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A COMPARATIVE STUDY TO EVALUATE THE ANALGESIC EFFECT OF AMITRIPTYLINE AND PREGABALIN IN ACUTE PHASE OF HERPES ZOSTER

Anaesthesiology

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ABSTRACT

INTRODUCTION: We present a study in which 90 patients of age ≥ 40 years, diagnosed as herpes zoster, divided into three groups and subsequently followed up for 14 weeks to assess the severity of pain using the Visual analogue scale (VAS) score.

MATERIAL AND METHODS: Patients in group A, B and C were given tab. amitriptyline 25 mg at night, tab. pregabalin 75 mg twice daily and only conventional analgesics for 12 weeks respectively. VAS score was assessed after every 2 weeks, for 14 weeks.

OBSERVATIONS AND RESULT: VAS scores were significantly lower in group A and group B as compared to group C at various time periods till 14 weeks ($p \leq 0.05$).

CONCLUSION: We conclude that starting tab. amitriptyline or tab. pregabalin in acute phase of herpes zoster can significantly reduce the severity of pain in later course.

KEYWORDS

Herpes zoster, amitriptyline, pegabalin.

INTRODUCTION

Herpes zoster (HZ) is caused by activation of varicella-zoster virus. It is divided into three phases i.e., acute, subacute and chronic phase. Pain is the predominant symptom in all phases of HZ disease. Acute phase usually subsides in days or weeks but, in some cases the pain persists. Post Herpetic Neuralgia (PHN) is the most common complication of the HZ, it is characterized by constant and/or intermittent paroxysmal pain persisting for ≥ 90 days after the onset of HZ rash. The chances of developing PHN in patients with herpes zoster increases with the age of the patient. Successful management of PHN can be complicated and challenging. Various studies suggest that amitriptyline and pregabalin are effective in reducing pain due to PHN and other neuropathies. There are multiple studies on management of pain of PHN but little has been explored on early treatment of acute herpetic neuralgia and impact on its sequelae (i.e. PHN). Only few studies are there on early treatment of acute herpetic neuralgia and out of which only limited are there on Indian population hence we evaluated the role of amitriptyline and pregabalin in reducing the pain of PHN, when started in acute phase of HZ.[1,2,3]

MATERIAL AND METHODS

This prospective, randomized and comparative study was conducted in the Department of Anesthesiology and Critical Care in collaboration with Department of Dermatology, in a tertiary care hospital. A total of 90 patients of acute herpes zoster infection, presenting with rash (above 40 years age), of either sex, willing to participate were included in the study. After obtaining informed written consent, they were randomly divided into three groups (n=30) and were followed up after every 2 weeks till 14 weeks.

All patients were subjected to detailed clinical history and examination in the pain clinic. All patients were assessed for the area of distribution of pain, the time since onset of rash (in days).

All the patients with acute HZ were managed as per the standard protocol which includes tab. acyclovir 800 mg five time per day for 7-10 days and for the pain relief tab. paracetamol 500 mg (SOS/TDS) or tab. diclofenac 50 mg (BD/SOS) or tab. tramadol 50 mg (BD/SOS) were given depending upon the pain relief of the patients. In addition to the above, the patients in the group A received tab. amitriptyline 25 mg at night, in group B received tab. pregabalin 75 mg twice daily while the patients in group C didn't receive either of the two for 12 weeks.

All the patients were assessed for pain (VAS score) and side effects on the day of visit and after every 2 weeks till 14 weeks. At the end of 14 weeks patient satisfaction was assessed regarding the pain control. The primary outcome measured in the study was the VAS score. The secondary outcomes measured included the development of PHN and side effects

STATISTICAL ANALYSIS

At the end of the study all the data was compiled and analyzed statistically. All the data collected was assessed using Statistical Package for the Social Sciences (SPSS 20.0). Analysis of variance (ANOVA) test was used to test the difference in age, time since onset of rash (in days) and VAS scores. Chi-square test/ Fischer's exact test was used to test the difference in sex distribution, area of distribution of rash and PHN. Independent student-t test was used to test the difference in VAS scores between the two groups at a time. For all statistical purposes, results were considered statistically significant if the p-value was ≤ 0.05.

OBSERVATIONS AND RESULTS

All the three groups were comparable regarding patient demographic profile (age and sex distribution), time since onset of rash (in days), area of distribution of rash and VAS score at presentation (p-value >0.05) (table 1).

In our study, the VAS scores in group A and group B were significantly lower than the VAS scores of group C at 2, 4, 6, 8, 10, 12 and 14 weeks (p-value<0.05) (table 2). However, there was no statistically significant difference in the VAS scores between the group A and group B (table 3) at various time intervals. In group A, B and C, 3(10%), 5(16.7%) and 8 (26.7%) patients respectively continued to have pain (i.e. developed PHN) though it was statistically not significant (figure 1).

The patients in group A predominantly complained of dry mouth and dizziness while in group B complained of somnolence, dizziness and gastrointestinal symptoms. Whereas, patients in group C predominantly complained of gastrointestinal symptoms and somnolence. There was no statistically significant difference noted between the three groups with respect to the total amount of analgesic consumed during the study period. Patient satisfaction was assessed at the end of the study and there was statistically and clinically significant difference among the three groups (p<0.05).

Table 1:- Comparison of demographic profile and clinical variables between the groups.

Variables		Group A	Group B	Group C	p-value
Age (in years)		58.37±9.19	60.70±9.52	61.77±6.97	.31
Time since onset of rash (days)		3.70 ± .915	3.87 ± .900	3.77 ± .774	.61
Sex	Male	18(60%)	16(53.3%)	21(70%)	.41
	Female	12(40%)	14(46.7%)	9(30%)	
Area of distribution of rash	Cervical	5(16.7%)	5(16.7%)	3(10%)	.642
	Thoracic	13(43.3%)	16(53.3%)	19(63.3%)	
	Lumbar	12(40%)	9(30%)	8(26.7%)	
VAS at day 1		88.67 ± 3.46	87.00 ± 5.96	88.33 ± 4.61	.365

Table 2:- Comparison of VAS scores between the groups at various time intervals.

Time	Group A Mean ± SD	Group B Mean ± SD	Group C Mean ± SD	p-value
VAS at day 1	88.67 ± 3.46	87.00 ± 5.96	88.33 ± 4.61	.365
VAS at 2 weeks	56.33 ± 6.69	56.67 ± 6.07	61.00 ± 8.03	.018*
VAS at 4 weeks	44.00 ± 5.63	45.67 ± 5.04	50.00 ± 5.87	.000***
VAS at 6 weeks	32.67 ± 5.83	33.33 ± 6.06	38.67 ± 7.67	.001**
VAS at 8 weeks	21.00 ± 8.85	21.33 ± 8.19	28.00 ± 11.27	.011*
VAS at 10weeks	8.67 ± 6.81	10.00 ± 7.88	16.00 ± 12.20	.007**
VAS at 12 weeks	2.33 ± 7.28	2.67 ± 6.92	9.33 ± 15.52	.020*
VAS at 14 weeks	1.67 ± 5.92	2.33 ± 6.26	8.33 ± 14.40	.016*

Table 3: Comparison of VAS score between the group A and group B at various time intervals

Time	Group A Mean ± SD	Group B Mean ± SD	p-value
VAS at day 1	88.67 ± 3.46	87.00 ± 5.96	.19
VAS at 2 weeks	56.33 ± 6.69	56.67 ± 6.07	.84
VAS at 4 weeks	44.00 ± 5.63	45.67 ± 5.04	.23
VAS at 6 weeks	32.67 ± 5.83	33.33 ± 6.06	.67
VAS at 8 weeks	21.00 ± 8.85	21.33 ± 8.19	.88
VAS at 10weeks	8.67 ± 6.81	10.00 ± 7.88	.48
VAS at 12 weeks	2.33 ± 7.28	2.67 ± 6.92	.85
VAS at 14 weeks	1.67 ± 5.92	2.33 ± 6.26	.67

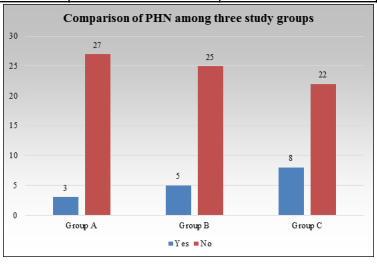

Figure 1:- Comparison of PHN among three groups

DISCUSSION

The present study demonstrates that patients receiving amitriptyline or pregabalin reported significantly greater reduction in the pain as compared to the control group at various time intervals, when treatment was started in the acute phase of the herpes zoster. Various studies have suggested the efficacy of long term treatment with amitriptyline or/and pregabalin in reducing PHN pain, infact both the above drugs are recommended in the treatment of PHN pain. Limited studies are there regarding the use of the above drugs in reducing pain in acute phase of herpes zoster.

Bowsher conducted a randomized trial using tab. amitriptyline 25 mg (at night) for 12 weeks in patients with acute herpes zoster and followed for 6 months. At 3 months, greater patients 28 (73.7%) versus 21 (61.75%) were pain free in amitriptyline versus placebo group respectively (statistically not significant). At 6 months the prevalence of PHN was reduced to half in amitriptyline group (15.8% versus 35.3% still in pain). The results in our study at 12 weeks suggested that, greater patients 27 (90%) versus 22 (73.3%) were completely pain free in amitriptyline versus control group (statistically not significant) (p-value = 0.236). The results in our study could be attributed to the relatively younger study population and uniform treatment to all patients with the use of antivirals at the earliest in the disease process.[4]

Kanodia & Singhal conducted a study of 4 weeks to assess the efficacy of pregabalin in acute phase of herpes zoster, there results suggested that there was a significant continuous decrease in VAS scores in pregabalin group (p-value<0.0001) vs the placebo group. In the above study none of the patients were reported to be totally pain free. The results in our study suggested that the pain was significantly lower in pregabalin group as compared to control group at various time intervals, till 12 weeks (p-value = 0.007) and 14 weeks (p-value = 0.028). The results in our study could be due to sustained levels of drug for 12 weeks, leading to steady reduction in pain.[5]

In our study, lesser number of patients in amitriptyline and pregabalin groups developed PHN i.e., 3(10%) and 5(16.7%) respectively as compared to 8(26.7%) patients in the control group at 14 weeks (statistically not significant, p-value= 0.236). In various studies the reported risk of developing PHN in patients with HZ varies widely from 5% to more than 30%.[6] In our study significantly greater number of patients were satisfied with the pain control, in group A (96.7%) and group B (96.7%) as compared to group C (76.7%) (p<0.05) which was not assessed in the study by Bowsher and Kanodia & Singhal. In our study all the patients irrespective of the group received uniform treatment i.e., with antiviral and analgesics. The systemic use of antiviral agents (acyclovir, famcyclovir and valacyclovir) had been recommended to shorten the healing process of acute herpes zoster, to alleviate pain, and to alleviate or prevent acute and chronic complications. In group A patients predominantly complaint of dry mouth and dizziness while in group B predominant complaint was of somnolence, dizziness and gastrointestinal symptoms. In group C patients predominantly complaint of gastrointestinal symptoms and somnolence at 2 weeks, which gradually improved with better tolerance of the drug. None of the patients discontinued medication because of side effects. Studies suggest that adverse affects with pregabalin are higher at a dose of 600 mg or more.[7,8,9]

PHN results from a combination of inflammatory and viral damage to primary afferent fibers of sensory nerve. Amitriptyline, a tricyclic antidepressant (TCA). The analgesic effect of amitriptyline is independent of its antidepressant effect. Pregabalin has anticonvulsant and analgesic properties. Both these drugs have diverse central and peripheral analgesic actions which include anti-inflammatory, anti-excitotoxic, anti-nociceptive and anxiolytic effects. These actions appear beneficial in reducing the ongoing neuronal damage in the patients with HZ that might lead to better outcome of pain management when started in acute phase of herpes zoster.[4,5]

CONCLUSION

In summary, this randomized controlled study on using amitriptyline or pregabalin in acute phase of herpes zoster showed that the patients who received the above drugs have significantly less severe pain as compared to those who didn't received these drugs. The study also showed a trend that lesser number of patients developed PHN in the group receiving amitriptyline or pregabalin as compared to the control group. Hence, starting tab. amitriptyline 25 mg at night or tab. pregabalin 75 mg twice daily as an adjunct to the standard practice for management in acute herpes zoster can provide better pain control.

However, further studies with optimal length of treatment, variables doses of drug, larger sample size, greater follow up and with diverse sample population are needed, so that the results can be directly extrapolated to a larger population.

REFERENCES

1. Hope-Simpson RE. The nature of herpes zoster: a long-term study and a new hypothesis. Proc R Soc Med 1965;58:9–20.
2. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. Br Med J open 2014;4:64-70.
3. Achar A, Chakraborty PP, Bisai S, Biswas A, Guharay T. Comparative study of clinical efficacy of amitriptyline and pregabalin in postherpetic neuralgia. Acta Dermatovenerol Croat 2012;20:89-94.
4. Bowsher D. The effects of pre-emptive treatment of postherpetic neuralgia with amitriptyline: A randomized, double-blind, placebo-controlled trial. J Pain Symptom Manag 1997;13:327-31.
5. Kanodia SK, Singhal K. A study on efficacy of Pregabalin in acute Herpetic Neuralgia. Ann Neurosci 2011;18:148-9.
6. Su M, Liang L, Yu S. Amitriptyline Therapy in Chronic Pain. Int Arch Clin Pharmacol 2015;1:15-9.
7. Verma V, Singh N, Singh Jaggi A. Pregabalin in neuropathic pain: evidences and possible mechanisms. Curr Neuropharmacol 2014;12:44-56.
8. Koshy E, Mengting L, Kumar H, Jianbo W. Epidemiology, treatment and prevention of herpes zoster: A comprehensive review. Indian Journal of Dermatology, Venereology, and Leprology. 2018 May 1;84(3):251.
9. Volpi A, Gross G, Hercogova J, Johnson RW. Current management of herpes zoster. American journal of clinical dermatology 2005;6(5):317-25.