

Pregabalin and Dexamethasone for Post Operative Pain Relief In Lower Limb Surgeries – A Randomized Controlled Study”

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Abstract:

Aims: In this study, we evaluated the pre-operative administration of pregabalin sufficiency and security in relieving post-operative pain after lower limb surgery and reducing the need for opioids and their possible side-effects. Also we evaluated the use of perioperative dose of dexamethasone in relieving post-operative pain and effects on adverse effects in adult surgical patients undergoing lower limb surgery under spinal anaesthesia.

Methods: This study is a randomized control trial. It was performed on 75 patients under lower limb surgery by spinal anaesthesia. Patients were randomly allocated to three groups, Groups were named, Group C: No drug given, Group P : Tab. Pregabalin 300 mg given orally 1 hour before surgery, Group D: Inj. Dexamethasone 8 mg i.v. + Tab. Pregabalin 300 mg given orally before 1 hour of surgery. In all three groups at 0, 2, 4, and 24 h after surgery, the patients were evaluated and the pain score, the score of sedation, incidence of nausea and vomiting was recorded. The results between the three groups were analysed statistically using ‘P’ value obtained by “chi square test” and “unpaired t test”.

Results: Visual analog pain scores at all hours in pregabalin group significantly reduced compared to the placebo group. Also, in the pregabalin group nausea, vomiting and opioids consumption have significantly been reduced.

Conclusion: A pre-operative oral dose of pregabalin reduces opioid consumption, improves postoperative analgesia, and yields higher patient satisfaction levels in patients undergoing lower limbs surgery.

Keywords: Pregabalin, Post operative pain, Opioid sparing effects.

I. Introduction

Most patients undergoing surgery experience post-operative pain. The path to pain relief was itself painfully slow and long. Pain therapy has undergone lot of metamorphosis since ages. Post-operative pain is usually perceived as nociceptive pain but surgical trauma also induces central and peripheral sensitization and hyperalgesia. Providing adequate analgesia after surgery is a major challenge as causes are multifactorial.

The current concept of multimodal postoperative analgesia is mainly based on combination of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol and perioperative administration of local anesthetics. Use of opioids may be limited by adverse effects. NSAIDs have prothrombotic properties, increase risk of stroke and cardiac ischemia. Interventional techniques such as epidural analgesia require additional work and carry potential risk of serious complications.

Pregabalin is a structural analogue of GABA. It acts by presynaptic binding to alpha-2-delta subunit of voltage gated calcium channels that are widely distributed in spinal cord and brain. By this mechanism, pregabalin modulates the release of several excitatory neurotransmitters, such as glutamate, norepinephrine, substance-P and calcitonin gene related peptide. It leads to inhibitory modulation of overexcited neurons and returns them to a “normal” state. Centrally, pregabalin could reduce the hyper excitability of the dorsal horn neurons that is induced by tissue damage.

Glucocorticoids have been used to reduce inflammation and tissue damage. Glucocorticoids have potent immunomodulatory and antiemetic properties. The efficacy of glucocorticoids for reducing pain and inflammation after surgery has recently been explored. Early studies in patients undergoing dental procedures showed that glucocorticoids were effective in reducing postoperative pain and oedema. A number of recent studies have investigated the potential analgesic benefit of a single perioperative dose of dexamethasone but have inconsistent findings.

Long-term treatment with glucocorticoids is associated with many side-effects. However, it is unclear if a single perioperative dose of dexamethasone increases the risk of these adverse effects. This is due to many of the published studies being underpowered to detect clinically relevant sideeffects, and many studies also excluded patients at the highest risk of glucocorticoid-related adverse effects.

We therefore performed this systematic review to determine if a single perioperative dose of dexamethasone in adult surgical patients undergoing surgery under spinal anaesthesia has a useful analgesic effect in the postoperative period. We also investigated whether the use of dexamethasone increases the risk of postoperative adverse effects.

II. Material And Methods

This Prospective Randomised Controlled study was conducted at our institute during the year 2011-2013, after written informed consent of 75 adult patients of either sex, between 30 - 65 years of age, ASA physical status I-II, and undergoing lower limb surgeries performed under spinal anaesthesia.

Patients were not admitted to study if any of the following criteria were present: (1) inability to cooperate, (2) allergy to any drug in the study, (3) treatment with antacids or antidepressants, (4) a history of diabetes or epilepsy, (5) known impaired kidney function, (6) alcohol, drug abuse, or both, (7) a daily intake of analgesics, except for non-steroidal anti-inflammatory drugs, cox-2 inhibitors, or acetaminophen and, (8) treatment with systemic gluco-corticoids within four weeks before surgery.

All patients were examined pre operatively as well as detailed history and investigations noted. All patients were premedicated with Tab. Lorazepam 1 mg. at 10:00 pm previous night of surgery and Tab. Diazepam 5 mg at 6:00 am on day of surgery. All patient received Tab. Acetaminophen 1 gm orally one hour before spinal anaesthesia.

All 75 patients were randomly divided into 3 groups(n=30). Groups were named, Group C: Control group (No drug given), Group P : Tab. Pregabalin 300 mg given orally 1 hour before surgery, Group D: Inj. Dexamethasone 8 mg i.v.+ Tab. Pregabalin 300 mg given orally before 1 hour of surgery.

Intravenous line was obtained with 18G canula and preloaded with ringer lactate/normal saline 10ml/kg body weight before spinal anesthesia. Patients was connected to multiparameter monitor for monitoring pulse,SPO2, ECG, NIBP. Under aseptic precautions Subarachnoid block was performed at L3-L4 interspace through a midline approach using 25G Quinke spinal needle and 3cc of 0.5% Bupivacaine heavy without any adjuvant was injected into subarachnoid space after confirming the clear and free flow of CSF. Patients was turned to supine posture immediately with the table kept flat and supplemental oxygen will be given. Pulse ,Blood Pressure, Respiratory rate, VAS score and Sedation score were monitored at beginning, then half hourly for 2 hours and there after every hourly till 24 hours.

In the post operative period patients were observed for VAS, vital signs, sedation, complication, side effects, requirement of rescue analgesia. Patients were monitored for post operative pain by VAS scale (scoring system of 0 -10, with no pain being 0 and most severe pain being 10) every 30minutes which was explained to the patients pre-operatively. When the VAS is >5 patient was given rescue analgesia of 75 mg Inj. Tramadol intravenously. Common complications such as nausea, vomiting, constipation, dizziness if present, were recorded and effectively treated.

The results between the three groups were analysed statistically using ‘P’ value obtained by “chi square test” and “unpaired t test”.

III. Results

75 ASA risk I & II patients undergoing elective lower limb surgery were studied and randomly assigned into three groups 25 patients each. They were assessed for post operative pain as mentioned previously.

GROUPS			
	Group C	Group P	Group D
N	25	25	25
Age(years)	50±9	49±7	47±8
Height (cm)	158±7	160±5	155±9
Weight (Kg)	51.6±3	48.6±8	47±6
Sex (M:F)	16:9	18:7	21:4
Duration of surgery(hr)	2.1±0.5	1.9±0.6	1.8±0.4

TABLE 1 : Demographic data (mean ± SD)

Table 1 shows that there were no significant difference in the age, weight, height, sex in all three groups & all groups are comparable. (P> 0.05)

TABLE 2 : Post operative VAS score (mean±SD)

Groups			
Time	Group C	Group P	Group D
0 hour	4.36±1.31	4.00±1.11	4.40 ±1.08
2 hour	4.56±1.00	3.04±0.73	2.92±0.70
4 hour	3.00±0.64	2.64±0.75	2.56±0.71
24 hour	2.72±0.54	1.80±1.00	1.99±1.02

Table 2 shows that VAS score of pain was not statistically different between all three groups at any time point of observation.

TABLE 3 : Changes in vital parameters (mean ± SD)

a) Pulse rate (beats/min)				
Time	0 hour	2 hour	4 hour	24 hour
Group C	88.68±9.71	85.6±8.10	76.44±4.99	73.2±5.36
Group P	85.92±11.92	82.0±6.02	76.76±4.87	72.16±6.62
Group D	85.76±8.19	81.36±6.67	76.36±6.96	70.68±8.04
b) Mean blood pressure (mm Hg)				
Time	0 hour	2 hour	4 hour	24 hour
Group C	87.68±11.36	83.52±10.08	75.52±9.11	75.28±8.66
Group P	84.36±9.78	83.4±6.51	76.04±8.74	77.44±8.16
Group D	83.4±10.48	88.6±8.43	80.8±7.51	77.68±6.90
c) Respiratory rate (/min)				
Time	0 hour	2 hour	4 hour	24 hour
Group C	14.84±1.92	14.76±1.92	14.72±1.59	14.84±1.79
Group P	14.72±1.92	14.56±1.26	14.12±1.64	14.84±1.7
Group D	14.4±1.63	15.04±1.83	14.48±1.22	14.96±1.54

Table 3 shows that pulse rate, mean blood pressure and respiratory rate at beginning (t=0 min) among all three groups were comparable. (P>0.05). The difference between all groups were not significant at any point of observation. (p>0.05)

TABLE 4 : Time of requirement of first dose of rescue analgesia(mean±SD)

Group	C	P	D
Time(min)	130.73±7.12	193.84±9.56	186.28±8.78

Table 4 shows that difference in mean time of requirement of first dose of rescue analgesia was statistically significant (p < 0.05) between Group C and Group P; and between Group C and Group D; while statistically not significant between Group P and Group D (p > 0.05); suggest pregabalin significantly increase mean time of requirement of first dose of rescue analgesia

TABLE 5 : Requirement of Analgesic Doses:

No. of Dose	Group C(n=25)	Group P(n=25)	Group D(n=25)
1	0	15	13
2	4	10	12
3	12	0	0
4	9	0	0

Table 5 suggest that requirement of analgesic doses were higher in Group C as compare to Group P and Group D. But, there was no significant difference in requirement of analgesic doses among Group P and Group D. Suggest that Pregabalin improve analgesia as compared to placebo. Adding of dexamethasone did not improve analgesia to pregabalin.

TABLE 6 : Side effects

Side effect	Groups		
	Group C	Group P	Group D
Nausea	4(16%)	3(12%)	4(16%)
Vomiting	4(16%)	6(24%)	1(4%)
Sedation	7(28%)	9(36%)	4(16%)

Table 6 shows that, for nausea there was no significant difference between all groups at any time point of observation. Incidence of vomiting was not significantly different between Group C and Group P. In Group D incidence of vomiting was significantly lower as compare to Group P. Number of patients having sedation in 24 hour were significantly lower in Group D as compared to Group P.

Above observations suggest that adding of Dexamethasone to Pregabalin decrease incidence of vomiting and sedation as compared to Pregabalin alone.

IV. Discussion

Current study is one such attempt to observe post operative pain relief with use of pregabalin and weather adding of dexamethasone has any improvement of pain relief or not.

In this study Mean age , weight, height and sex distribution was found comparable in 3 Groups. The majority of previous studies have similar results as MATHIESE.O et al [1] and Godrat Akhavanakbari et al. Pain was evaluated by VAS. There were no significant differences in VAS score between all three groups which was comparable with observations of O. Mathiesen et al [1] Monica kohli et al [2] and Elina M. Tiippana et al [3] . Our study shows that pulse rate, mean blood pressure and respiratory rate at beginning (t=0 min) among all three groups, the difference were not significant at any point of observation.(p>0.05) which was comparable with study of Scott s. Reuben et al[4].

We have selected Tramadol as as a rescue analgesic because Tramadol has a low potential for abuse and psychological dependence. Preoperative administration of pregabalin resulted in reduction in number of patient requiring frequent Tramadol dosing compared to placebo group. But there was no difference in number of patient requiring Tramadol dosing in group D compared to group P. The combination of pregabalin and dexamethasone had no effect on pain or opioid requirements compared with pregabalin alone. One reason for this finding could be that the dose of dexamethasone (8 mg) was too low.

Romundstad L et al[5] suggested a somewhat higher dose of 0.2–0.4 mg / kg dexamethasone i.v. required to produce analgesic effect of dexamethasone. But we used only 8 mg of total dexamethasone IV which was almost one third dose of total required dose, so on adding of dexamethasone to pregabalin we did not observed any significant improvement in pain relief. Another reason for no effect of dexamethasone on pain could be the low pain score at most time points in all groups, because many study concluded that adequate sensitivity in to analgesics for acute pain may only be achieved when patients are experiencing at least moderate pain[6, 7, 10].

In spite of the relatively large reduction in tramadol consumption, we did not observe any reduction of nausea or vomiting with pregabalin compared to placebo. The well-known anti-emetic effect of dexamethasone was seen as a significant reduction in vomiting in patients receiving the combination of pregabalin and dexamethasone compared with pregabalin alone in our study which was comparable with observations of Iris henzi et al [8] and Henrik Kehlet et al [9].

Sedation and dizziness are well-known side-effects of gabapentinoids, and we observed increased sedation in patients receiving pregabalin alone in the early postoperative period. When adding dexamethasone to pregabalin (Group D), sedation diminished and we observed no significant differences in mean sedation score between Group C and Group D. Elina M. Tiippana et al [3] observed most common side effect were sedation and dizziness.

V. Conclusion

- In patients undergoing lower limb surgery, Preoperative dose of pregabalin is an effective method for reducing post-operative pain and has a significant opioid-sparing effect in the first 24 h after surgery. Added dexamethasone reduced vomiting and sedation compared with pregabalin alone but no additional effects on pain or opioid requirements could be demonstrated.

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