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A Comparative Study of Oral Gabapentin Versus Oral Pregabalin In Acute Post-Operative Pain Management In Patients Undergoing Urological Procedures Under Sub-Arachnoid Block.

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I. Aims:

Prove the efficacy of pre-emptive use of pregabalin and gabapentin in the control of post-operative pain by its anti-allodynic and antihyperalgesic activity.

II. Objective:

To assess and compare the efficacy of pregabalin (150mg) and gabapentin (600mg) on pre-emptive administration, in post-operative pain management among patients undergoing urological procedures under sub-arachnoid block.

III. Introduction:

Pain is defined by International Association for Study of Pain (IASP) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage [1]. Acute pain occurs following tissue injury associated with surgery which resolves during the healing process [17]. More than 80% of patients who undergo surgical procedures experience acute post-operative pain [18]. In 75% of patient's severity is reported as moderate, severe or extreme. Less than half of the patients who undergo surgery report adequate pain relief [18]. Inadequately controlled pain negatively affects quality of life, function and functional recovery, the risk of post-surgical complications and persistent post-surgical pain [18].

Traditionally, pain management has been post-operative [3]. Use of opioids, NSAIDs and local anaesthetics have been the routine tools of acute post-operative management [3].

Pre-emptive analgesia is the new modality to reduce post-operative pain, which has proven to be successful [7]. Pre-emptive analgesia is defined as an anti-nociceptive treatment that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain [7]. Pre-emptive analgesia consequently decreases the incidence of hyperalgesia and allodynia after surgery, by decreasing the altered central sensory processing [7]. Drugs such as local anaesthetic injection, opioids, non-steroidal anti-inflammatory drugs, cyclooxygenase-2-inhibitor, Paracetamol, gabapentin, pregabalin, clonidine and dexmeditomidine are routinely used pre-emptive analgesics [2].

The newer anti-epileptics pregabalin and gabapentin act on the $\alpha_2\delta_1$ subunits of the presynaptic voltage-dependent calcium channel [10]. Gabapentin binds to the 21 subunits of the presynaptic voltage gated calcium channels, which are up regulated in the dorsal root ganglia and spinal cord after surgical trauma. It functions by inhibiting the release of substance P, calcitonin and gene-related peptide from the primary afferent nerve fibres in the pain pathway [8]. Pregabalin is a structural analogue of the inhibitory neurotransmitter γ-amino butyric acid. It binds to $\alpha_2\delta_1$ subunit of voltage-gated calcium channels and reduces the release of excitatory neurotransmitters and blocking the hyperalgesia and central sensitization [4]. Pregabalin has a much favourable pharmacokinetic profile, including dose-dependent absorption [8].

The primary aim of this study is to administer oral pregabalin (150mg) and oral gabapentin (600mg) to two groups of patients undergoing elective urological procedure under sub-arachnoid block. Pain levels is assessed through visual analogue scale (VAS).

IV. Materials And Methods:

Source of data: Patients admitted for urological procedures in Sapthagiri Institute of Medical Sciences and Research Institute.

Methods of Collection of Data:
Study Design – Comparative study.
Study Type – Non randomized, multi-arm clinical trial.
Sample Size – 33 per group.

$$n = 2\frac{S^2(Z1 + Z2)^2}{(M1 - M2)^2}$$

M1	Mean VAS Scores in Group A	2.80*
M2	Mean VAS Scores in Group B	2.40*
S1	Standard deviation of VAS Scores in Group A	0.6*
S2	Standard deviation of VAS Scores in Group B	0.5*
S	Pooled SD	0.55
AH	Two sided Alternative Hypothesis	2
1-α	level of confidence	0.95
1-β	level of power of test	0.80
Z1	Z value associated with alpha	1.96
Z2	Z value associated with beta	0.84
n	Minimum sample size	30

Substituting the values in the above formula, sample size obtained is 30.
Since there are 2 groups, total sample size is 30*2= 60.
Considering 10% attrition rate, total sample size is 60+6=66(33 per group).
**Source: Bafna U et al. A comparison of effect of pre-emptive use of oral gabapentin and pregabalin for acute post-operative pain after surgery under spinal anaesthesia. Journal of anaesthesiology clinical pharmacology. 2014; vol 30(3): 373-377.*

Statistical Analysis:
SPSS (Statistical Package for Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] will be used to perform the statistical analysis

- Data will be entered in the excel spread sheet.
- Descriptive statistics of the explanatory and outcome variables will be calculated by mean, standard deviation/median and IQR (based on normalcy test- Shapiro wilk test) for quantitative variables, frequency and proportion for qualitative variables.
- Chi-square test will be applied to find the association of qualitative variables.
- Independent sample t test / Mann-Whitney test (based on data distribution) will be applied to compare the quantitative parameters between the groups.
- Test (based on data distribution) will be applied to compare the quantitative parameters between the groups.
- Data will be represented graphically wherever necessary using Pie diagram, Bar graph.

Inclusion Criteria:
1. Patients willing to give written informed consent.
2. Patients undergoing urological procedure.
3. ASA Grade – 1 & 2 patients.
4. Age – 18 to 70 years.

Exclusion Criteria:
1. ASA Grade – 3 and above.
2. Age less than 18 years or more than 70 years.
3. Patients with known allergy to pregabalin, history of intake of NSAIDs within 48 hours of surgery, coagulation abnormalities.
4. Patients on anticoagulant and antiplatelet medications.

Methodology:
After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent (Annexure – 1).

Demographic details of the patients were recorded as per the case record form (Annexure – 2).

After a thorough pre-operative evaluation, visual analogue score (VAS) was explained to the patient. Patients were pre-medicated with Tab. Pantoprazole 40mg. Patients were divided into two groups by alternate random technique, while they were unaware as to which group they belong.

Group A received T. Pregabalin 150mg and Group B received T. Gabapentin 600mgPatient was shifted to the operating room, sub-arachnoid block was given with Inj. Bupivacaine heavy (0.5%) at a dose of 0.3mg/kg body weight with maximum dose limited to 20mg and the level was assessed.

After surgery, patients were shifted to the recovery room. All patients were given Inj. Tramadol 50mg IV or Inj. Paracetamol 1gm IV as rescue analgesia, once VAS exceeds 4. The patients were subsequently shifted to ward.

Post-operatively VAS score was assessed at 0,2,4,6 and 12 hours after surgery. Total amount of analgesic administered was recorded. Any adverse events like giddiness, nausea, vomiting in the first 24 hours of post-operative period was noted.

V. Results:

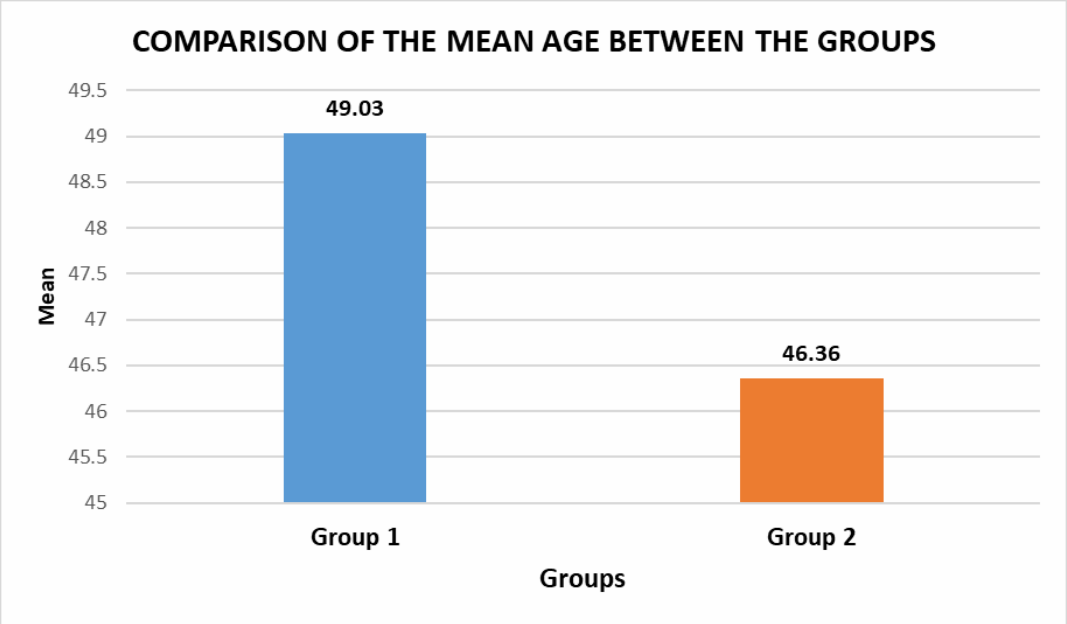
This comparative study was done on patients undergoing urological procedures under spinal anaesthesia in a tertiary care centre in South India. 66 patients were included in the study during the period of June 2024 – August 2024. A thorough preoperative anaesthetic assessment was done and candidates who qualified the inclusion criteria were selected. Suitable measures were taken to include various age groups and both sexes into the study. **SPSS (Statistical Package for Social Sciences)** version 20. (IBM SPASS statistics [IBM corp. released 2011] was be used to perform the statistical analysis.

Table – 1 & Graph – 1 suggest that, the mean age of the patients belonging to Group – 1 was 49.03 and Group – 2 was 46.36. The two groups are comparable as the 'p' value > 0.05.

Table 1: Comparison Of The Mean Age Between The Groups Using Independnent Sample T Test.

Groups	Minimum	Maximum	Mean	S.D	Mean Diff	P Value
Group 1	20.0	75.0	49.03	15.30	2.66	0.516
Group 2	23.0	85.0	46.36	17.81		

Graph 1: Comparison Of The Mean Age Between The Groups Using Independnent Sample T Test.



As depicted in Table – 2 & Graph – 2, maximum subjects belong to the age group between 20 to 35 years (28.8%) and 51 to 65 years (28.8%), followed by 36 to 50 years (25.8%) and >65 years (16.7%). All the groups are comparable as the 'p' value > 0.05.

Table 2: Distribution Of The Subjects Based On Age Groups.

Age Groups		Groups		Total
		Group 1	Group 2	
20 to 35 years	Count	6	13	19
	%	18.2%	39.4%	28.8%
36 to 50 years	Count	11	6	17

	%	33.3%	18.2%	25.8%
51 to 65 years	Count	11	8	19
	%	33.3%	24.2%	28.8%
>65 years	Count	5	6	11
	%	15.2%	18.2%	16.7%
Total	Count	33	33	66
	%	100.0%	100.0%	100.0%
Chi-square value-4.61				
p value-0.202				

Graph 2: Distribution Of The Subjects Based On Age Groups.

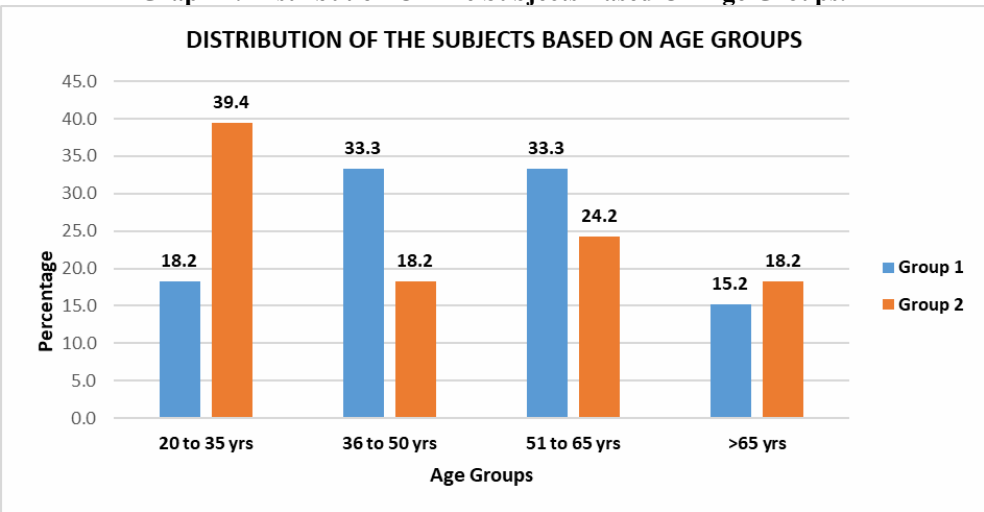
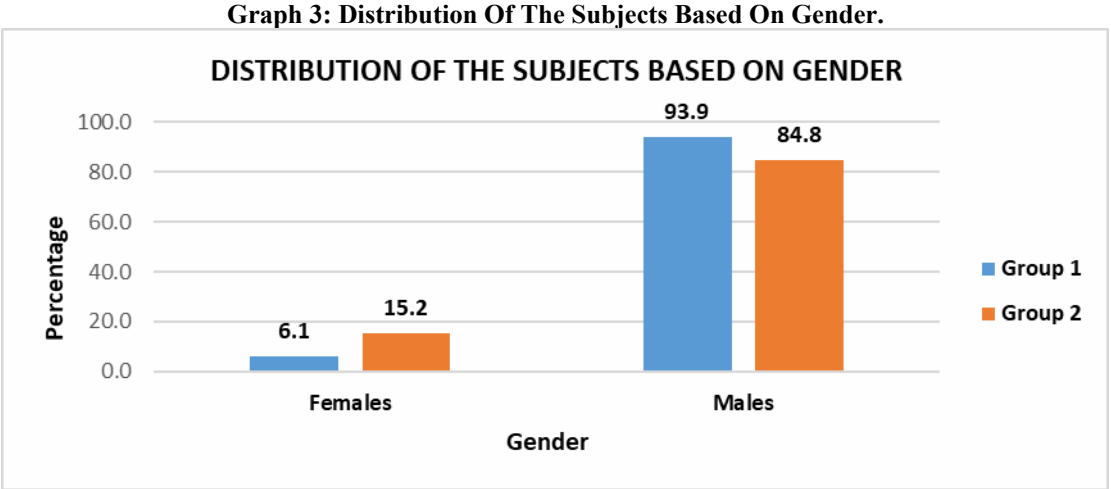


Table – 3 indicates that predominantly males (89.4%) were recruited.

Table 3: Distribution Of The Subjects Based On Gender.

Gender		Groups		Total
		Group 1	Group 2	
Females	Count	2	5	7
	%	6.1%	15.2%	10.6%
Males	Count	31	28	59
	%	93.9%	84.8%	89.4%
Total	Count	33	33	66
	%	100.0%	100.0%	100.0%
Chi-Square Value- 1.43				
P Value-0.23				

Graph 3: Distribution Of The Subjects Based On Gender.

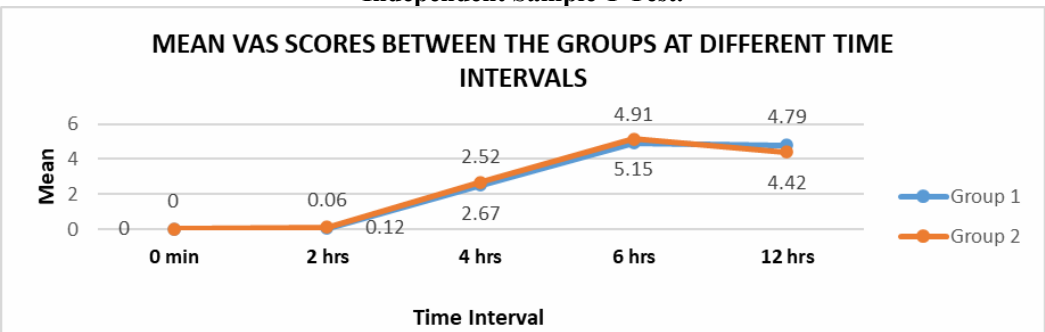


As shown in Table – 4, at 0 minutes the mean VAS is 0, while at 2 hours the mean VAS is 0.06 for Group – 1 and 0.12 for Group – 2, with a 'p' value > 0.05 which suggests that the two groups are comparable. At 4 hours, mean VAS of Group – 1 is 2.52 and that of Group – 2 is 2.67, with a 'p' vale >0.05, which suggests the two groups have a comparable mean VAS. At 6 hours, mean VAS of Group – 1 is 4.91 while that of Group – 2 is 5.15, with 'p' value > 0.05, indicating the similarity between the two groups. At 12 hours post procedure, the mean VAS among Group – 1 is 4.79 and Group – 2 is 4.42 with a 'p' value >0.05, suggesting the two groups have a comparable VAS. From the table, it can be observed that the highest VAS scores were noted at 6 and 12 hours; mean VAS score was noted to be highest at 6 hours in Group – 2.

Table 4: Comparison Of The Mean Vas Scores Between The Groups At Different Time Intervals Using Independent Sample T Test.

Vas Score	Groups	N	Minimum	Maximum	Mean	S.D	Mean Diff	P Value
0 Min	Group 1	33	0.0	0.0	0.00	0.00	-	-
	Group 2	33	0.0	0.0	0.00	0.00		
2 Hrs	Group 1	33	0.0	2.0	0.06	0.35	-0.06	0.562
	Group 2	33	0.0	2.0	0.12	0.48		
4 Hrs	Group 1	33	0.0	6.0	2.52	1.39	-0.15	0.58
	Group 2	33	0.0	4.0	2.67	0.78		
6 Hrs	Group 1	33	2.0	8.0	4.91	1.38	-0.24	0.487
	Group 2	33	2.0	8.0	5.15	1.44		
12 Hrs	Group 1	33	3.0	8.0	4.79	1.34	0.36	0.231
	Group 2	33	2.0	6.0	4.42	1.09		

Graph 4: Comparison Of The Mean Vas Scores Between The Groups At Different Time Intervals Using Independent Sample T Test.

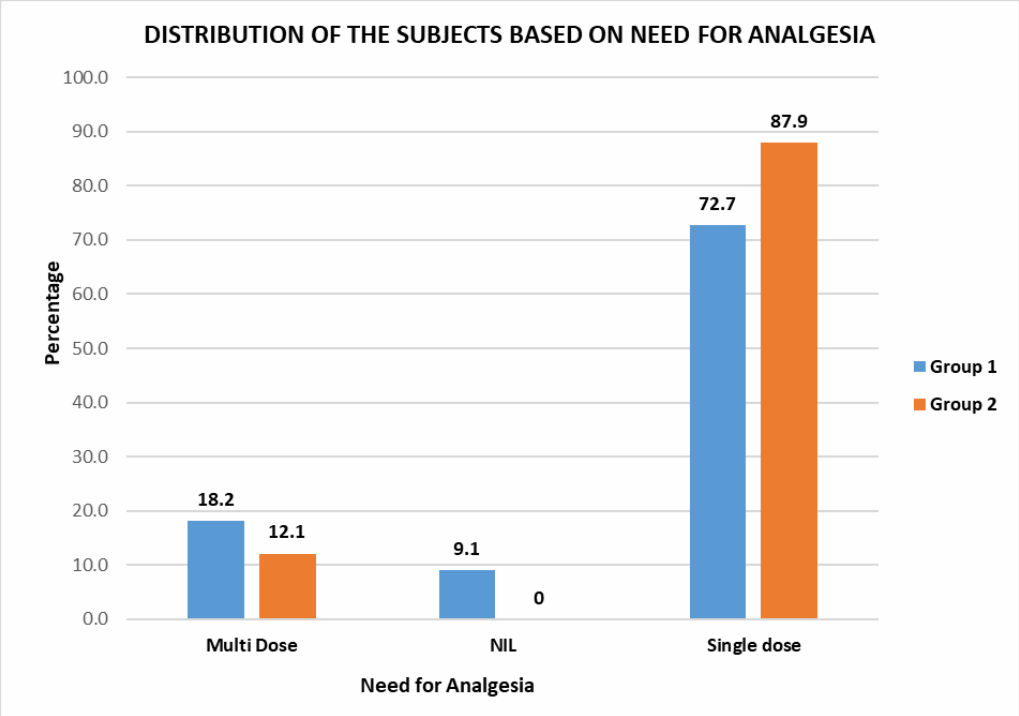


Data from table 5 suggests that, requirement of rescue analgesia is higher among individuals of Group – 2 as compared to Group – 1. Multi-dose analgesia requirement was higher among participants of Group – 1 over Group – 2.

Table 5: Distribution Of The Subjects Based On Need For Analgesia

Need For Analgesia		Groups		Total
		Group 1	Group 2	
Multi Dose	Count	6	4	10
	%	18.2%	12.1%	15.2%
Nil	Count	3	0	3
	%	9.1%	0.0%	4.5%
Single Dose	Count	24	29	53
	%	72.7%	87.9%	80.3%
Total	Count	33	33	66
	%	100.0%	100.0%	100.0%
Chi-Square Value- 3.87				
P Value-0.144				

Graph 5: Distribution Of The Subjects Based On Need For Analgesia



VI. Discussion:

In this comparative study, we assessed post-operative pain among 66 patients, using VAS score as the tool and compared the two drugs under study. It can be concluded that pre-emptive analgesia significantly prolonged analgesia and reduced the need for rescue analgesia in the immediate post-operative period. The two drugs under study, Pregabalin and Gabapentin had comparable outcome with slight differences. Need for rescue analgesia was slightly higher among subjects receiving Gabapentin while need for multidose analgesia was higher among those with Pregabalin. Post-operative recovery was uneventful. Gabapentinoids such as gabapentin and pregabalin show anti-allodynic by reducing the hyper-excitability of dorsal horn neurons induced by tissue damage [4].

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