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Evaluation of Efficacy of Pregabalin and Tramadol on Anxiety and Sedation in Total Knee Arthroplasty Patients

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Abstract: ***Background**: Anticonvulsant medications are established treatments for neuropathic pain, role of pregabalin was studied in the latest research that it has a role in the Acute and post operative pain. Pregabalin was taken up for the study to primarily assess anxiety and sedation when compared to tramadol in patients undergoing elective Total Knee Arthroplasty. **Methods**: Study group included 50 patients between 20-60 yrs belonging to ASA-I and II, The patients were randomly allocated into 2 groups of 25 each. Tramadol group received 100mg capsule while the pregabalin group received 150mg capsule orally 1hr before the anesthetic induction. Multimodal analgesia included femoral nerve 3 in 1 nerve block and rescue analgesics diclofenac was used. The primary outcome in our study was Anxiety and sedation. **Results**: Pregabalin showed statistically significant anxiolytic effects compared to tramadol but was associated with less sedation to tramadol. Whereas Pregabalin had less number of postoperative complications of nausea, vomiting and drowsiness. **Conclusion**: The results of this study support, the clinical use of pregabalin in the post surgical setting for relieving Anxiety alone. Whereas tramadol was better in only post operative pain and mild sedation.***

Keywords: pregabalin, Tramadol, Total knee arthroplasty, sedation, Anxiety

1. Introduction

Pregabalin (S-[+]-3-isobutylgaba) a structural analogue of gamma amino butyric acid has been used for treatment of various neuropathic pains and also as an adjunctive therapy for adults with partial onset seizures [1]. The search for new Drugs are increasing and the anticonvulsants which are useful in chronic pain are under the study in the present era. In this context anticonvulsant drugs gabapentin and pregabalin have been targeted by researchers. The study was aimed at anxiolysis and sedation as there was lot of research on pain but very less on the sedation and anxiolysis.

Drugs which are treated for the trigeminal neuralgia [2,3] have been assessed for its analgesic potency in treating neuropathic pain associated with diabetic peripheral neuropathy [4,5] and post herpetic neuralgia.[6,7] Also its analgesic efficacy after a variety of surgical procedures[8,9] Two such drugs especially pregabalin and gabapentin which are alfa-2-delta (α2-δ) subunit calcium channel ligands have been widely studied. Pregabalin binds potently to the α2-δ subunit and modulates calcium influx at nerve terminals, and, thereby, reduces the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P. [10-14] Thus the present study was aimed to compare and assess the anxiolysis and sedation in patients undergoing total Knee arthroplasty.

2. Material and Methods

The study was conducted on 50 patients of either sex or age group between 20-60 yrs belonging to ASA-I and II patients, undergoing elective Total Knee Arthroplasty under spinal anesthesia. The patients were randomized into 2 groups of 25 each by computer generated random number table and sealed opaque envelope technique. Exclusion criteria were known allergy or sensitivity to the drug, renal insufficiency, ongoing therapy with sustained release opioids and seizure disorders. Group I (pregabalin) received 150mg capsule orally the night before the surgery, Group II (tramadol), received 100mg capsule Sedation scores were given as awake and alert or tense-4, Awake and not alert-3, Drowsy-2, Asleep-1, Asleep and not arousable -0. Anxiety scores were given as; Frightened/terrified -4, very upset and worried -3, Worried and anxious -2, uneasy-1, calm and comfortable -0. Post operatively blood pressure, heart rate, respiratory rate, level of sedation as measured by sedation scoring, side effects like nausea, vomiting, constipation, drowsiness and other complications if any were also recorded at preop, 1hr, 2 hr, 4 hr, 6, hrs.

Statistical analysis

Pilot study was conducted to assess the sample size on 5 patients and Power analysis of ANOVA was done with PASS (power analysis and sample size system) software (trial version), in two groups, standard deviation 2, power of 80% and alpha = 0.05. (ANOVA) was performed for repeated measures for anxiety and sedation.

3. Results

The demographic data of all the two groups is shown in the Table1. The groups were matched in terms of age, gender, weight, duration of surgery. No significant difference was observed in the mean systolic and diastolic blood pressures at preop, 1hr, 2hr, 4hr and 6hrs postoperatively. Anxiety and sedation scores at different time intervals are shown in Table

3. The mean anxiety scores were lower in pregabalin which is significant when compared to tramadol and. Preoperatively the sedation scores were significantly lower in tramadol patients when compared to pregabalin. The adverse effects observed in the three groups are given in. The complications like nausea, vomiting and drowsiness were higher in tramadol patients and least in pregabalin patients though statistically insignificant. (Table 3).

Table 1: Demographic Profile

Variables	Group 1 pregabalin (Mean ± S.D)	Group 2 Tramadol (Mean ± S.D)
Age (years)	41.8 ± 12.43	45.36 ± 11.04
Weight (kg)	69.44 ± 7.51	61.4 ± 7.91
Sex ratio (male: female)	5:19	6:16
Duration of surgery (minutes)	190 .4 ± 51.17	245.6 ± 38.72

Table 2: Hemodynamic Changes

	Group1 pregabalin		Group 2 Tramadol	
	SBP	DBP	SBP	DBP
Pre op	121.64±23.90	81.48 ± 9.18	110.72±18.67	85.44±8.48
1min After surgery	138.64±18.95	75.16 ± 16.53	155.36±19.58	90.56±12.63
1hr After Surgery	114.32 ± 14.59	77.92 ± 6.46	110.8 ± 9.96	83.6 ± 5.68
2hr After Surgery	112.4 ± 12.34	85.68 ± 7.34	147 ±11.64	80.96 ± 4.16
4hr After Surgery	119.4 ± 10.52	95.52 ± 7.68	135.56±10.40	82.24 ± 3.843
6hr After Surgery	120.76 ± 12.08	110.92 ± 8.82	155 .28±13.87	82.72 ± 5.79

Table 3: Anxiety and sedation scores

Variables	Time point	Group 1: Pregabalin	Group 2: Tramadol
Anxiety score	Pre op	0.28 ± 0.84	1.52 ± 0.62
	1 min After Anesthesia	0.48 ± 0.50	1.48 ± 0.97
	5 min After Anesthesia	0.36 ± 0.7	1.66 ± 1.2
	2hr After Surgery	0.92 ± 0.90	1.5 ± 1.15
	4hr After Surgery	0.28 ± 0.84	1.32 ± 0.62
	6hr After Surgery	0.48 ± 0.50	1.30 ± 0.97
Sedation scores	Pre op	2.68 ± 1.09	3.56 ± 2.12
	1hr After Surgery	2 ± 1	2.6 ± 1.15
	2hr After Surgery	2.04 ± 0.92	2.64 ±1.25
	4hr After Surgery	2.98 ± 1.09	3.56 ± 2.12
	6hr After Surgery	2.11 ± 0.66	3 ± 2.06

Table 4: Adverse Effects

	Group 1: Pregabalin	Group 2: Tramadol
Nausea	7 %	26%
Vomiting	8 %	30%
Drowsiness	12%	6%

4. Discussion

The anxiety scores were significantly lower in pregabalin when compared to tramadol groups. Whereas anxiety scores in pregabalin group was found to be significantly higher than tramadol group. This clearly signifies that pregabalin has an anxiolytic effect than tramadol. This anxiolytic effect of pregabalin may be beneficial as patients may be anxious in perioperative period. Our observation is in line with previous studies. [15,16] We also observed that preoperatively the sedation scores were significantly higher in tramadol when compared to pregabalin. From this we infer that pregabalin has good anxiolytic effect without excessive sedation. Pregabalin had no effect on heart rate, which is consistent with animal experiments showing that intrathecal administration of the related compound gabapentin does not alter resting or acutely evoked autonomic out flow. [17] drowsiness was less with pregabalin 10 % when compared to tramadol 25 % even though it is statistically insignificant. Fewer patients experienced nausea 7% and vomiting 8 % in pregabalin group and in tramadol Nausea 26 %, vomiting 30 % groups. This infers that the tramadol has a significant incidence of nausea and vomiting,

5. Conclusion

Pregabalin has statistically significant anxiolytic effect compared to tramadol with less sedation when compared to Tramadol in patients undergoing total knee arthroplasty under regional anesthesia.

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