Original Research Article

An observational study to compare the effect of pregabalin with pregabalin and dexamethasone for post operative analgesia in orthopedic surgeries under spinal anesthesia

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Abstract

Background: Post-operative pain is a troublesome problem after orthopedic surgeries. Pregabalin acts as a synthetic analog of the neurotransmitter gamma-aminobutyric acid (GABA) with analgesic, anticonvulsant, and anxiolytic effects. Pregabalin is effective in controlling postoperative pain and in decreasing analgesic consumption. Glucocorticoids have strong anti-inflammatory effects and exhibit antiemetic and analgesic efficacy. Dexamethasone increases the efficacy of analgesia when given alone or in combination with other drugs.

Material and methods: The aim was to determine the efficiency of pregabalin alone and the combination with dexamethasone to the orthopedic operations regarding postoperative pain control and analgesic consumption. It was an observational study in which participants were allocated in two groups of 30 each. In group P – Tab Pregabalin: 300 mg and in group D –Tab Pregabalin: 300 mg + Inj. Dexamethasone: 16 mg IV was given. Pain was assessed by Visual analogue scale at 0, 2, 4, 6, 12, 24 hours post-operatively. Any patient with the visual analogue scale more than 3 were given Inj. diclofenac 1.5 mg/kg IM. Time since spinal anesthesia to the first dose of analgesic and total dose of analgesic in first 24 hours was recorded. $P<0.05$ was considered statistically significant.

Results: Rescue analgesia was not required only in 1 (3.3%) case in Group D. Those who required analgesia, maximum proportion of patients required two doses in Group P (n=17, 56.6 %) while in Group D the max proportion of patients required one dose (n=15; 50.0%). Statistically, the number of patients requiring more number of rescue analgesia was significantly higher in Group P as compared to Group D ($p<0.001$).

Conclusion: Combined administration of pregabalin and dexamethasone conferred analgesic benefits superior to those of pregabalin alone, by reducing the requirement of rescue analgesia and side effects.

Key words

Pregabalin, Dexamethasone, Orthopedic surgeries, Spinal anesthesia.

Introduction

Post-operative pain is a troublesome problem after orthopedic surgeries. Appropriate management of post-operative pain is known to reduce the length of the hospital stay and to make patients more comfortable by reducing pain-associated complications [1]. Opioids are most commonly used analgesic for intra-operative and post operative pain relief. But these are associated with a number of side effects such as nausea, sedation etc which are highly undesirable. During the last few years new drugs namely gabapentin and pregabalin have been used to alleviate post operative pain [2, 3, 4]. In contrast to gabapentin, pregabalin has better pharmacokinetic properties and due to lack of hepatic metabolism has less drug interactions. Pregabalin essentially acts as a synthetic analog of the neurotransmitter gamma-aminobutyric acid (GABA) with analgesic, anticonvulsant, and anxiolytic effects [5].

In a number of studies, it is found that dexamethasone increases the efficacy of analgesia when given alone or in combination with other drugs. Hence we have chosen a combination of Pregabalin and Dexamethasone and compared it with Pregabalin alone.

Aim

The aim was to determine the efficiency of pregabalin alone and the combination with dexamethasone to the orthopedic operations regarding postoperative pain control and analgesic consumption.

Material and methods

Inclusion criteria

- Number of patients: 60
- ASA risk category I or II
- Patients in age group of 20-50 years.
- No known history of allergy, sensitivity or other form of reaction to local anesthetics of the amide type.

Exclusion criteria

- Patient refusal.
- Patients on anti epileptics, analgesics, anti platelets, or on anticoagulants.
- Known allergy to the trial drugs.
- ASA III or more.
- Contraindication to spinal anesthesia.

It was an observational study in which participants were allocated in two groups of 30 each. In group P – Tab Pregabalin: 300 mg and in group D –Tab Pregabalin: 300 mg + Inj. Dexamethasone: 16 mg IV was given. Pregabalin was given orally 1 hour prior to administration of the spinal anesthesia in both the groups. Before the administration of spinal anesthesia, IV dexamethasone 16 mg was given in group D.Multipara monitoring in the form of NIBP, Pulse Oximetry and ECG was attached. Patients were preloaded with 10 ml/kg RL IV.

Spinal anesthesia was instituted with 3.5 ml of 0.5% Heavy Bupivacaine in L3-L4 inter-vertebral space in sitting position. Patients were monitored intra-operatively for pulse rate, blood pressure, SpO_2, ECG and complications if any.

Pain was assessed by Visual analogue scale at 0, 2, 4, 6, 12, 24 hours post-operatively. Any patient with the visual analogue scale more than 3 were given Inj. diclofenac 1.5 mg/kg IM. Time since spinal anesthesia to the first dose of analgesic and total dose of analgesic in first 24 hours was recorded. *P*<0.05 was considered statistically significant.

Results

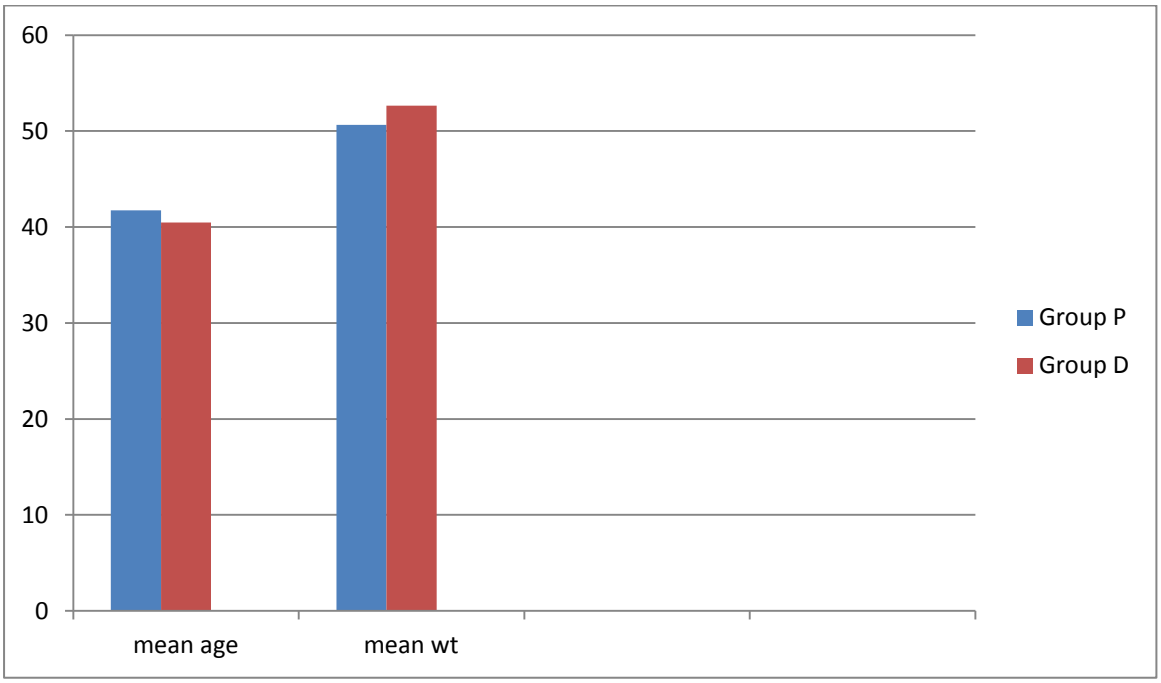
The present study was carried out at Dhiraj Hospital, Piparia on 60 ASA-I and II patients undergoing orthopaedic surgery under spinal anesthesia for comparative evaluation of post-operative analgesic benefit in patients administered Pregabalin or Pregabalin with Dexamethasone as premedication. Patients were divided into two groups of 30 each (Group P were given oral Pregabalin 300 mg, Group D were given oral Pregabalin 300 mg with IV Dexamethasone 16 mg.

The distribution of patients with respect to age and weight was comparable in both the groups. Age and weight wise distribution of cases were as per **Graph – 1** and **Table - 1**.

Table – 1: Distribution of cases according to age and weight.

	Mean ± SD		**"p" value**
	Group P (n=30)	**Group D (n=30)**	
Mean age	41.73 ± 7.72	40.46 ± 6.03	0.489
Mean weight	50.63 ± 8.45	52.63± 10.15	0.41

Graph – 1: Distribution of cases according to age and weight.



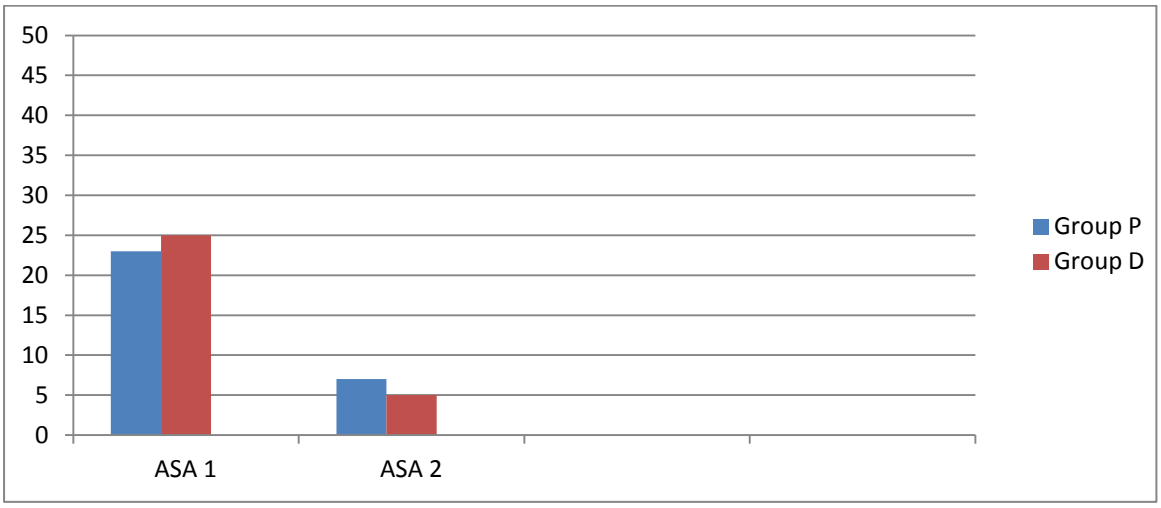
Distribution of cases as per ASA was as per **Table – 2** and **Graph – 2**. There was majority of ASA I patients in both the groups (76.7% in Group G versus 83.3% in Group P). The distribution of patients with respect to ASA grading was comparable in both the groups (p value > 0.05) as per **Table – 2** and **Graph - 2**. Hemodynamically, there was no statistically significant difference between the groups in terms of pulse rate at all-time intervals for both the groups (P>0.05) as per **Graph – 3**.

Table - 2: American Society of Anesthesia (ASA) Grade.

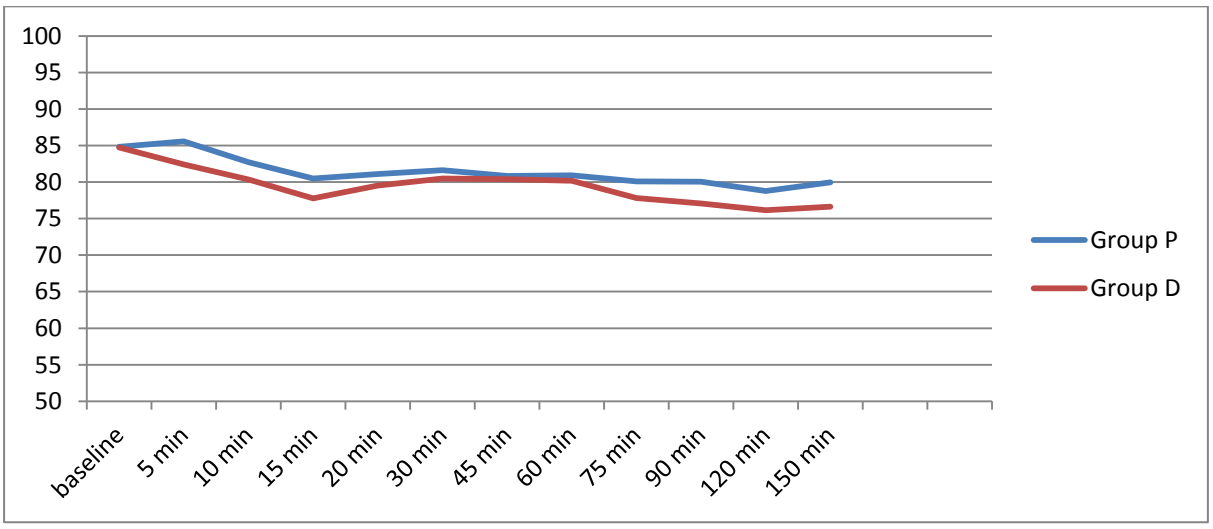
ASA Grade	Group P	Group D	P value
I	23 (76.7%)	25 (83.3%)	0.519
II	7 (23.3%)	5 (16.7%)	0.621

Chi-Square p-value 0.519.

Graph – 2: Distribution of cases according to ASA grading.



Graph – 3: Distribution according to pulse rate.



There was no statistically significant difference between the two groups regarding SBP and DBP (P>0.05) as per **Graph – 4** and **Graph – 5.**

Intra operatively and postoperatively no statistically significant difference in SpO_2 was observed between two groups (p value > 0.05) as per **Graph - 6**.

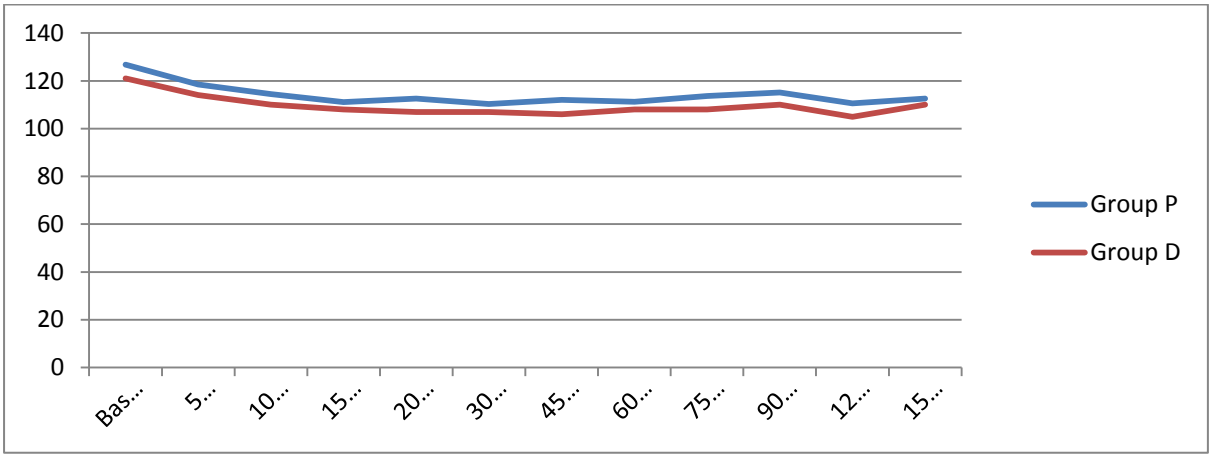
Duration of surgery was as per **Graph – 7** and **Table – 3**. The mean duration of surgery was 88.83 ± 30.16 min in Group P and 97.83 ± 38.34 min in Group D which was comparable and statistically not significant (p value > 0.05).

VAS was used to assess pain score at 2 hour interval after being shifted out of OT and that

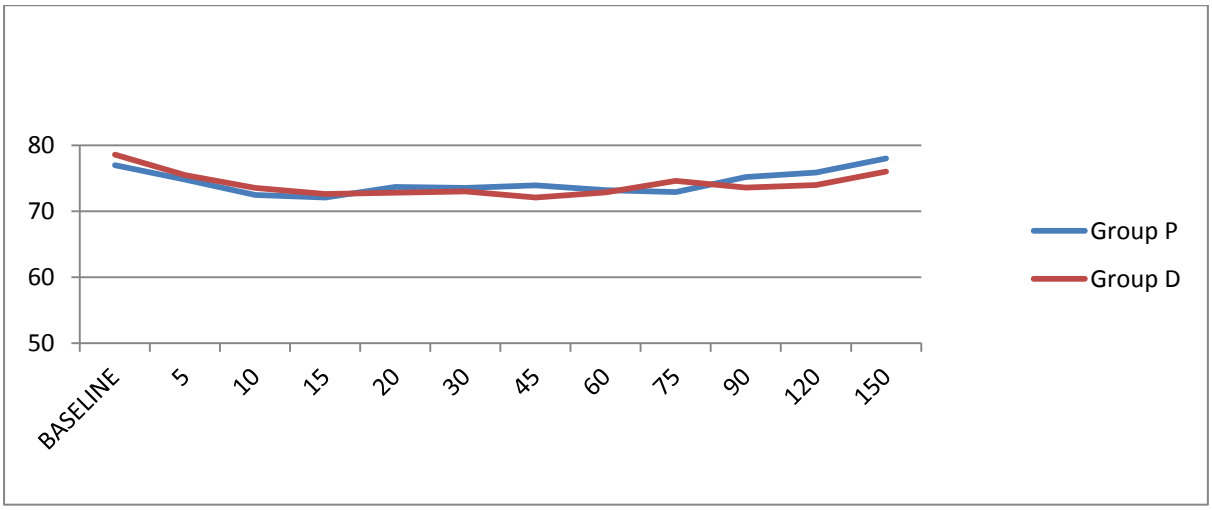
was significant statistically. (P<0.05) (**Table – 4**, **Graph – 8**)

Rescue analgesia was not required in 3.3% case in Group D in 24 hours. 56.6% of patients in group P required 2 doses of rescue analgesia as against 46.6% in group D, which was statistically highly significant (p<0.001). There was no statistically significant difference in the requirement of 1 dose in both the groups (**Graph – 9, 10** and **Table – 5, 6**).

Graph – 4: Distribution according to systolic blood pressure.



Graph – 5: Distribution according to diastolic blood pressure.



Complications like bradycardia, sedation, nausea were seen slightly more in group P as compared to group D, which were statistically non significant (p> 0.05) as per **Table – 7**.

Discussion

Pain after surgery is normally perceived as nociceptive pain. However, surgical trauma has been known to induce hyperalgesia, which can contribute to persistent postoperative pain after surgery [6]. In contrast to traditional analgesics that are anti nociceptive, gabapentinoids such as gabapentin and pregabalin reduce the hyperexcitability of dorsal horn neurons induced by tissue damage rather than reduce the afferent input from the site of tissue injury [7]. Central neuronal sensitization may result in an amplification of postoperative pain, and that

preoperative administration of gabapentinoids, may reduce the degree of central sensitization. Because of the absence of hepatic metabolism, Pregabalin has good pharmacokinetic properties and fewer drug interactions which make it a better drug than Gabapentin [8].

Graph – 6: Comparison of Oxygen Saturation in study groups at different time intervals.

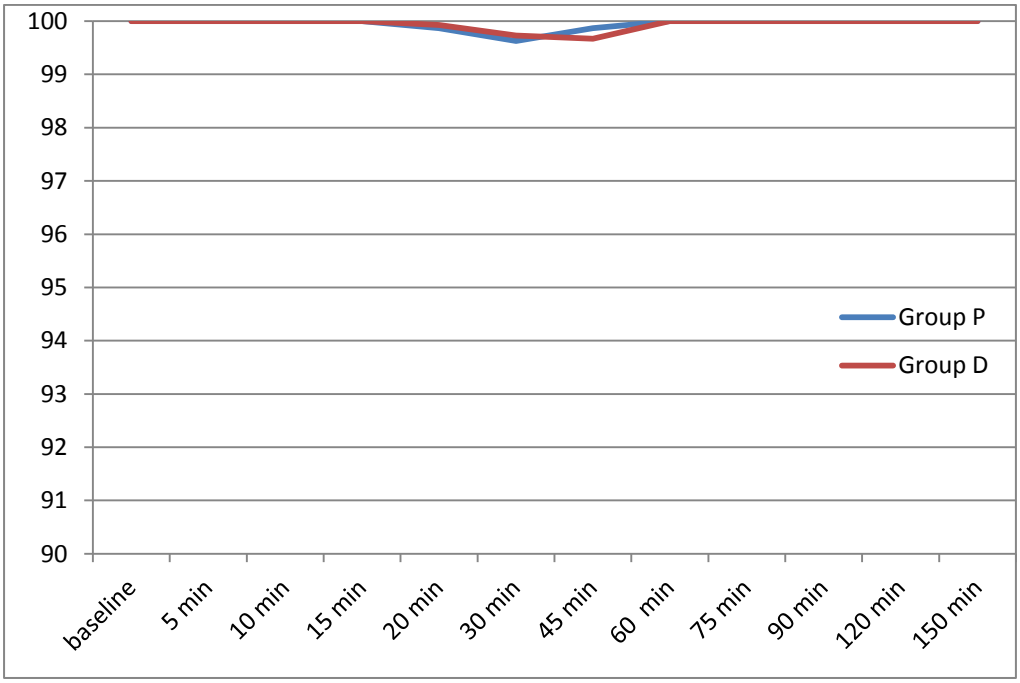


Table – 3: Duration of surgery.

	Group P	Group D	P value
Mean Duration of Surgery	88.83 + 30.16	97.83 + 38.34	0.202 (non significant)

Graph – 7: Distribution according to duration of surgery.

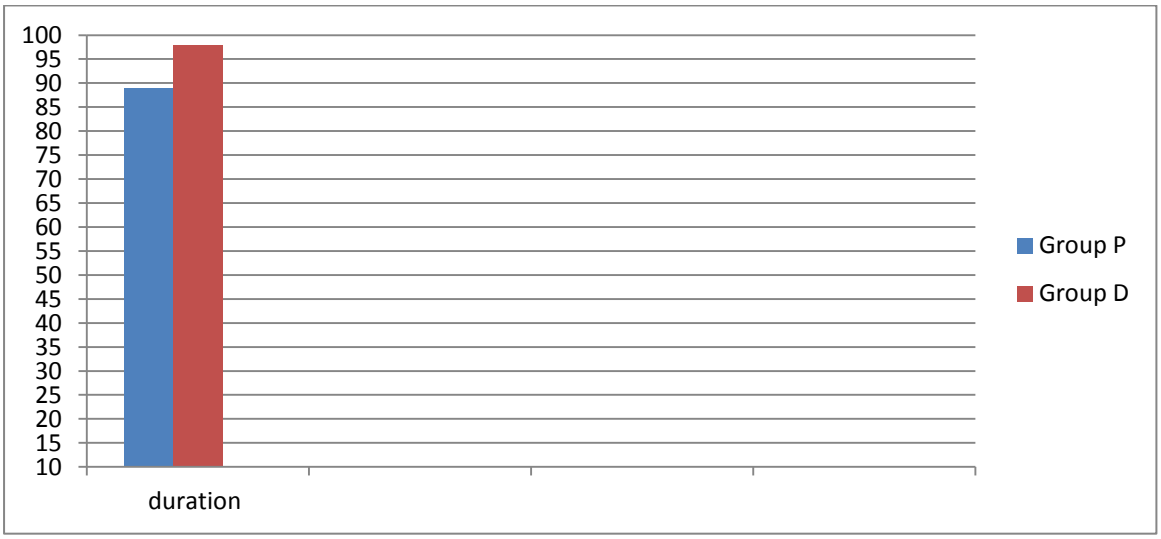
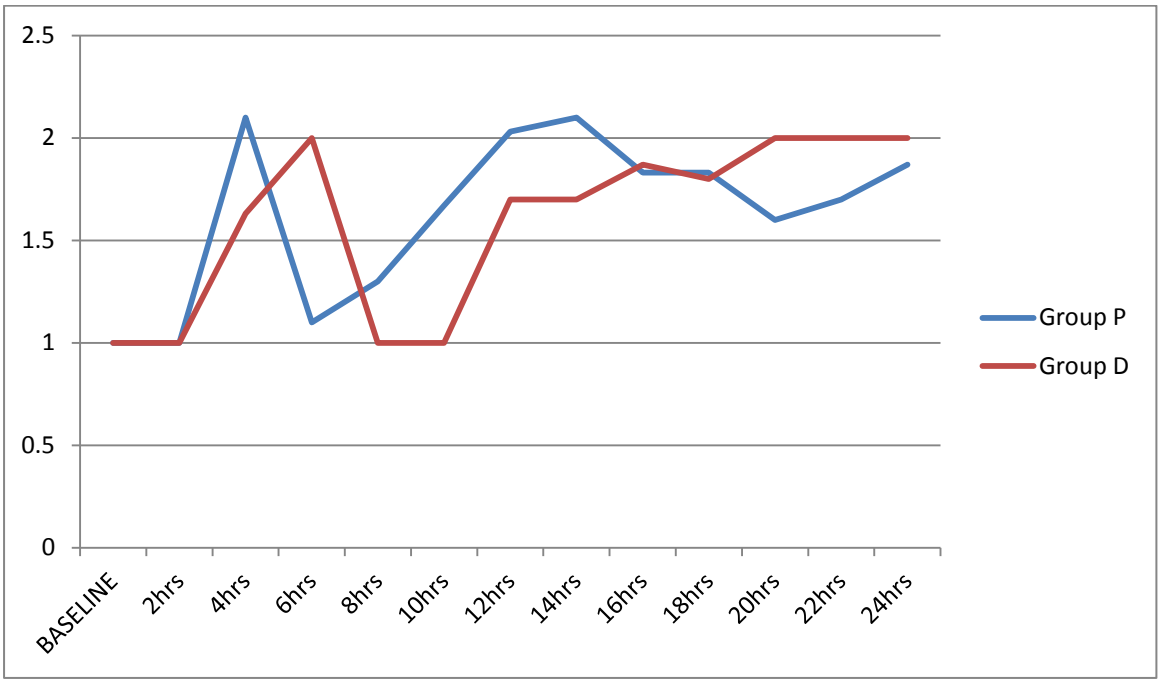


Table - 4: VAS Score (hours) in both groups at different time interval post operatively.

Time (hours)	Group		p-value
	P	D	
Baseline	1±0	1±0	NA
2	1±0	1±0	NA
4	2.1±0.403	1.63±0.49	0.061
6	1.1±0.305	2±0.643	0.082
8	1.3±0.466	1±0	0.001
10	1.67±0.479	1±0	0.007
12	2.03±0.49	1.7±0.466	0.009
14	2.1±0.607	1.7±0.651	0.017
16	1.83±0.648	1.87±0.434	0.816
18	1.83±0.791	1.8±0.484	0.845
20	1.6±0.563	2±0	0.096
22	1.7±0.596	2±0	0.008
24	1.87±0.346	2±0	0.039

Graph – 8: VAS Score (hours) in both groups at different time interval post operatively.



Studies conducted by Hill, et al.; Wichai, et al. and R. Jokela, et al.; found that pain relief and pain intensity was better in group using 300 mg of pregabalin [9, 10, 11]. Pregabalin has oral bio availability of 90% and reaches its maximum plasma concentration within 1 hour. Sedation and dizziness are well known side effects of gabapentinoids. To minimize the incidence of side effects, some adjuvants can be added.

Dexamethasone is a potent synthetic corticosteroid derivative with analgesic, antiemetic and potent anti inflammatory activities. Studies conducted by Mathesian, et al.; using combination of 300 mg of pregabalin and

8 mg of dexamethasone found 50% reduction in postoperative morphine requirements in patients receiving pregabalin [12, 13]. Addition of dexamethasone 8 mg did not provide any beneficial effects on pain and opioid requirements. One reason for this finding could be that the dose of dexamethasone was too low. A higher dose of 0.2-0.4 mg/kg dexamethasone iv is recommended by some authors [14]. Hence we have chosen an optimal dose of 300 mg Pregabalin orally along with 16 mg dexamethasone IV and compared it with pregabalin 300 mg alone, in terms of pain relief and side effects if any.

Graph – 9: Duration of rescue analgesia.

Graph – 10: Rescue analgesia.

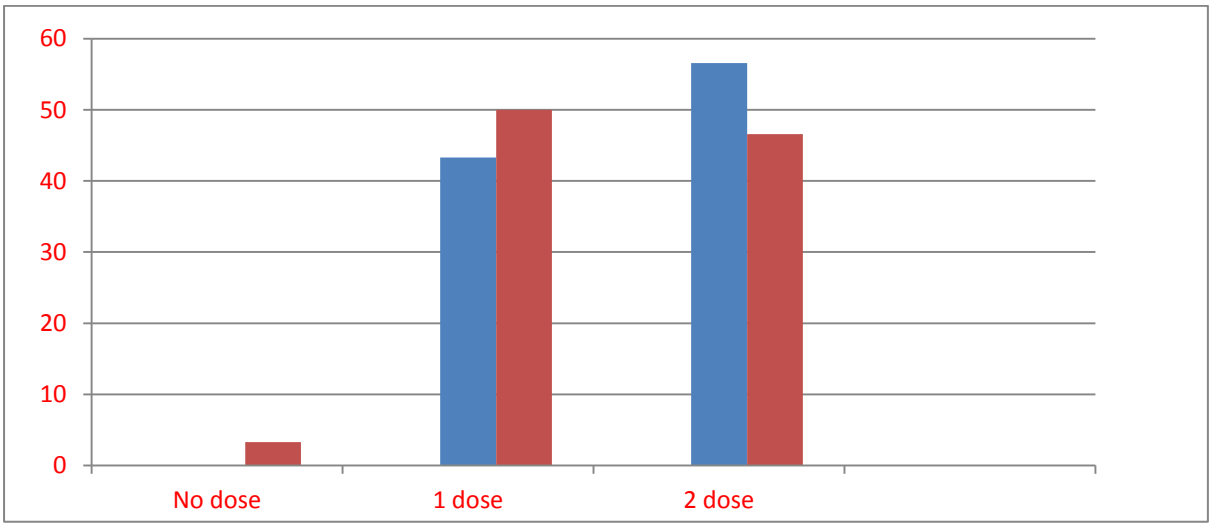


Table – 5: Duration of analgesia.

Duration of Analgesia	Mean±SD		p value
	Group P	Group D	
	10.26+0.382	14.36+ 0.485	0.042

Table – 6: Rescue analgesia.

Group	No Dose		1 Dose		2 Doses	
	No.	%	No.	%	No.	%
P (n=30)	0	0	13	43.3	17	56.6
D (n=30)	1	3.33	15	50.0	14	46.6.0

Table – 7: Complications.

Complications	Group P	Group D	P VALUE
No complications	12 (40%)	23 (76.6%)	0.003
Bradycardia	3 (10%)	2 (6.6%)	0.64
Sedation	8 (26.6%)	3 (10%)	0.09
Headache	1 (3.3%)	0	0.31
Nausea	3(10%)	1 (3.3%)	0.30
Vomiting	3 (10%)	1 (3.3%)	0.30
Visual disturbances	0	0	NA

Conclusion

Preoperative administration of a single dose of 300 mg Pregabalin along with 16 mg Dexamethasone provided analgesic benefits superior to that of pregabalin alone, by reducing the requirement of rescue analgesia. Though not statistically significant, the combination reduces the side effects in 24 hours.

References

1. P. F. White. The changing role of non-opioid analgesic techniques in the management of postoperative pain. Anesthesia and Analgesia, 2005; 101(5): S5–S22.
2. Ho KY, Gan TJ, Habib AS. Gabapentin and postoperative pain. a systematic review of randomized controlled trials. Pain, 2006; 126; 91-101.
3. Hurley RW, Cohen SP, Williams KA, Rowlingson Al, Wu CL. The analgesic effects of perioperative gabapentin on postoperative pain: a meta-analysis. Reg Anesth Pain Med., 2006; 31: 237-247.
4. Mathiesen O, Meniche S, Dahl JB. Gabapentin and postoperative pain: a qualitative and quantitative systematic review, with focus on procedure. BMC Anesthesiol., 2007; 7: 6.
5. N. M. Gajraj. Pregabalin: its pharmacology and use in pain management. Anesthesia and Analgesia, 2007; 105(6): 1805–1815.
6. Field MJ, Holloman EF, McCleary S, Hughes J, Singh L. Evaluation of gabapentin and S-(+)-3-isobutylgaba in a rat model of postoperative pain. J Pharmacol Exp Ther 1997; 282: 1242–6.
7. Gilron I. Gabapentin and pregabalin for chronic neuropathic and early postsurgical pain: current evidence and future directions. Curr Opin Anaesthesiol., 2007; 20: 456–72.
8. Shnekar BF, mCAuley JW.Pregabalin:a new neuromodulator with broad therapeutic indications. Ann Pharmacother., 2005; 39: 2019-37.
9. Hill CM, Balkenohl M, Thomas DW, Walker R, Mathe H, Murray G. Pregabalin in patients with postoperative dental pain. Eur J Pain, 2001; 5: 119–24.
10. Ittichaikulthol Wichai, Virankabutra Tanit, Kunopart Mutita, Khamhom Wachirapol, Putarawuthichai Pipat, Rungphet Suyawej. BN J Med Assoc Thai., 2009; 92(10): 1318–23.
11. Jokela R, Ahonen J, Tallgren M, Haanpaa M, Korttila K. A randomized controlled trial of perioperative ad-ministration of pregabalin

for pain after laparoscopic hysterectomy. Pain, 2008; 134: 106–12.

12. O. Mathiesen, D. G. Jorgensen, K. L. Hilsted, et al. Pregabalin and dexamethasone improves post-operative pain treatment after tonsillectomy. Acta Anaesthesiologica Scandinavica, 2011; 55(3): 297–305.
13. O. Mathiesen, M. L. Rasmussen, G. Dierking et al. Pregabalin and dexamethasone in combination with paracetamol for postoperative pain control after abdominal hysterectomy. A randomized clinical trial. Acta Anaesthesiologica Scandinavica, 2009; 53(2): 227–235.
14. L. Romundstad, A. Stubhaug. Glucocorticoids for acute and persistent postoperative neuropathic pain: what is the evidence? Anesthesiology, 2007; 107(3): 371–373.