well as chronic pain.[2,3] Chronic postoperative pain has neuropathic causes. Neuropathic pain is also seen in the early stages of postoperative pain.[4] Although opioids are widely used to control postoperative pain, they are associated with many complications, including nausea, vomiting, respiratory depression, and hypotension. Drugs such as nonsteroidal anti-inflammatory drugs, acetaminophen, and nonpharmacological techniques are also used to control acute pain, with less complications, but are not as effective as opioids.[5]

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For this reason, traditional drugs used to treat neuropathic pain are increasingly used as an adjuvant to control the pain of surgery. These drugs include antidepressants (amitriptyline), anticonvulsants (gabapentinoids), aspartate receptor antagonists (ketamine and magnesium), membrane stabilizing agents (Lidocaine), and alpha 2 agonists (dexmedetomidine and clonidine).[6]

The effectiveness of postoperative pain control regimens depends on various factors such as psychiatric status, personality type of the patient, receipt and nonreceipt of alcohol and opioids prior to surgery, age, and type of surgery. It has been shown that the use of combination analgesics is capable of reducing postoperative pain and postoperative complications.[3] Various studies have demonstrated that drugs such as pregabalin are not only able to reduce the severity of acute postoperative pain and opiate doses but also may contribute to the prevention of chronic postoperative pain. A systematic and meta-analysis by Clarke *et al.* interpreted eight studies on gabapentin and three studies on pregabalin that indicated that the incidence of chronic pain and the use of analgesic drugs decreased in the long term in four studies with perioperative administration of gabapentin and in all three trials of pregabalin. Of the six trails with long-term assessment of patient's function, four studies have shown that perioperative administration of gabapentin and pregabalin was capable of improving postsurgical patient function.[7] Pregabalin is a gamma-aminobutyric acid analog and anticonvulsants drug used in neuropathic pain and adjuvant therapy in adult partial seizures.[8] The effect of pregabalin on acute postsurgical pain reduces stimulation of posterior horns of neurons caused by tissue damage.[9] This medication has a few side effects and causes dizziness and drowsiness, and has no effect on blood pressure and heart rate.[10] Another commonly used analgesic for pain relief is acetaminophen, which has analgesics, anti-fever, and mild anti-inflammatory properties.[11] Studies have examined the effect of pregabalin and apothecary drugs on postoperative pain alone. On the other hand, in view of the faster and stronger effects of pregabalin, we decided to carry out a study in which two drugs of pregabalin and apotel were used to improve pain after lower limb orthopedic surgery.

Materials and Methods

This randomized, double-blind clinical trial was conducted on 75 patients undergoing orthopedic surgery in the lower limb, referred to Valiasr Hospital of Arak, Iran. Patients were divided into three groups according to inclusion and exclusion criteria.

Inclusion criteria: candidate for lower limb orthopedic surgery, aged 17–65 years, both sexes. Exclusion criteria: coagulation disorders, severe hemodynamic instability, liver and kidney disease, cardiovascular disease, allergy to pregabalin and apotel, unwillingness to participate in the study.

The first group received a 150-mg pregabalin capsule (from the company Sobhan, Iran) 2 h before the surgery. The other group as control received a placebo capsule that was replaced by starch. In the third group, 1 g of apotel was given in 200 mL of normal saline, 20 min before surgery.

In each of the three groups, the pain was assessed at 2, 4, 12, and 24 h after surgery, and the patient's pain score was recorded based on Visual Analogue Scale using a ruler. The amount of opioid use was recorded in the first 24 h in milligrams. Patient sedation was recorded by Ramsey scale at 2, 6, 12, and 24 h after surgery. It should be noted that double-blind procedure was performed by an orthopedic resident who was not aware of the groupings. Finally, the results were analyzed using SPSS version 20.

Results

This study was a double-blind, one-stage clinical trial on 75 patients undergoing orthopedic surgery in the lower limb, referred to Valiasr Hospital of Arak in Iran. Samples were randomly divided into three groups. The minimum age was 15 years and the maximum age was 69 years. The mean age of patients was 39.17 ± 15 years. About 14.7% (11 cases) of patients were women, and 85.3% (64) of the 75 patients entered were men.

The most common type of fracture was tibia fracture (33.3%). The results showed that there was no significant difference between the three groups in terms of age ($P = 0.118$). In addition, no significant difference was found between three groups in terms of gender ($P = 0.474$). Additionally, no significant difference was observed between the three groups regarding the type of fracture ($P < 0.05$).

As shown in Figure 1, pain in the pregabalin and apotel groups was less than placebo, but the apotel group showed less pain than the other intervention group. There was a significant difference in pain between the three groups at 2, 4, 12, and 24 hours after surgery ($P = 0.0001$).

According to Table 1, there was a significant difference between the three groups ($P < 0.05$) at all times (2, 6, 12, and 24 h after surgery). At all times, the highest Ramsey score was related to pregabalin group.

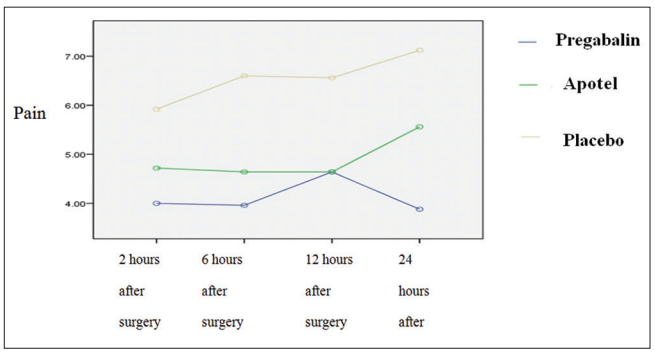

Figure 1: Comparison of pain at different times in three groups of pregabalin, apotel, and placebo

As indicated in Table 2, the amount of opioid consumed in the first 24 h had a significant difference between the three groups ($P = 0.0001$); the least amount was attributed to the apotel group.

Discussion

The minimum age was 15 years and the maximum age was determined as 69 years in this study. The mean age of patients was recorded to be 39.17 ± 15 years. About 14.7% (11 cases) of patients were women, and 85.3% (64) of the 75 patients entered were men.

The most common type of fracture was found to be tibia fracture (33.3%). The finding revealed no significant difference between the three groups in terms of age ($P = 0.118$). Furthermore, no significant difference was demonstrated between three groups in terms of gender ($P = 0.474$). Moreover, no significant difference was found between the three groups regarding the type of fracture ($P < 0.05$). A significant difference was revealed in pain between the three groups at 2, 4, 12, and 24 h after surgery ($P = 0.0001$), but the apotel group exhibited less pain as compared with the other intervention group.

Based on the findings presented herein, significant differences were observed between the three groups at all times (2.6, 12, and 24 h after surgery; $P < 0.05$). At all times, the highest scores were for the pregabalin group. The amount of opioid consumed in the first 24 h exhibited a significant difference in the three groups ($P = 0.0001$). The lowest amount was also for the apotel group.

Shakeri *et al.*, in 2016, conducted a study to compare morphine-apotel and Ketorolac for controlled anesthesia in patient's candidate for plating surgery. Based on their results, the mean score of pain in both groups was significantly decreased by the time ($P < 0.05$). There was no significant difference between the two groups in the hours 0, 6, and 12. Based on the results of this study, it can be concluded that the use of nonopioid analgesics has not been superior to opioid analgesics.[12] Their results were not consistent with our study. In our study, the pain was lower in the apotel group and the Ramsey score in the pregabalin group was found to be higher. The cause of the difference can be different types of drugs.

Naderi Nabi *et al.* in 2014 conducted a study to evaluate the effect of single dose oral pregabalin on acute pain control after orthopedic surgeries. Patients' pain score was lower in the pregabalin group at recovery time and at 6 and 12 h after operation ($P < 0.05$). In addition, the level of intravenous pethidine in the pregabalin group was found to be lower as compared with the control group ($P = 0.001$).

They stated that administration of a single dose of 150 mg oral pregabalin an hour before orthopedic surgery under spinal anesthesia significantly reduced postoperative pain and reduced the need for opioid drugs.[13] Their results were not consistent with our study. In our study, apotel was better in controlling pain than pregabalin, whereas Ramsey score in the pregabalin group was higher and the amount of pethidine consumed in the apotel group was lower.

Talebi *et al.*, in 2014, conducted a study aimed at the effect of intravenous apotel and opioid use during and after orthopedic surgery in patients with radius shaft fracture.

The mean of opioid use in the apotel group was reported to be low. There was no significant difference in pain score in any of the recovery times, 4, 12, and 24 h after the operation. The interval to first analgesic request for the apotel group was 254.71 ± 28.2 min, and for the placebo group was 198.28 ± 34.22 min. Significantly, the interval to first analgesic request in the apotel group was reported to be longer. Aforementioned study indicated that apotel was effective as a premedication in reducing opioid consumption during and after orthopedic surgery;[14] therefore, their results were consistent with our study.

Rahimzadeh *et al.* in 2013 conducted a study to compare the analgesic effect of paracetamol and ketamine on pain control after hysterectomy surgery. They reported that administration of intravenous acetaminophen was more effective than ketamine in controlling pain after abdominal hysterectomy;[15] thus, it could be said that their results were in line with our study.

Akhavan Akbari *et al.* in 2012 conducted a study with the aim of relieving postoperative pain after lower limb orthopedic surgery by oral pregabalin in patients suffering from fractures of the lower limb. It has been shown that the mean of visual analog pain scores in the pregabalin recipient group was significantly lower than

Table 1: Comparison of mean and standard deviation of Ramsey score in three groups of pregabalin, apotel, and placebo

Group Ramsey score	Pregabalin, SD±Mean criterion	Apotel, SD±Mean criterion	Placebo, SD±Mean criterion	*P*
2 h after surgery	0/57±2/08	0/27±1/08	0/27±2/04	0/0001
6 h after surgery	0/52±1/88	0/50±1/40	00/00±1/00	0/0001
12 h after surgery	0/50±1/52	0/47±1/32	0/37±1/16	0/025
24 h after surgery	0/45±2/04	0/48±1/64	0/50±1/40	0/0001

Table 2: Mean and standard deviation of drug consumption in three groups of pregabalin, apotel, and placebo

Group Variable	Pregabalin, SD±Mean criterion	apotel , SD±Mean criterion	placebo , SD±Mean criterion	*P*
Pethidine (mg)	2/70±6/50	1/81± 4/70	2/25± 10/80	0/0001

that of the placebo group. Aforementioned study indicated that nausea and vomiting scores at all hours decreased. Furthermore, sedation levels at 2 and 6 h after operation, and pethidine use in all hours showed a remarkable decrease ($P < 0.05$).

Prescribing pregabalin before surgery can provide better control of postoperative pain and may reduce problems of opioid use by reducing pethidine consumption.[16] Their results were not consistent with our study. In our study, the effect of apotel in analgesia was better and could be due to sample size of our study.

Conclusion

Our results indicate that apotel has a greater effect on pain management, when pain was less at all times in apotel group as compared with the other two groups, whereas pregabalin has had a better effect on the sedation of the patients, where the degree of sedation of the patients was found to be significantly higher in the pregabalin group.

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Conflicts of interest

There are no conflicts of interest.

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