‘‘Which One Should Be Preferred in Cervical Percutaneous Epidural Neuroplasty?’’

Statistical Analysis

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Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 32.0 (IBM Corp. , The study was conducted using Armonk , NY, USA. The distribution characteristics of continuous variables were examined; variables conforming to a normal distribution were presented as mean ± standard deviation, variables not showing a normal distribution were presented as median and interquartile range (IQR), and categorical variables were presented as number and percentage. One-way analysis of variance (ANOVA) or Kruskal -Wallis test was used to compare baseline characteristics among the three groups, depending on the distribution of the data. Categorical variables were evaluated using the chi-square test, and in cases where the expected number of cells was low, the exact /Monte Carlo methods were used. Bonferroni correction was applied for necessary multiple comparisons . The change in NRS and NDI scores over the follow-up period was evaluated using linear mixed models, taking baseline values into account. The effects of group, time, and the combined effect of group and time were examined in the models, and adjusted values were used. estimated marginal This was reported with 95% confidence intervals. The temporal variation of pregabalin dose was similarly linear , taking into account the initial dose. The analysis was performed using a mixed model. Temporal variation in opioid use was generalized due to its binary structure. estimating The results were evaluated using the Genetic Equation (GEE). Patients showing a ≥50% reduction in NRS from baseline were also defined as responders, and these rates were compared between groups. All tests were performed two-way, and $p<0.05$ was considered statistically significant. The graphs for the study were prepared using Python / Matplotlib in the Google Colab environment .

3. Findings

Initially, 75 patients were evaluated, seven patients were dropped out of follow-up, and five patients declined the intervention. The final analysis was performed on 63 patients. 21 patients were in the 0.9% saline group, 20 in the 5% saline group, and 22 in the 10% saline group. Follow-up data from months 1 , 3, 6, and 12 were included in the analysis. There were no significant differences between the saline groups in terms of age, pain duration, gender, target level, and baseline NRS score.

The pre-procedure NDI score showed a borderline significant difference between the groups (p=0.046). In the Tukey post-hoc pairwise comparison, this difference was found only between the 0.9% and 5% saline groups (mean difference 3.98 points; 95% CI 0.05–7.91; adjusted p=0.047). While there was no significant difference between the groups in terms of pre-procedure opioid dose (p=0.057), there was a significant difference between the groups in terms of pre-procedure pregabalin dose (p=0.031), and in the pairwise comparison, this difference was found between the 5% and 10% groups (Bonferroni adjusted p=0.036). Pre-procedure characteristics of the groups are presented in Table 1.

Table 1. Pre-treatment demographic and clinical characteristics of the groups.

Variable		**0.9% (n=21)**	**5% (n=20)**	**10% (n=22)**	**p**
Age (years), mean ± SD		42.52 ± 9.59	38.90 ± 10.02	40.45 ± 11.71	0.544
Pain duration (months), mean ± SD		17.81 ± 2.80	17.95 ± 2.80	18.41 ± 3.29	0.789
Gender n (%)	Male	8 (38,1)	9 (45.0)	9 (40,9)	0.903
	Woman	13 (61,9)	11 (55.0)	13 (59,1)	

Target level n (%)	C4-5	1 (4,8)	1 (5.0)	1 (4,5)	0.757
	C5-6	7 (33.3)	5 (25.0)	10 (45.5)	
	C6-7	10 (47.6)	10 (50.0)	10 (45.5)	
	C7-T1	3 (14,3)	4 (20.0)	1 (4,5)	
Target side n (%)	Right	12 (57,1)	8 (40.0)	11 (50.0)	0.545
	Left	9 (42,9)	12 (60.0)	11 (50.0)	
NRS		6.67 ± 0.97	6.60 ± 1.10	6.73 ± 0.94	0.863
NDI		28.43 ± 6.04	24.45 ± 4.93	25.45 ± 4.66	**0.046**
Opioid Dose, Median (IQR)		20 (15-50)	10 (10-20)	10 (9-22.5)	0.057
Pregabalin Dose, Median (IQR)		300 (150-300)	300 (150-300)	300 (300-337.5)	**0.031**

P values indicate the overall group comparison. For NDI, the post-hoc comparison for 0.9%-5% was p=0.047; for pregabalin starting dose 5%-10%, the Bonferroni corrected p=0.036. Mean : mean, SD: standard deviation, NRS: numeric Rating Scale , NDI: Neck Disability Index, IQR: interquartile range .

NRS scores decreased significantly in all groups after the procedure and remained at low levels until the 12th month (Table 2). In the analysis adjusted for baseline NRS values, there was no overall significant difference between the groups during the follow-up period (p=0.713). The change between the 1st , 3rd, 6th, and 12th month measurements was also not significant (p=0.209). The trend of change over time was similar for the groups (p=0.848). No significant difference was found between the groups at each follow-up time (p=0.560, p=0.845, p=0.677, and p=0.709 for the 1st , 3rd, 6th, and 12th months, respectively). A significant relationship was found between pre-procedure NRS levels and follow-up scores (p<0.001), and this relationship did not change over time (p=0.319).

In the categorical analysis, where clinical response was defined as at least a 50% reduction from the baseline NRS score, the overall response rate was 90.5% at month 1, 92.1% at month 3, 92.1% at month 6, and 93.7% at month 12. There were no significant differences between the saline groups in these rates across all follow-up periods (Table 2) . (Figure 4)

NDI scores decreased in all groups after the intervention. Since baseline NDI values differed between groups, follow-up analyses were corrected to account for this baseline difference. In the corrected analysis, no overall significant difference was found between groups during the follow-up period (p=0.417). However, NDI scores showed a significant change over time (p=0.017), and the pattern of this change differed between groups (p=0.015). However, when the corrected NDI values at months 1 , 3, 6, and 12 were evaluated separately, no significant difference was found between the groups (p=0.780, p=0.595, p=0.274, and p=0.132, respectively). In addition, baseline NDI levels were significantly associated with follow-up scores (p<0.001).

In within-group comparisons, the time effect for NDI was significant in all three groups (0.9%: p=0.006; 5% and 10%: p<0.001). In Bonferroni -adjusted comparisons, the 1-3 and 1-6 month differences were significant in the 0.9% group (p=0.009 and p=0.008). In the 5% group, the 3rd , 6th, and 12th month values were lower than the 1st month values (all p<0.001). In the 10% group, the 1-3 month (p=0.016), 1-6 month (p<0.001), and 1-12 month (p<0.001) differences, as well as the 3-6 month (p=0.001) and 3-12 month (p<0.001) differences were significant; no additional change was detected between 6-12 months (p=0.265). These results show that while there are some differences in the timing of improvement, there is no superiority at any particular follow-up time. (Table 2) .: (Figure 4)

Table 2. NRS, NDI, and clinical response outcomes.

Conclusion	Time	0.9%	5%	10%	p
NRS (Mean ± SD)	Pre-procedure	6.67 ± 0.97	6.60 ± 1.10	6.73 ± 0.94	0.863
	1st month	2.48 ± 1.54	2.05 ± 1.39	2.45 ± 1.26	0.560
	3rd month	2.29 ± 1.42	2.05 ± 1.19	2.23 ± 1.11	0.845
	6th month	2.19 ± 1.44	1.90 ± 1.21	2.00 ± 1.20	0.677
	12th month	2.33 ± 1.32	2.10 ± 1.25	2.14 ± 1.25	0.709
NDI (Mean ± SD)	Pre-procedure	28.43 ± 6.04	24.45 ± 4.93	25.45 ± 4.66	**0.046**
	1st month	9.52 ± 4.85	7.65 ± 3.17	7.59 ± 3.40	0.780
	3rd month	7.90 ± 4.57	5.80 ± 2.24	6.59 ± 3.22	0.595
	6th month	7.90 ± 4.91	5.55 ± 2.21	5.73 ± 2.64	0.274
	12th month	7.86 ± 5.25	5.10 ± 2.07	5.27 ± 2.51	0.132
≥50% NRS response n /N (%)	1st month	18/21 (85.7)	19/20 (95.0)	20/22 (90.9)	0.772
	3rd month	18/21 (85.7)	19/20 (95.0)	21/22 (95.5)	0.512
	6th month	18/21 (85.7)	19/20 (95.0)	21/22 (95.5)	0.512
	12th month	19/21 (90.5)	19/20 (95.0)	21/22 (95.5)	0.838

Pre-treatment p-values represent baseline comparisons. Follow-up NRS and NDI p-values represent group comparisons at each time point in a longitudinal model adjusted for baseline scores; clinical response p-values represent Fisher-Freeman-Halton Monte Carlo comparisons.

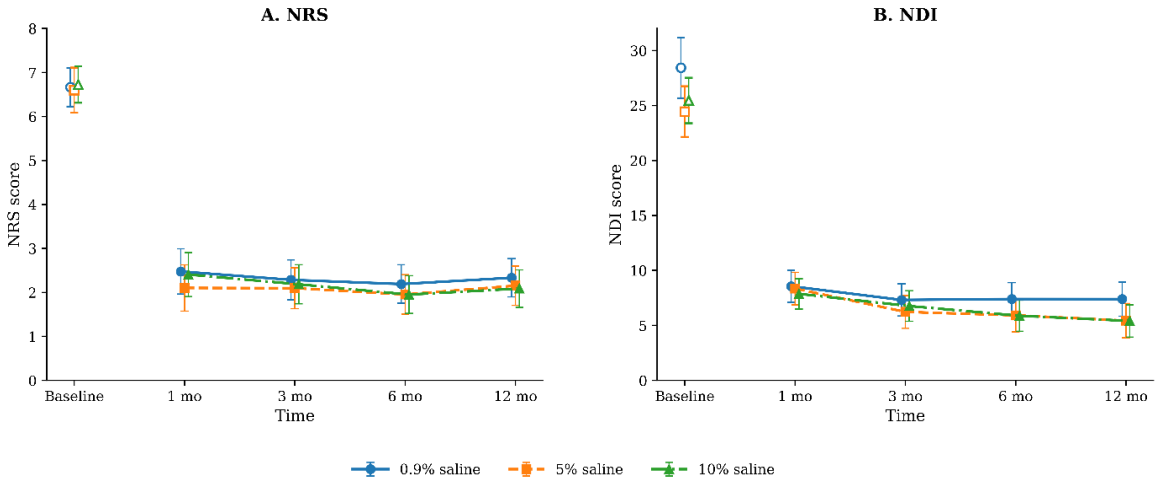


Figure 4. Saline The temporal trend of NRS and NDI scores according to concentration .
Open symbols represent observed baseline averages, while filled symbols represent estimated marginal averages adjusted for baseline values over follow-up periods. Error bars indicate 95% confidence intervals.
For NRS, the group effect (p=0.713), time effect (p=0.209), and group×time interaction (p=0.848) were not significant. For NDI, the group×time interaction was significant (p=0.015); however, the adjusted intergroup difference was not significant at any follow-up time point.

opioids was 61 (96.8%) at the pre-procedure period, 31 (49.2%) at 1 month, 15 (23.8%) at 3 months, 9 (14.3%) at 6 months, and 5 (7.9%) at 12 months. In repeated measures analysis, the probability of not using opioids increased significantly over time (p<0.001); there was no significant difference between groups during the follow-up period (p=0.624), and the course of change was similar to saline. There was no difference according to concentrations (p=0.883). The corrected likelihood of opioid non-use was 51% (95% CI 39%-63%), 77% (65%-86%), 86% (75%-93%), and 92% (82%-97%) at 1, 3, 6, and 12 months, respectively. In Bonferroni - adjusted comparisons, the differences at 1-3, 1-6, and 1-12 months were significant at p<0.001, and the difference at 3-12 months was significant at p=0.006; however, the differences at 3-6 months (p=0.076) and 6-12 months (p=0.278) were not significant. Opioid dose changes from baseline were also not different between groups at any follow-up time (p=0.207, p=0.211, p=0.158 and p=0.141 for months 1 , 3, 6 and 12, respectively). (Table 3)

Pregabalin was used in all patients before the procedure, at 1 month, and at 3 months. The discontinuation rate was 9.5% at 6 months and 14.3% at 12 months. Discontinuation rates were not different between groups at 6 months (p=0.150); although numerically higher in the 5% group at 12 months, the difference did not reach statistical significance (p=0.070).

pre-treatment pregabalin doses differed significantly between groups, follow-up doses were adjusted to baseline values. In the adjusted analysis, there was no overall significant difference

between groups during the follow-up period (p=0.847). The overall change between follow-up time points was also not statistically significant (p=0.065). However, although the pregabalin dose decreased in all groups during the follow-up period, the magnitude and timing of the decrease differed between groups (group × time interaction, p=0.038). Nevertheless, no significant difference was found between groups at any follow-up time point. The baseline dose was strongly correlated with follow-up doses (p<0.001). In contrast, adjusted doses did not differ between groups at any single follow-up time point (p=0.252, p=0.351, p=0.668, and p=0.592 for months 1 , 3, 6, and 12). The within-group time effect was significant in all three saline groups (all p<0.001). Bonferroni -adjusted within-group comparisons were significant in the 0.9% group at 1-3, 1-6, and 1-12 months (all p<0.001) and 3-12 months (p=0.027); in the 5% group at 1-6 and 1-12 months (p<0.001), 3-6 months (p=0.003), and 3-12 months (p<0.001); and in the 10% group at 1-3, 1-6, 1-12, 3-12, and 6-12 months (all p<0.001). Unconsidered crude pregabalin dose comparisons at 1 , 3, and 6 months were nominally significant (p=0.014, p=0.011, and p=0.040), but not at 12 months (p=0.363). In the dose change analysis from baseline, only the overall group comparison at 12 months was significant (p=0.040); however, pairwise comparisons remained insignificant after multiple test correction (10%-0.9% p=0.085; 10%-5% p=0.089; 0.9%-5% p=1.000). (Table 3) (Figure 5)

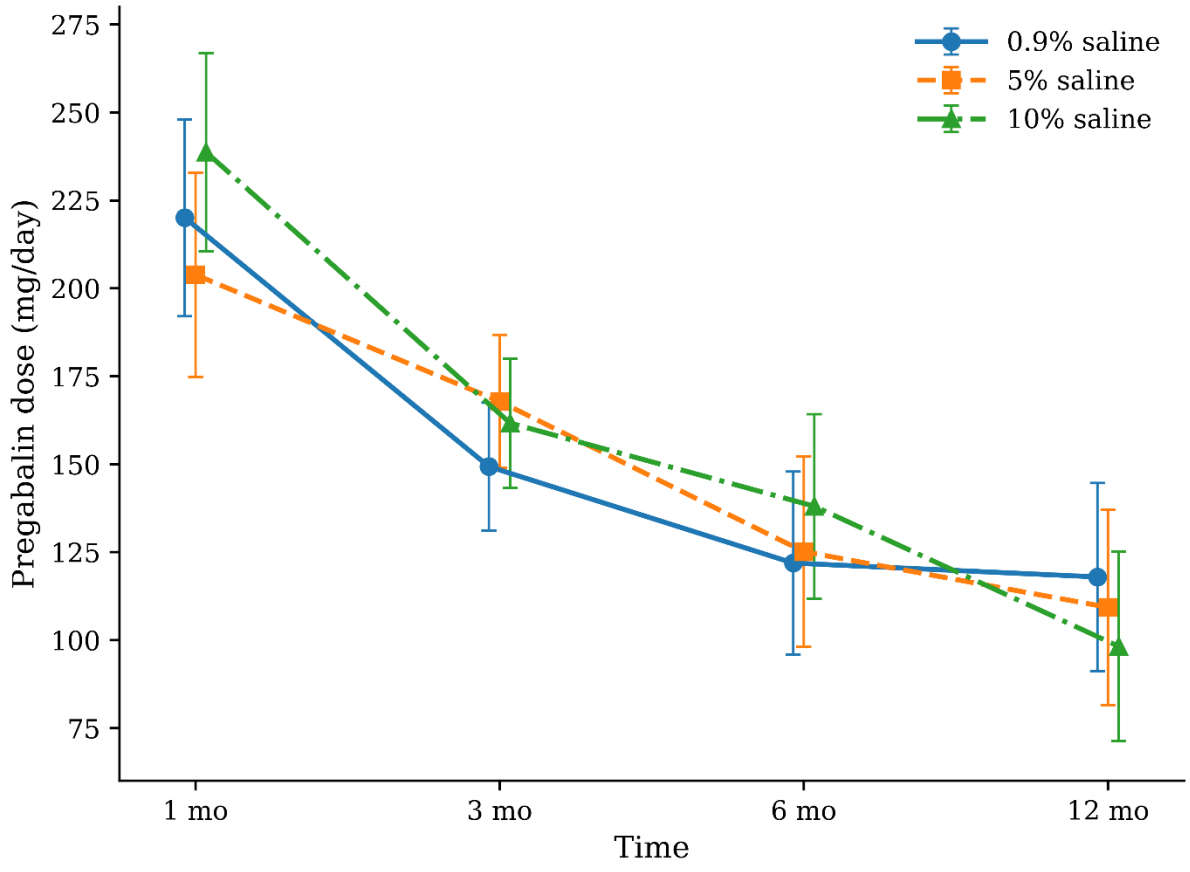


Figure 5. Estimated marginal mean pregabalin doses adjusted for baseline pregabalin dose at follow-up periods according to saline concentration .
Error bars indicate 95% confidence intervals.
The group×time interaction was significant (p=0.038); however, adjusted intergroup comparisons were not significant at any follow-up time point.

Table 3. Opioid and pregabalin dosages and usage rates.

Medicine	**Time**	**0.9%**	**5%**	**10%**	**Use p**	**Dose p**
Opioid Median (IQR) n /N (%)	1st month	10 (0-25) 12/21 (57.1)	0 (0-17.5) 8/20 (40.0)	5 (0-12.5) 11/22 (50.0)	0.567 [a]	0.207 [b]
	3rd month	0 (0-15) 7/21 (33.3)	0 (0-0) 3/20 (15.0)	0 (0-2.5) 5/22 (22.7)	0.405 [a]	0.211 [b]
	6th month	0 (0-0) 3/21 (14.3)	0 (0-0) 2/20 (10.0)	0 (0-0) 4/22 (18.2)	0.902 [a]	0.158 [b]
	12th month	0 (0-0) 2/21 (9.5)	0 (0-0) 1/20 (5.0)	0 (0-0) 2/22 (9,1)	1,000 [a]	0.141 [b]
Pregabalin Median (IQR) n /N (%)	1st month	150 (150-300) 21/21 (100)	150 (93.75-300) 20/20 (100)	300 (150-300) 22/22 (100)	-	0.252 [c]
	3rd month	150 (75-150) 21/21 (100)	150 (75-150) 20/20 (100)	150 (150-300) 22/22 (100)	-	0.351 [c]
	6th month	150 (75-150) 18/21 (85.7)	75 (75-150) 17/20 (85.0)	150 (131.25-150) 22/22 (100)	0.150 [a]	0.668 [c]

	12th month	75 (75-150) 19/21 (90.5)	75 (0-150) 14/20 (70.0)	75 (75-150) 21/22 (95.5)	0.070 [a]	0.592 [c]

[a]: Comparison of usage rates by Fisher – Freeman – Halton groups The exact /Monte Carlo test was used. [b]: For opioids , p-values show the Kruskal -Wallis test for group comparison of dose change from baseline at the respective follow-up time. [c]: For pregabalin , p-values show the adjusted group comparison at each follow-up time in a linear mixed model considering the baseline pregabalin dose. Since pregabalin was used by all patients at months 1 and 3, no comparable variability was found between groups, and a p-value was not calculated.