



# Comparison of the anxiety and satisfaction level of the patients under fracture plating treatment type c1 and c2 of distal femur in the two groups of combination drugs (gabapentin, celecoxib, and acetaminophen) and placebo

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## ABSTRACT

**Introduction:** Prevention through pain killer drugs can be very useful compared to the treatment of the pain.

**Aims:** Therefore, this study sought to investigate the effect of the three compound prodrugs (celecoxib, acetaminophen, and gabapentin) on the post-operation anxiety and satisfaction level of the patients under distal femur fracture plating treatment.

**Methods:** This study is a clinical trial conducted on 100 patients in which two groups are compared respecting the levels of anxiety, satisfaction, time, morphine doses, and side effects. One hour before surgery, the case patients were given three drugs celecoxib, acetaminophen, and gabapentin with doses of 200, 500, and 400 mg, respectively. The control group patients were given the same placebos. 15 minutes before the operation, the patients were gone under spinal anesthesia through injecting epinephrine 0.2 mg and 5%-lidocaine 100 mg. After entering the ward at 1, 2, 4, 8, 12, and 00:00 O'clock following the operation, the tranquilizer intake and the first time for requesting analgesia was recorded after the elimination of spinal anesthesia.

**Result:** There was a significant difference between the two groups respecting the comparison of the time of consuming the first morphine and its dose, anxiety level, and satisfaction. Other comparisons were not significant.

**Conclusion:** The compound of celecoxib, acetaminophen, and gabapentin is an appropriate one so as to reduce orthopedic surgery post-operation pain. The results of this study can confirm the effect of non-drug palliative drugs on the reduction of the anxiety level and satisfaction increase.

**Keywords:** multiple drugs, anxiety, satisfaction, plating treatment, distal femur

## INTRODUCTION

The thigh is a part of the lower limb that has been located between the pelvis and the knee. This part of lower limb includes a long bone in its center that is named thigh bone of Femur. This bone is very powerful and strong and contributes at upside in the formation of thigh joint and at downside in the formation of the knee joint. The thigh bone or Femur is the biggest and longest bone of the body. The long of thigh bone of a mature human is about 0.5 meter and its diameter in the center is about one inch. This bone can bear the weight 30 times the weight of a human. The distal femur fractures consist of severe and complex damages which can be resulted in the long-term disabilities and are of special importance because of being near to the knee joint (1). From 100 thousand members, the distal femur fractures are appeared in about 37 members in a year (2). These fractures include Metaphysis Distal Femur (Supracondylar) and Joint Level Distal Femur (Intracondylar) that is created in the young individuals by the mechanism of trauma with higher energy and in the old women by the mechanism of trauma with lower energy. This fracture can cause a long-term inability in the patients especially in the cases of severe damages of soft tissue, hard damage of articular cartilage and considerable crushing of bones (3). The treatment of Distal Femur Fracture is one of the most important treatment challenges because of the high level of its complications and almost all specialists emphasize the surgery to achieve favorable results (4). In these kinds of fractures, because of being near to knee joint (for the reason of the exorbitant use of this joint and also bearing the weight on that), the pain derived the surgery should be treated very soon. As we can

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get an acceptable result, the time of hospitalization would be reduced and the patient would begin to move earlier. So, the use of different anti-pain methods in these kinds of surgeries are of special importance. The triple therapy which is applied nowadays by some orthopedists to reduce the pain after TKA surgeries have had valuable results. The Cyclooxygenase – II such as Celecoxib don't have the side effects of Non-Steroidal Anti-inflammatory Drugs (NSAIDs). Of course, it should be noticed that the gastrointestinal, hemostasis effects and bad effects on the bone healing is reduced by the consumption of COX-2 Inhibitor in comparison to the usual NSAIDs but there is no difference in renal effects (5). The incident effects of this drug include tiredness and stress, depression, anger, paresthesia, nausea, anorexia, vomit, constipation, and xerostomia. The potential of Gabapentin in controlling the pain and its effect on the procedure of feeling the pain in the central nerve system caused that the clinical use of this drug would increase (6). The incident effects include drowsiness and dizziness and also swelling limbs. These effects often have a severity from light to average and may be disappeared by the passage of time. The other effects include nausea and vomit, diarrhea, cough, and tiredness. Acetaminophen or Paracetamol is an anti-pain and anti-fever drug and it seems that its effect is for the reason of reducing the production of Prostaglandins by the body. The prostaglandins are the materials which cause inflammation and fever. In spite of the other anti-inflammatory drugs that cause reducing the production of prostaglandins in all parts of the body, Acetaminophen reduces the production of this material just in the central nerve system (brain and spine). In a research which was done by Karvonen et al. in 2008, the effect of edible Acetaminophen and Ketoprofen in the management of pain, reduction of consumption of iPod and side effects of narcotics after the big orthopedic surgery was studied. In this study, after the surgery, the level of pain (measured by Score VAS), respiration number, oxygen saturation, level of the environmental artery, heartbeat, blood pressure and side effects were registered every 4 hours during 20 hours. In a 20 hours period, the case group consumed 0.22 Fentanyl less than the placebo group in average ( $p>0.05$ ). The frequency of side effects didn't reduce by the use of non-narcotic downers (7). Niruthisard et al. in 2013 studied the effect of using separately and also the combination of two placebos, Pregabalin (150 mg) and Celecoxib (400 mg) in the improvement of anti-pain effect of intra-spine Morphine in the patients under Total Knee Arthroplasty (TKA). In this study, 100 patients were randomly categorized into four groups (pregabalin, celecoxib, pregabalin- celecoxib and placebo). The pain score when moving at 2 hours, in comparison to the placebo group, was meaningfully lower in pregabalin- celecoxib group ( $p<0.05$ ). Furthermore, a considerable reduction was observed in anxiety scores of this group at 2 hours after the surgery and also in celecoxib group at 6 and 24 hours after the surgery ( $p<0.05$ ). The side effects and also the effects after surgery, except spo2 in pregabalin group, were similar in all groups at the end of surgery. The patient's satisfaction was similar in all groups at 24 and 48 hours after the surgery (8). In the other study which was done in 2007 by Reuben et al., the efficiency of celecoxib in the reduction of pain of patients who were under the arthroscopic therapy of Anterior Cruciate Ligament, was studied. They categorized 200 patients into two groups. One group consumed Acetaminophen (1000mg) and celecoxib (400 mg) and the other group used Acetaminophen and placebo. This regime began from one or two hours before the surgery and kept until 14 hours after the surgery. They found that the patients of celecoxib group felt less pain after the surgery ( $p>0.01$ ), needed less amount of iPod to reduce their pain ( $p>0.001$ ), released earlier from the hospital and felt less nausea and vomit ( $p>0.05$ ). Furthermore, the patients of celecoxib- Acetaminophen experienced less pain in the move and rest at home and used less amount of Oxycodone (anti-pain drug given them) (9). Therefore, with regard to the different results and studies about the effect of multidrug treatment model on the prevention of pain in different methods of orthopedic surgery, the present research aims to study the effect of consumption of three prodrugs (CAG) on the amount of stress and satisfaction after the surgery in the patients under the of plate of distal femur fracture according to Multi Analgesia Model.

## METHOD AND MATERIALS

The present research is a clinical and quasi-experimental trial. From the beginning of 2013, 100 patients who were the voluntary of surgery of distal femur plate with the fracture of C1 and C2 types under the spinal anesthesia that the criteria of entrance to the study, like the age between 25 and 45, is the patient's satisfaction with the entrance to ASA (American Society of Anesthesiologists class) I and II. The patients were randomly categorized into two groups of Mord (the patients to whom three edible drugs of celecoxib 200mg, Acetaminophen 500mg and gabapentin 400 mg were given) and control group (the patients to whom the similar placebo have been given). The patient, after receiving 500cc Normal saline in the sitting situation, was put under the spinal anesthesia at one turn by transfusing 0.2mg of Adrenaline and 100mg of Lidocaine %5 by Whitaker Spinal Syringe No. 24 in the L4- L5 intervertebral space. For the purpose of all patients' having less pain after the surgery, all of them were gone under the surgery without a tourniquet. The Titanium

**Table 1: Comparison of the First Morphine Consumption and the Amount of Dose**

		Groups					P
		Mean	SD	Median	Minimum	Maximum	
Time of the first morphine dose (min)	Prodrug group	235.70	11.56	235	210	265	0.0001
	Placebo group	170.90	13.50	170	135	200	
Morphine dose (mg)	Prodrug group	7.56	2.52	8	4	15	0.0001
	Placebo group	46.01	7.98	45.50	29	62	

Locking Plate was done in all patients by lateral cutting of distal femur and knee joint. After being sure of proper locking and the control by fluoroscope and proper draining and washing, all the layers of the wound were stitched and then splinted. After the entrance of patients into the department and reduction of spinal anesthesia to the level lower than T10 after the surgery, amount of pain, consumed tranquillizer and the first time of requesting the analgesic drug after the removal of spinal anesthesia were registered at 1, 2, 4, 8, 12 and 24 hours after the surgery. Every 6 hours, 5mg Morphine IM was transfused into both groups. The quality of patients' satisfaction with the anesthesia during 24 hours after the surgery was evaluated in excellent, good, average and improper criteria. Ultimately, the questionnaire of evaluation of the amount of patients' stress was given to them. This questionnaire includes 40 questions which consist of self- evaluation separate indexes for measuring the obvious and hidden stress. The obvious stress index (y-1 form of STAI) consists of 20 sentences which evaluate the individual's feelings "in this moment and the time of answering". Also, the hidden stress index (y- 2 form of STAI) includes 20 sentences that evaluate the general and usual feelings of the individuals. In testees' answering to the obvious stress index, a number of choices have been presented for each sentence that the testees should choose the choice which expresses his/ her feeling in a better way. These choices include very little, little, much, so much. In answer to the hidden stress index, the testees should choose choice which is the indicative of usual and natural feeling of them, in a four- choices indexes as following: almost never, often, most of the times, almost always. The criteria except the study included: existence of background diseases (such as diabetes) or organic regurgitation, drug and alcoholism addiction, vascular problems or apoplexy and heart- failure, sensitivity to iPods and gabapentin and celecoxib, renal failure, multiple trauma, fatness (BMI<35), pathologic fractures, liver diseases, emotional disorders, pregnancy, lactation, IBD, consumption of Aspirin or Warfarin and the individuals who consume permanently analgesic drugs for any reason. Data were analyzed by the use of SPSS- 21 software. The Independent T test was used in a normality form for the purpose of comparing the amount of consumption of Morphine and Paracetamol and the time of anesthesia in two groups and otherwise, the non-parametric Mann Whitney test was used for the purpose of determining the amount of effect of combinative drugs on the amount of pain after the surgery by controlling the effects of background variables and the new changed models (Giz) in a GEE method for studying the consumption of Morphine and Paracetamol. The level of significance of the tests in the present study was evaluated with  $p < 0.05$  and the tests were studied in a two- sided form.

## RESULTS

In this research, 50 members in the group of combinative drugs (celecoxib, Acetaminophen, and gabapentin) and 50 members as the placebo group were studied in the regard of the level of stress and satisfaction. The findings o present research revealed that the percentage of man to woman in the group of combinative drugs was %86 to %14 and in the placebo group was %88 to %12 that this difference has not been statistically meaningful with regard to Chi Square Test ( $p = 0/766$ ). The average of relative standard deviation in the group of combinative drugs has been  $9/27 \pm 9/3$  years and in the placebo group was  $1/28 \pm 9/3$  that the age of two studied groups was similar and has no meaningful difference ( $p = 0/915$ ). Also, there was no meaningful difference in the body mass index of two groups ( $p = 0/973$ ). With regard to the time of surgery, the group of combinative drugs from the minimum time of 95 to 125 minutes had  $107/5 \pm 7/6$  minutes average and standard deviation and in the placebo group, from minimum surgery time of 90 and 120 minutes, the average and standard deviation have been  $104/4 \pm 7/9$  minutes. Although the surgery time of two groups has been meaningful ( $p = 0/0046$ ), but this difference (3 min) is not clinically important in **Table 1**.

**Table 2** shows the comparison of first morphine use time and its dose use. With regard to Mann Whitney U Test, the table data shows a meaningful difference in the time of beginning of morphine use ( $p < 0/0001$ ) and also in its dose use ( $p < 0/0001$ ) that in both measured variable the first morphine use time in the group of combinative drugs ( $235/7 \pm 11/6$ )

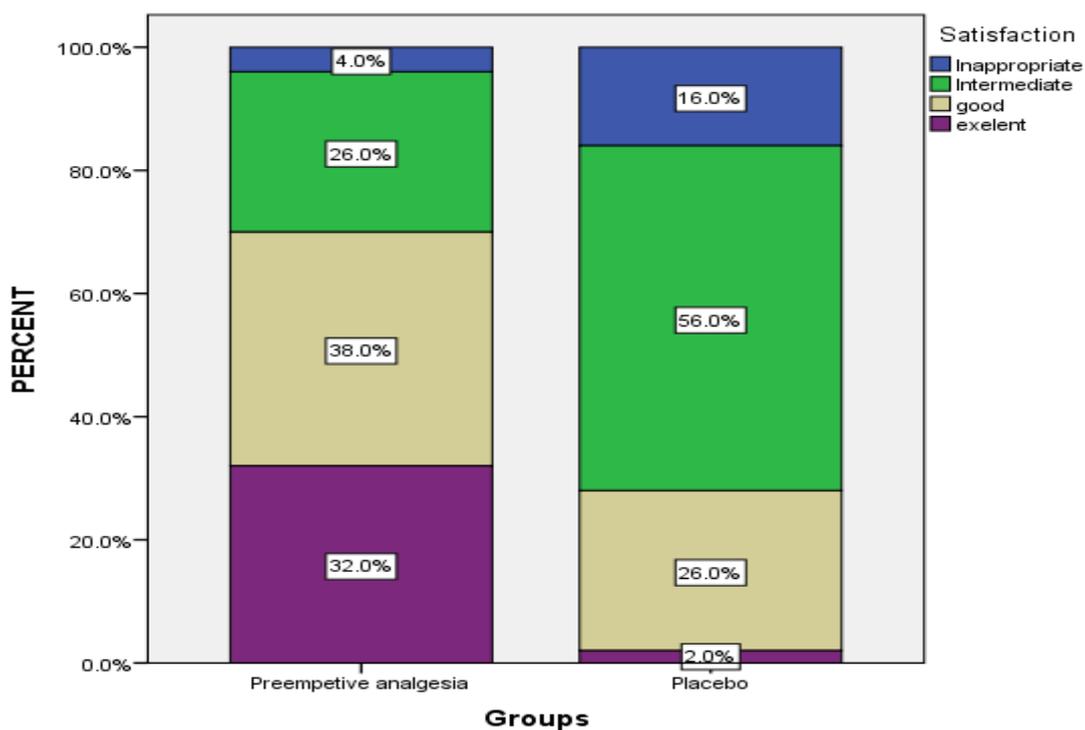
**Table 2:** Comparison of the Anxiety Level Based on Score Stae

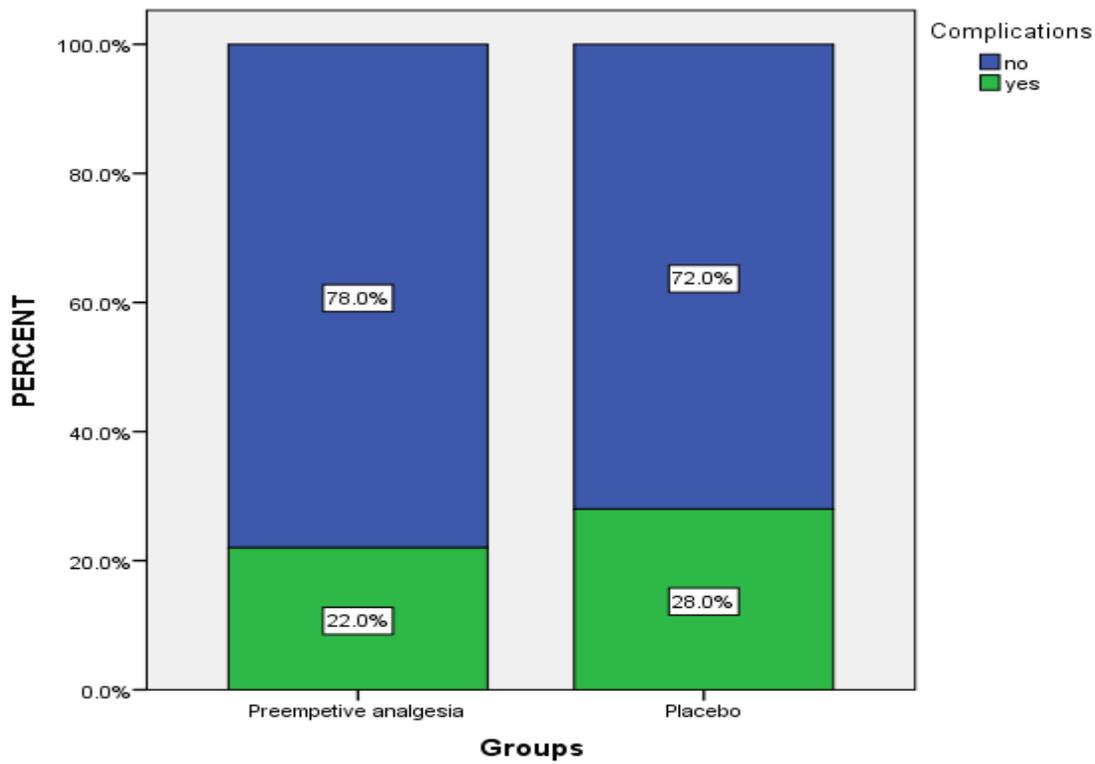
Variable	Groups				P	
	Prodrug group		Placebo group			
	No.	Percentage	No.	Percentage		
Anxiety level	20-31 mild anxiety	12	24	4	8	0.0001
	32-42 mild anxiety to moderate	26	52	14	28	
	43-53 moderate anxiety to severe	7	14	10	20	
	54-64 relatively severe	1	2	8	16	
	65-75 severe	2	4	7	14	
	76 very severe	2	4	7	14	
	total	50	100	50	100	
	Average amount	39		62		
Satisfaction level	dissatisfaction	2	4	8	16	0.0001
	moderate	13	26	28	56	
	good	19	38	13	26	
	excellent	16	32	1	2%	
	total	50	100	50	100	
	Average amount	63.37		37.63		
Complications	Without complication	39	78	36	72	0.488
	With complication	11	22	14	28	
	total	50	100	50	100	

is more than the time in the placebo group ( $170/9 \pm 13/5$ ) and also in the regard of dose of consumption, the group of combinative group ( $7/6 \pm 2/5$ ) is less than the placebo group ( $46 \pm 7/9$ ). The comparison of the first morphine consumption and the amount of dose is shown in **Figure 1**. In the comparative study of severity of stress with regard to anxiety score, **Table 3** shows a meaningful difference in the anxiety severity of both two groups (combinative and placebo) ( $p < 0/0001$ ) in a way that the percentage of relatively severe and severe and very high anxiety in the group of combinative drugs (39) has been less than the placebo group (62) (**Figure 2**). The data of **Table 3** shows a meaningful difference in the regard of the level of satisfaction ( $p < 0/0001$ ), in such a way that the percentage of level of good and excellent in the group of combinative drugs has been almost %60 but in the placebo group has been %28. The ranking mean of the level of satisfaction in the group of combinative drugs has been almost more than 22 ranks (63/37 versus 37/63) (**Figure 3**). Also, in the regard of the amount of effects, the table data reveals that the percentage of effects in the group of combinative drugs has been %22 and in the placebo group %28; but the amount of effects has had no meaningful difference statistically ( $p = 0/488$ ) (**Figure 4**). In the comparison of effect of the combinative drugs with the placebo group on the amount of pain by the moderation of effects of morphine use time and also dose of morphine and surgery time with regard to the statistic method of Variance Analysis ANCOVA of moderation of data revealed that the effect of combinative drugs in comparison to the effect of placebo on the amount of pain ( $p = 0/518$ ) by controlling the amount of morphine use and its use time has not been statistically meaningful; but the used morphine dose ( $p = 0/008$ ) and morphine use time ( $p = 0/013$ ) have been of effective factors in the amount of pain. Also, the moderation between two groups studied and the used morphine dose is meaningful ( $p = 0/044$ ). The other comparisons and the surgery time have not been meaningful ( $p > 0/05$ ).

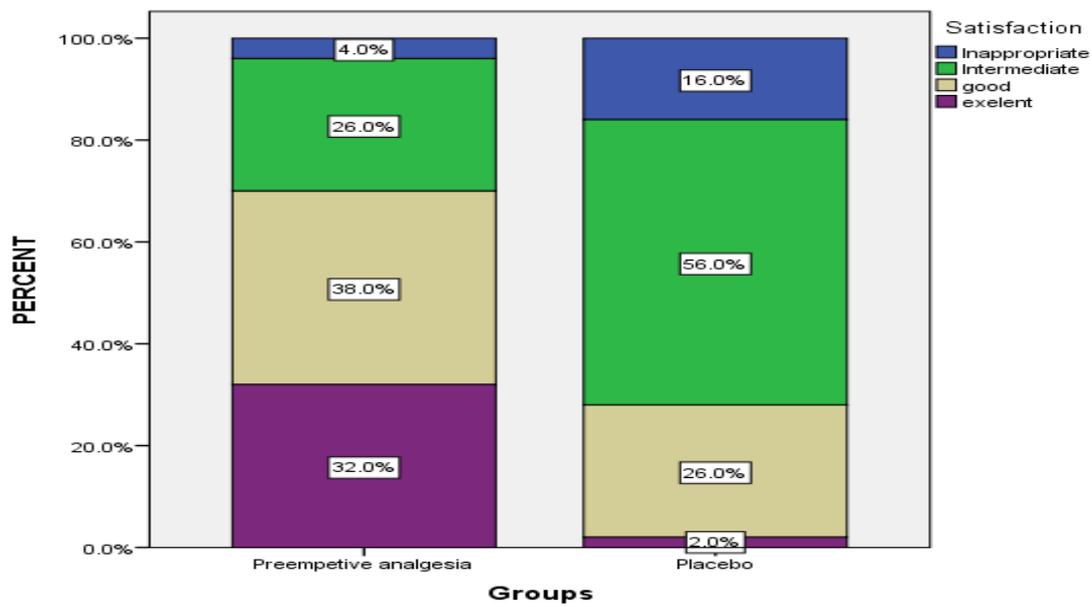
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Variable	Groups				P	
	Prodrug group		Placebo group			
	No.	Percentage	No.	Percentage		
Anxiety level	20-31 mild anxiety	12	24	4	8	0.0001
	32-42 mild anxiety to moderate	26	52	14	28	
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	54-64 relatively severe	1	2	8	16	
	65-75 severe	2	4	7	14	
	76 very severe	2	4	7	14	
	total	50	100	50	100	
Average amount	39		62			
Satisfaction level	dissatisfaction	2	4	8	16	0.0001
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	good	19	38	13	26	
	excellent	16	32	1	2%	
	total	50	100	50	100	
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Complications	Without complication	39	78	36	72	0.488
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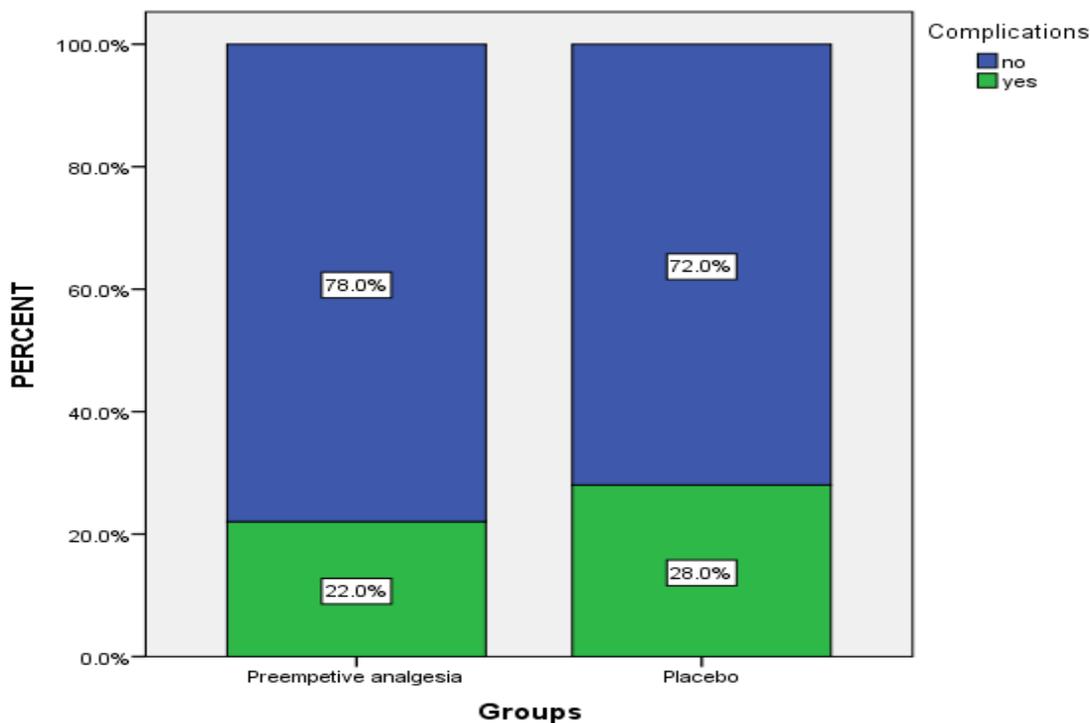
**Figure 1:** The Mean of the Post-operation Satisfaction Score based on VAS in the Two Groups



**Figure 2:** The Amount of Complications Caused by Surgery in the Two Groups



**Figure 3:** The Mean of the Post-operation Satisfaction Score based on VAS in the Two Groups



**Figure 4:** The Amount of Complications Caused by Surgery in the Two Groups

## DISCUSSION AND CONCLUSION

According to the results in the regard of surgery time, the group of combinative CAG drugs had minimum time of 95 min to 125 min with the mean and standard deviation of  $107/5 \pm 7/6$  and in the placebo group, the minimum time of surgery has been 90 min to 120 min with the mean and standard deviation of  $104/4 \pm 7/9$ , that the surgery time of two groups has been statistically meaningful. But, this difference (3 min) is not clinically important. Perhaps, the reason for this difference is that the use of analgesic drugs has reduced the need to anesthesia and analgesic drugs during the surgery and finally has reduced the time of surgery (10). Gabapentin is the structural analog of Gama Amino butyric acid (GABA). This drug at first for the treatment of seizure, then it was used effectively in alleviating the neuropathic pains. The mechanism of its action is by applying an inhibitive effect on the entrance of calcium by the activated channels with high voltage that includes subunit alpha- 2 delta- 1 and causes the reduction of release of Neurotransmitter and postsynaptic excitation (11) and it is recently used as an effective drug to reduce the pain after surgery (12). Celecoxib which is of the group of alternative inhibitive cyclooxygenase enzyme- 2, has been expressed as a substitute for the use of non-alternative Non- Steroidal Anti- inflammatory drugs; because, in comparison to the classic Non- Steroidal Anti- inflammatory drugs, it has anti- pain effects and has no side effect on the platelet, gastrointestinal mucus system and renal function (13). On one side, Acetaminophen is one of the relative new drugs which is used to reduce the pain of patients and acts as anti- pain and anti- fever and also has anti- inflammatory tinge. Mechanism of action is accompanied by the inhibition of santes prostaglandins. The Acetaminophen has been used in an edible and rectal form and recently in the transfusing form. Acetaminophen is relatively safe and has fewer side effects and also has limited contraindication; also, it has not obvious interactions with the other drugs. With regard to being safe of the aforesaid drugs, it seems that the combinative use of them can help reduce the pain, even during many hours after the surgery. According to the obtained results, the first morphine use time in the group of combinative drugs is more than the placebo group and also, the morphine use dose in the group of combinative drugs has been less than the placebo group. The results of Imani and his colleagues' study revealed that the mean of morphine use during the first 24 hours in the Gabapentin group was less than control group that there was statistically no meaningful difference between two groups (14). The results of Poornajafian and his colleagues' study which compares the painlessness after surgery in the patients under the surgery of shin fracture with the prescription of celecoxib as placebo at different times before the surgery, showed that the mean of time of requesting downer from the termination of spinal anesthesia in the group of celecoxib 400mg was  $196/5 \pm 121$  minutes that was meaningfully more than the group of celecoxib 200 mg ( $127/5 \pm 68$ ) and group of control ( $122/7 \pm 44$ ); but in the regard of dose of received downer, there observed no statistic meaningful relationship between

three groups. In the study done by Niruthisard et al. about morphine use first time and its dose, there observed no meaningful difference between the placebo group and the group received pregabalin- celecoxib that this result contradicts with the present study. The control and reduction of severe pains of the patients are so important and significant, the use of anti- pain narcotics as a prodrug is current in the general anesthesia and is generally used during the surgery as fixing the hemodynamic of the patients, too. But for the reason of side effects of these combinations such as nausea, vomit, respiratory weakness, urinary retention and ..., the similar non- narcotics are recently used for controlling the pain of patients. It seems that the combination of aforesaid drugs can reduce the need for the narcotics for the control and reduction of anxiety and ultimately, the side effects of the narcotics is reduced, too. Also, the results of present study showed that there was a meaningful difference in the anxiety severity of two combinative drugs and placebo groups, in such a way that the percentage of relatively severe, severe and very high anxiety in the group of combinative drugs has been meaningfully less than the placebo group (39 versus 62). The results of the study done by Niruthisard and his colleagues revealed that the anxiety score in the patients received celecoxib and pregabalin, was reduced two hours after the surgery. Talebi et al. in a research titled study of effect of educational- combinative interference on level of anxiety in patients voluntary in orthopedic surgery, revealed that there was a statistic meaningful difference in the amount of anxiety of two groups of interference and control at the first post- test (before surgery). Ghaneii and his colleagues in a research titled study of the relationship of anxiety before surgery with pain after cesarean showed that there observed a meaningful statistic relationship between the obvious and hidden anxiety before surgery with the pain after surgery (15). The anxiety is very usual in the patients voluntary for surgery and can cause problems at the time of surgery and after surgery. The results of the present research show that the use of a combination of downers before the surgery has resulted in the peace and reduction of anxiety in the patients. It seems that inasmuch as the pain is an effective factor in the creation of anxiety; so, the reduction of pain reduces the anxiety in the patients. In the regard of the level of satisfaction, there was a meaningful difference between two groups. In such a way that the percentage of good and excellent satisfaction in the group of combinative drugs was about %60 and in the placebo group was about %28. The ranking mean of the level of satisfaction in the group of combinative drugs has been more than 22 ranks (63/37 versus 37/63). The results of the study done by Tavakkoli et al., revealed that 70/55 percent of the patients were completely dissatisfied with the reduction of their pain and 29/45 percent have weak and average satisfaction, too (16) that the results of this study contradict with the present study. The results of Bamshaki and colleagues' study titled amount of severe pain after surgery and patients' satisfaction in Laparotomy, Cholecystectomy, and Herniorrhaphy, revealed that %921/3 of patients had relative to perfect satisfaction with the amount of controlling their own pain. And only %7/7 of patients expressed levels of dissatisfaction (17). It seems that if the pain of patient be controlled better and be reduced, it would result in the increase of satisfaction and tranquility of the patients. In the study of the effect of combinative drugs and placebo group, there was a meaningful difference between two groups in the comparison of anxiety severity and satisfaction. Although the moderation between two groups studied and the amount of morphine used was meaningful. The other comparisons and the surgery time were not meaningful. The present study shows that the combination of three drugs (Gabapentin- Celecoxib- Acetaminophen) is a proper combination for the reduction of anxiety and increase of satisfaction after orthopedic surgery. The results of present research can be used as a guide in the next studies for further verification of effect of non- narcotic downer drugs in the reduction of pain.

## REFERENCES

1. Intramedullary fixation of distal femoral fractures. *Rev Med Chir Soc Med Nat Lasi*. 2006;110(4):917-920.
2. Zlowodzki M, Bhandari M, Marek D, Cole PA, Kregor P. Operative Treatment of Acute Distal Femur ractures. *J Orthop Trauma*. 2006 May;20(5):366-71. <https://doi.org/10.1097/00005131-200605000-00013> PMID:16766943
3. Zlowodzki M, Bhandari M, Marek DJ, Cole PA, Kregor PJ. Systematic Review of 2 Comparative Studies and 45 Case Series (1989 to 2005). *J Orthop Trauma*. 2006;20:366-371. <https://doi.org/10.1097/00005131-200605000-00013> PMID:16766943
4. Link BC, Babst R. Current concepts in fractures of the distal femur. *Acta Chir Orthop Traumatol Cech*.2012;79(1):11-20. PMID:22405544
5. Fanlli A, Romualdi P, Viganò R, Lora Aprile P, Gensini G, Fanlli G. Non-selective non-steroidal anti-inflammatory drugs (NSAIDs) and cardiovascular risk. *Acta Bio MED*. 2013;84(1):5-11
6. Maneuf YP, Gonzalez ML, Sutton KS, Chung FZ, Pinnock RD, Lee K. Cellular and molecular action of the putative GABA-mimetic, gabapentin. *Cell Mol Life Sci*. 2003;60(4):742-750. <https://doi.org/10.1007/s00018-003-2108-x> PMID:12785720

7. Karvonen S, Salomaki T, Olkkola KT. Efficacy of oral paracetamol and ketoprofen for pain management after major orthopedic surgery. *Method Find Exp Clin Pharmacol.* 2008;30(9):703-706. <https://doi.org/10.1358/mf.2008.30.9.1316919> PMID:19229379
8. Niruthisard S, Earsakul A, Bunburaphong P, Chinda P, Anutinmanee R, Prapreuttham S. Preoperative pregabalin and/or celecoxib for pain management after total knee arthroplasty under intrathecal morphine: a randomized controlled trial. *Asian Biomedicine.*2013;7(4):579-585.
9. Reuben SS, Ekman EF, Charron D. Evaluating the Analgesic Efficacy of Administering Celecoxib as a Component of Multimodal Analgesia for Outpatient Anterior Cruciate Ligament Reconstruction Surgery. *International Anesthesia Research Society.* 2007;105(1):222-227. <https://doi.org/10.1213/01.ane.0000265440.98491.e2>
10. Talebi H , Kamali AR, Moshiri ES, Yazdi BJ, Hosseini MO. Efficacy of intravenous acetaminophen injection on pain intensity and opioid consumption in patients undergoing radius shaft fracture surgery. *Journal of Anesthesiology and Pain.* 2014;5(1):64-72.
11. Saghilini, H, Ghorbanian, E. Comparison of effect of Gabapentin, Pregabalin and Acetaminophen in headache after spinal anesthesia. *J Clin Neurosci.* 2011;18(10):1365-8.
12. Clarke H, Pereira S, Kennedy D. Gabapentin decreases morphin consumption and improves functional recovery following total knee arthroplasty. *Pain Res Manage.* 2009;14:217-222. <https://doi.org/10.1155/2009/930609>
13. Pournajafian AL, Sehat M, Ghodrati MR, Rokhtabnak F, Kholdbarin AR. Comparison of post-operative pain in patients with leg fracture surgery with celecoxib administration in different preoperative times. *Anesthesiology and pain J.* 2011;1(4):61-71.
14. Imani F, Hasani V, Bazargani B, Entezari SR, Mirdehghan MH. Evaluation of Oral Gabapentin Premedication on Postoperative Pain after Thoracotomy. *Razi Journal of Medical Sciences.* 2009;16(62):73-79.
15. Ghaneii, R. 2012. Study of relationship of anxiety before surgery with pain after cesarean surgery. *The Iranian Journal of Obstetrics.* 2012;15(39):16-22.
16. Tavakoli A, Norouzi M, Hajizadeh E. Patients' Satisfaction from Pain Soothing after the Surgery in Kerman Hospitals. *J Clin Diagn Res.* 2005;10(7):IC01–IC04.
17. Bameshki AL, Jahanbakhsh SS, Jangjoo A, Zahndi H, Fathi M. Evaluation of acute postoperative pain and patient satisfaction in laparotomy, cholecystectomy and herniorrhaphy. *JAP.* 2013;3(4):196-201.



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