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Original Article

Role of Systemic Lignocaine in Neuropathic Pain

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ABSTRACT

***Objective*:** To study analgesic efficacy of lignocaine in patients having neuropathic pain.
Study Design: Quasi-experimental study.
Place and Duration of Study: Department of Pain Management, Combined Military Hospital, Rawalpindi Pakistan, from Jan to Dec 2019.
***Methodology*:** A total of 46 patients, fulfilling the inclusion criteria, were divided into two groups, where Group X (n=23), received 0.9% normal saline (2 ml/kg) as a placebo and Group Y (n=23) received lignocaine (2 mg/kg) in 100 ml continuous infusion, over 30 minutes, administered twice a week for a period of 12 weeks as an outdoor procedure. Pre and post infusion parameters were recorded at baseline, 6 weeks and 12 weeks. Douleur Neuropathique 4 (DN4) questionnaire was used to measure pre and post infusion outcome parameters and response to treatment.
***Results*:** There was reduction in parameters when compared at baseline with 12 weeks as, DN4 score reduced from 7.78±1.04 to 7.04±0.82 in Group X (*p*-value=0.167) and 7.52±0.89 to 3.43±0.72 in Group Y (*p*-value=0.03). Baseline values between Group X and Y (7.78±1.04 and 7.52±0.89), showed no statistical significance (*p*-value=0.08) when compared to 12-week scores (7.04±0.82 for Group X vs 3.43±0.72 for Group Y) with *p*-value <0.0001. On comparison within groups at baseline, 6 weeks and 12 weeks, the *p*-value for Group X was 0.07 and Group Y was 0.02.
***Conclusion*:** Intravenous lignocaine was noted to be effective in reducing neuropathic pain severity among patients which may be helpful in preventing long term disability.

Keywords: Efficacy, Lignocaine, Neuropathic Pain.

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INTRODUCTION

The World Health Organization (WHO) has reported that 22% of primary care patients globally had chronic debilitating pain, making it a global dilemma which needs to be addressed by all health care professionals.[1] There are broadly two categories of chronic pain: neuropathic and nociceptive, where neuropathic pain arises as a direct consequence of a lesion or disease affecting somatosensory system,[2] occurring in approximately 8-20% of patients with shingles and diabetes mellitus.[3] Neuropathic pain is further divided into central and peripheral components, according to the site of lesion, with post-stroke pain, multiple sclerosis, components of cancer pain, phantom pain, post-herpetic neuralgia, nerve entrapment syndrome and peripheral neuropathies being a few examples.[4] The incidence of neuropathic pain increases with age, with higher risk of neuropathic pain in older adults.[5] Neuropathic pain is challenging to diagnose because there is a lack of validated diagnostic tools, however one of the most validated tools is the Doleur Neuropathique (DN4) questionnaire[6] with predictive value of 86%, specificity of 89% and sensitivity of 83%,[7] greatly aiding physicians in screening patients. While pharmacotherapy remains the mainstay of treatment, patients still suffer from moderate to severe pain despite all medications[8] including opioids, cannabinoids, anticonvulsants, topical agents, tricyclic anti-depressants, neuraxial blocks and biopsychosocial interventions.[9] Lignocaine, exerts analgesic effects by blocking peripheral and central sodium channels in the spinal dorsal horn or inhibition of ectopic discharges at neurons evidence of use of Intravenous lignocaine in managing neuropathic pain syndrome including postherpetic neuralgia, headache, central pain, postoperative and cancer pain with no documented serious side effects at therapeutic dose.[10] Delay in treating neuropathic component of pain, will result in permanent disability, thus the basic purpose to conduct this study was to reduce morbidities associated with neuropathic pain through early intervention with systemic lignocaine at the time of diagnosis.

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METHODOLOGY

After obtaining approval from the Ethics Review Committee (vide certificate ERC/CMH-RWP) and informed patient's consent, this quasi-experimental study was conducted at the Department of Pain Medicine, Combined Military Hospital, Rawalpindi Pakistan, from January to December 2019, lasting 1 year. WHO sample size calculator was used to calculate sample size. Significance of 5%, power of 95%, anticipated chronic pain prevalence in young Asian population (proportion-1) P1 of 42% and prevalence of chronic pain in Asian geriatric population (proportion 2) P2 of 90.8% was set and sample size was calculated to be 46 and 23 in each group.[1] Non-probability consecutive sampling was used to enroll participants after all risks and benefits were explained to patients and their informed, written consent was obtained.

Inclusion Criteria: Patients of either gender, with age ranging from 20 to 70 years, presenting to Outpatient Department with neuropathic pain, including post-herpetic neuralgia, trigeminal neuralgia, brachialgia secondary to carcinoma, sciatica, central post-stroke pain, complex regional pain syndrome, with duration of more than six months and scoring DN4 score of ≥4 were included.

Exclusion Criteria: Patients who were pregnant, had known allergy to lignocaine, terminal illness, cardiovascular instability, end-stage renal and/or liver disease, heart block, abnormal cognition, on beta-blockers, with disease duration of less than six months and DN4 questionnaire score <4 were excluded.

All patients were divided into two groups, labelled X and Y, by following a computer-generated allocation. As per protocols, all enrolled patients were informed and counseled about the procedure after which a brief history was taken, clinical examination and investigations were reviewed and vitals were recorded. Patients were administered a continuous infusion, over 30 minutes, of 0.9% normal saline (2 ml/kg) in Group X as a placebo and lignocaine (2 mg/kg in 100 ml) in Group Y. Vitals were continuously monitored during the infusions which were scheduled as an outdoor procedure, twice a week and continued for a total period of 12 weeks. The preset pre and post infusion parameters were recorded at baseline, 6 weeks and 12 weeks. DN4 questionnaire used to screen neuropathic pain and used to measure pre and post infusion response to treatment where total score was 10 and cutoff of lower limit of score to diagnose neuropathic pain was 4. In both groups, scores at baseline and at 12 weeks were recorded and compared. Data was analyzed using Statistical Package for Social Sciences (SPSS version 22.0). For quantitative variables, mean and standard deviation was calculated, while qualitative variables were presented as frequency and percentage. Chi square test and independent sample t-test was used to compare means between the groups and to test significance along with one-way ANOVA to compare means within groups and to test significant difference among the sample means within groups where a *p*-value of ≤0.05 was considered as statistically significant.

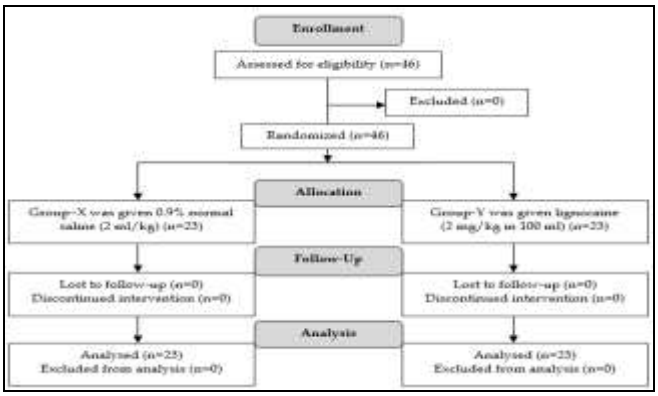

Figure: Patient Flow Diagram (n=46)

RESULTS

A total of 46 patients were enrolled in each group, these being Group X (Placebo, n=23) and Group Y (Lignocaine, n=23) where mean age of the patients in Group X and Group Y were 59.30±8.33 and 51.57±7.58 years (*p*=0.46) respectively. Majority of the patients in both groups were male (Group X=12, 52%, Group Y=14, 60%) with other demographic details shown in Table-I. Table-II shows distribution of cases between both groups. Table-III shows details of DN4 scores at each interval, where in Group X, there was a reduction in parameters when baseline was compared with 12 weeks as DN4 score reduced from 7.78±1.04 to 7.04±0.82 and 7.52±0.89 to 3.43±0.72 in Group Y. On comparing baseline values between Group X and Group Y (7.78±1.04 vs 7.52±0.89), no statistical significance was seen (*p*-value=0.368), when compared to 12-week scores for Group X and Group Y (7.04±0.82 vs 3.43±0.72), *p*-value was <0.0001. There was significant reduction in DN4 score from 0 to 12 weeks in Group Y when compared to Group X and DN4 score declined below the limit of neuropathic pain criteria of 4. To test significant difference among

sample means within groups by using analysis of variance, the Mean values at baseline, 6 weeks and 12 weeks were compared and *p*-value was 0.0398 in Group X and <0.001 in Group Y, respectively.

Table-I: Demographic Variables of Participants (n=46)

Variables		Group X (n=23) (Mean±SD)	Group Y (n=23) (Mean±SD)	*p*–value (≤0.05)
Age (years)		59.30±8.33	51.57±7.58	0.46
Weight (kg)		66.04±9.34	69.43±8.23	0.62
Gender n(%)	Male	12(52.2%)	14(60.9%)	0.58
	Female	11(47.8%)	09(39.1%)	

Table-II: Distribution of Cases (n=46)

Distribution of Cases	Group X (n=23)	Group Y (n=23)
Brachialgia (CA Breast)	07(30.4%)	06(26.1%)
Central Post Stroke Pain	03(13%)	04(17.4%)
Complex regional pain syndrome	01(4.3%)	01(4.3%)
Post Herpetic Neuralgia	08(34.8%)	05(21.7%)
Trigeminal Neuralgia	04(17.4%)	05(21.7%)
Sciatica	-	02(8.7%)

Table-III: Mean DN4 Score at Each Recording Interval, (n= 46)

Outcome Parameters	Group X (n=23) (Mean±SD)	Group Y (n=23) (Mean±SD)	*p*–value (≤0.05)
DN4 at Baseline	7.78±1.04	7.52±0.89	0.368
DN4 at 6 Weeks	7.26±1.09	3.96±1.06	<0.001
DN4 at 12 Weeks	7.04±0.82	3.43±0.72	<0.001

DN4: Douleur Neuropathique 4

DISCUSSION

The diagnosis and management of neuropathic pain remains a dilemma for pain physicians despite recent advances in treatment modalities as the precise pathophysiological mechanism of neuropathic pain is still under investigation.[11] Different patho-physiological mechanisms have been postulated[12] as electrophysiology and molecular biology studies have revealed changes in neuronal sodium channel expression and impact of focal inflammatory process rather than axonal destruction[13] with the basis of antiarrhythmic action of lignocaine found to be its sodium channel blocking properties, however, the half-life of lignocaine (90-120 minutes) and its pharmacological effect lasts longer therefore, lignocaine may have central and peripheral mechanisms of action[14] as the analgesic effects of narcotic opiates and lignocaine were similar where lignocaine can generate selective block of afferent evoked activity in the spinal cord.[15] Similar findings to ours were reported in diabetic neuropathic pain while using higher doses of lignocaine 5mgkg–1 during 30 minutes[16] while another author reported that the concentration-effect and graded quantal dose-response relationship for intravenous lignocaine was characterized by greater pain relief with minimal increase in dosages. The concentration-effect relationship was also steep with pain scores abruptly decreasing over a range of 0.62 g ml-1 of lignocaine.[17] One researcher administered lignocaine infusion to achieve plasma concentrations of 0.5, 1, 1.5, 2 and 2.5 g ml-1 where a considerable plasma concentration dependent decrease in pain scores starting at 1.5 g ml-1 was reported and a decrease in the size of the receptive field to which pain was referred.[18]

LIMITATIONS OF STUDY

This study has several notable limitations. The small sample size of 46 patients per group reduces statistical power and increases the risk of type II errors, particularly given the marginal p-value in the treatment group. The study was conducted at a single center, limiting generalizability to diverse populations or healthcare settings. Additionally, reliance on the self-reported DN4 questionnaire as the sole outcome measure may be subject to response bias, and longer-term follow-up beyond 12 weeks was not performed to assess the durability of analgesic effects or potential relapse.

CONCLUSION

Intravenous lignocaine has shown to be effective in reducing neuropathic pain severity and ultimately helps in preventing long term disability.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SMW & RAK: Data acquisition, data analysis, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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