Traditional Versus Additive Analgesia in Post-Operative Pain Control in Surgery around the Knee- A Randomized Controlled Trial.

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ABSTRACT

Objective: To compare the efficacy of Diclofenac sodium and Pregablin in reducing post operative pain in patients with surgeries around the knee.
Methods: This randomized controlled trial was conducted in Department of Orthopedics Surgery and Traumatology Mayo Hospital Lahore from 23rd December 2017 to 23rd December 2020. All adults patients of either gender and age with surgeries around the knee fulfilling the inclusion criteria were randomly divided into two equal groups as group A (Diclofenac sodium 50 mg BD) and group B (Pregablin 75 mg BD). The drugs were administered orally for two days after surgery. Post operative pain intensity was determined with visual analogue score (VAS). Comparison of VAS in both group was done and *P* value calculated with paired-t test. *P* value < 0.05 was considered significant.
Results: The total number of patients were 80 and equally divided into group A and group B. In group A 26 (65%) were male and 14 (35%) were females. In group B 25 (62.5%) were male and 15 (37.5%) females. The mean age of group A patients was 30.5±7.33 and group B 31.15±9.97 years. The mean VAS in group A was 4.08±0.95 and in group B was 4.012±0.96 (P value 0.5) on first post-operative day. On second post-operative day group A had mean VAS 4.012±0.96 and group B 1.55±0.59.(*P* value 0.001)
Conclusion: Post-operative oral Pregablin is more effective than Diclofenac sodium in reducing postoperative pain in patients with surgeries around the knee.
Keywords: Analgesia, Diclofenac sodium**,** Pregablin**,** Visual analogue score.

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INTRODUCTION

Injuries around the knee are very common due to road traffic accidents and sports.[1-3] After surgeries around the knee pain control is of paramount important for achieving early rehabilitation, return to sports or profession and improving the quality of life.[4] Different modalities of pain control medication are non-steroidal anti-inflammatory drugs (NSAIDs), opioids and pregabalin are used following surgery around the knee.[5,6] Both NSAIDs and opioids have been reported with sever adverse effects when used in immediate post operative period.[7-11]

Pregabalin can provide added effect in control of neuropathic pain as it binds with presynaptic neurons at the α 2 δ-1 and α 2 δ-2 subunits of voltage-gated calcium channels and thus inhibits the release of excitatory neurotransmitter responsible for pain.[12] Studies have shown that oral Pregablin can serve as an active agent in reducing pain intensity and morphine dose in multimodality pain control regimen following limb surgery.[7,13,14]

The objective of our study was to compare the efficacy of Diclofenac sodium and Pregablin in reducing post operative pain in patients with surgeries around the knee. We hypothesized that oral

Pregablin is better than Diclofenac sodium in reducing post-operative pain in patients with surgeries around the knee.

METHODS

We conducted this randomized controlled trial in Department of Orthopedics Surgery and Traumatology Mayo Hospital Lahore from to 23rd December 2017 to 23rd December 2020.

Adult patients of either gender and age with injury around the knee including isolated fracture of patella, distal femur, proximal tibia and torn anterior cruciate ligament (ACL) and meniscus who required surgical intervention were included in this study. Open fractures, pathological fractures, revision surgeries, hypertensive patients, peptic ulcer patients, pregnant patients, patients with compartment syndrome and poly trauma patients requiring multi-disciplinary surgical interventions were excluded. The study was approved by the Ethical Committee of our hospital. Informed written consent was taken from all study participants. After initial resuscitation and stabilization complete history, physical examination and relevant investigations (including 3D CT for intra articular fractures) were ordered. All the surgeries were performed under general anaesthesia and tourniquet control by the same surgical team following identical standard protocol. Per operative and post-operative pain on the surgery day was controlled with intra venous Nalbuphine 10 mg (®Nalbin) in all patients. Postoperative randomization of patients were done with computer generated random lists. Group A patients were administered 75 mg Diclofenac sodium (Cap. Mobikare DR®) BD while group B was administered Pregablin 75mg (Cap. Gabica®) BD by staff nurse starting on first post-operative day till second day with total of 4 doses in each group. Patients who had received additional analgesics were excluded from analysis. No other analgesics were allowed. Pain intensity at 10 PM was recorded daily as per VAS scale in both groups by an Orthopaedic consultant who was not part of this study.

We followed CONSORT guidelines[15] for conducting and reporting of our study. Data was entered into SPSS version 21.0 for analysis. Frequency and percentage was calculated for qualitative variables while mean and standard deviation for quantitative variables.

Mean VAS in both groups were compared and *P* value was calculated with paired-t test. *P* value < 0.05 was considered significant. Data was presented in table where necessary.

RESULTS

In this study 120 patients with surgeries around the knee were assessed for eligibility as per CONSORT flow diagram (Fig I) but 80 patients fulfilled the inclusion criteria and consented for the study. They were randomly divided into two equal groups each group containing 40 patients each. In group A (Diclofenac sodium) 26 (65%) were male and 14 (35%) were females. In group B (Pregablin) 25 (62.5%) were male and 15 (37.5%) females. The mean age of group A patients was 30.5±7.33 and group B31.15±9.97 years. There was no statistically significant difference between the demographic characteristics of both the groups.(table I) No statistically significant difference in VAS was found between the two groups on first post-operative day(mean VAS in group A 4.08±0.95 versus group B VAS 4.012±0.96 and P value 0.5).However on the second post-operative day group B had statistically lower VAS than group A (1.55±0.59 versus 4.012±0.96 with P value 0.001).No significant difference was noted in VAS when data stratification was done for gender, side or type of surgery.(P ≥0.05).No adverse effects like dizziness, sedation and visual disturbances were noted in Pregablin group. No gastric irritation or dyspepsia was noted in Diclofenac group.

Table 1: Comparison of demographic profiles of both groups.

Variables	Group A (n=40)	Group B (n=40)	*P* value
Gender			
Male	26 (65%)	25 (62.5%)	0.5
Females	14 (35%)	15 (37.5%)	0.4
Age	30.5±7.33	30.5±7.33	
Side of injury			
Right	29 (72.5%)	24 (60%)	0.8
Left	11 (27.5%)	16 (40%)	0.7
Types of surgeries			
Distal femoral locking plate	11(27.5%)	9(22.5%)	0.3
Proximal tibia locking plate	10(25%)	12(30%)	0.1
TBW patella	6(15%)	7(17.5%)	0.2
ACL reconstruction	7(17.5%)	5(12.5%)	0.8
Meniscectomy/repair	6(15%)	7(17.5%)	0.5

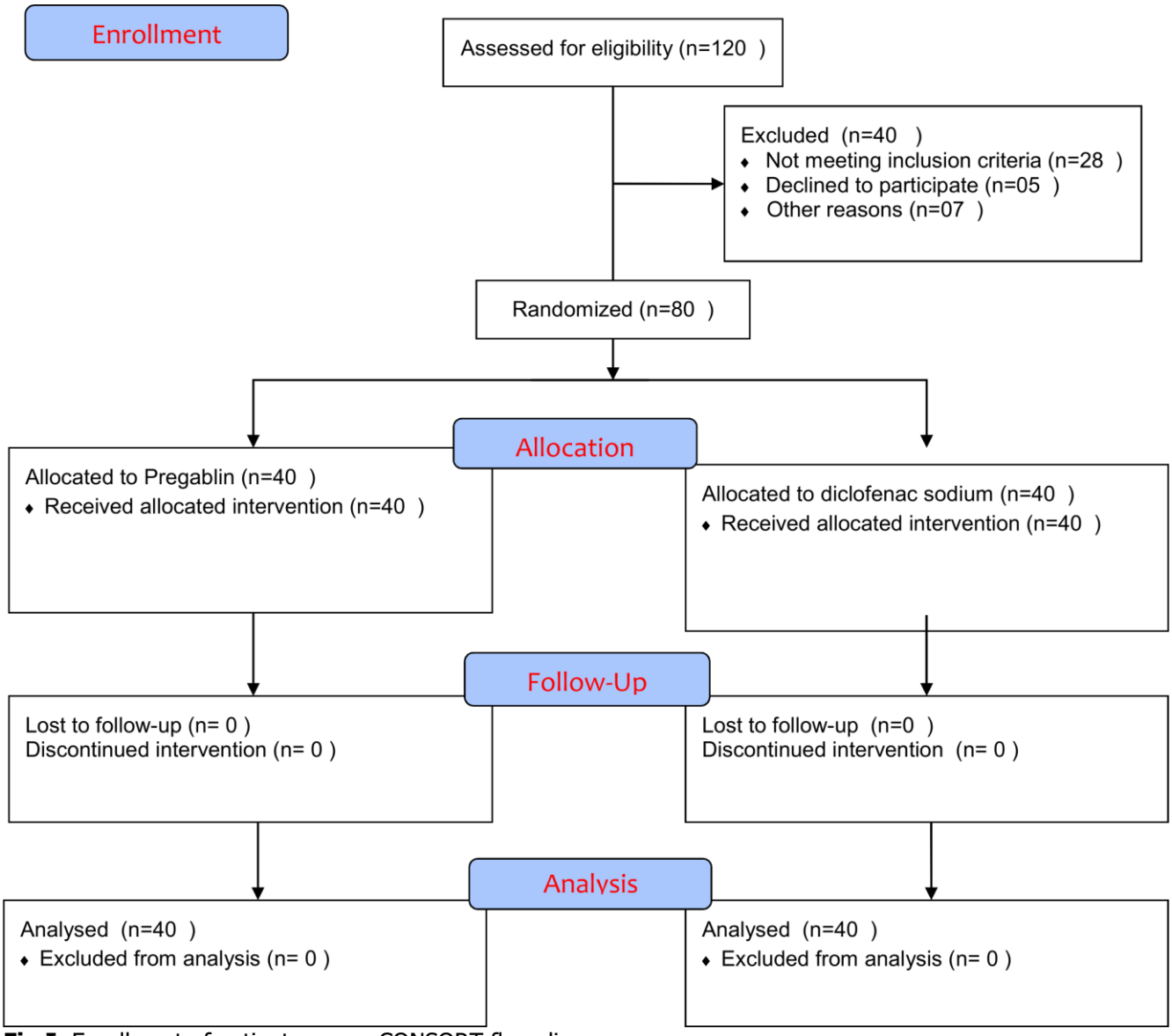

Fig I: Enrollment of patients as per CONSORT flow diagram.

DISCUSSION

Several studies have shown that preoperative Pregabalin reduces postoperative pain.[16-19] Dierking had demonstrated that administration of Pregablin can reduce the post-operative morphine requirement by 50%.[20] Buvanendran and colleagues[13] showed that perioperative administration of Pregablin in total knee patients significantly reduced knee pain and consumption of opioids. They however, documented sedation and confusion with high dose (300mg).In a systematic narrative review Dauri[22] had shown that Pregablin significantly reduced post-operative pain and opioid consumption when compared with placebo.

We included those patients who were operated under general anaesthesia. This was due to that fact that literature had shown that Pregablin was more effective in reducing post-operative pain in patients who were operated under general anaesthesia than regional anaesthesia.[23,24]

In our study 12(30%) patients of tibia fracture were treated with Pregablin and 10(25%) with Diclofenac sodium. Eraghi[25] compared the efficacy of Pregablin with Clonidine in 64 patients with tibia fracture surgery and noted significantly lower VAS score in patients with Pregablin than Clonidine.

In our study we used 150 mg of Pregablin post operatively for two days. No consensus can be found in the literature regarding the optimum time, dose

and duration of Pregablin usage due to heterogeneity of clinical trial. [26] Higher doses of Pregablin however, can cause dizziness, sedation and visual disturbances but none was reported in our series.

In our study 5(12.5%) patients received Pregablin and 7(17.5%) Diclofenac sodium after ACL reconstruction. Nimmaanrat[27] had demonstrated no pain reduction or decreased morphine requirements in patients with ACL reconstruction. Contrary to this study Cho and colleagues[28] in a randomized double blinded placebo trial showed that Pregablin significantly reduced post-operative pain in patients with ACL reconstruction.

We had noted significant pain reduction in our patients who received Pregablin after surgeries around the knee. Durkin[29] was of the opinion that Pregablin is a safe and effective drug and advocated the use of Pregablin in surgeries involving acute neuropathic pain. Besides surgeries around the knee for traumatic causes Pregablin has also been used successfully for pain reduction and opioid sparing effects in patients with spinal fusion, total knee replacement and total hip replacement.[31,32] We did not include these patients in our study.

Our study had few limitations. Our sample size was small. The number of surgical procedures in both groups were not equal. We recommend further studies to verify our results.

CONCLUSION

Post-operative oral Pregablin is more effective than Diclofenac sodium in reducing postoperative pain in patients with surgeries around the knee.

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