CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com *Research Article*

PAIN MANAGEMENT BY A COMBINATION OF CARBAMAZEPINE, HALOPERIDOL AND TRAMADOL

Dr. Hafsa Saeed[1], Dr. Aneeqa Mumtaz[2], Dr. Sibgha Saliha[3]

[1] University College of Medicine and Dentistry, Lahore

[2] Punjab Medical College Faisalabad

[3] Kind Edward Medical University, Lahore

Article Received: May 2020 **Accepted:** June 2020 **Published:** July 2020

Abstract:

Aim: *To investigate the effectiveness of haloperidol, carbamazepine and tramadol in the treatment of pain in patients burned during the first seven days of hospitalization.*

Patients and methods: *30 patients with burns (12 to 45 years old) admitted to the burn unit of Jinnah Hospital Lahore. In our study, haloperidol (0.05-0.15 mg / kg orally once daily) and tramadol (300 mg to 400 mg continued) and carbamazepine (administered orally at a dose of 100-200 mg twice daily) for 12 hours) was given. During the study, the pain was monitored by using a pain scale for adults and children, and behavior of patients was monitored by using an observational pain assessment scale. Vital parameters like pulse rate, systolic and diastolic blood pressure, duration of sleep for each patient were recorded on the first day of treatment with these drugs up till the seventh day.*

Results: *Systolic and diastolic blood pressure dropped (95% CI: 9-21 mmHg, respectively; 4-13 mmHg), respectively, and the heart rate dropped (95% CI: 25 to 37 b / min); sleep duration increased to 6-7 hours a day in 19 patients (95% CI: 0.45-0.81). The median total pain score of 30 burn patients decreased from 9 to 1 in seven days; and 18 of 30 patients (95% CI: 0.4-0.75) became more calm, cooperative, relaxed, normal tones, without crying and no negative reaction to touching the wound.*

Conclusion: *The combination of tramadol, oral infusion of haloperidol and oral carbamazepine effectively reduces pain in burn patients.*

Key words: *tramadol, haloperidol, carbamazepine, burn patients.*

Corresponding author:

Dr. Hafsa Saeed,

University College of Medicine and Dentistry, Lahore

QR code

Please cite this article in press Hafsa Saeed et al, ***Pain Management By A Combination Of Carbamazepine, Haloperidol And Tramadol.,*** *Indo Am. J. P. Sci, 2020; 07(07).*

INTRODUCTION:

Pain is an unpleasant sensory and emotional experience resulting from actual or potential tissue damage mediated by specific nerve fibers in the brain[1-2]. Pain is a subjective experience, no machine can measure pain, the only person who can determine the presence and degree of pain is the patient. Appropriate pain assessment and drug selection training was minimal for most healthcare providers. Because pain is a subjective phenomenon, direct patient inquiry is the only way clinicians can detect the presence or severity of pain. A useful way of assessing pain and assessing the effectiveness of analgesia is to ask the patient to assess the degree of pain along with a numerical or visual pain scale, as shown in Figure 1. Direct communication with the patient is the best method for determining comfort needs, and not just that it is a source of comfort for patients[3-4].

Drugs used to treat pain.

Opioids: the most commonly used pain relievers and mild sedation. It is more effective at relieving dull pain, less effective at acute intermittent pain, and relatively ineffective at neuropathic pain. Misconceptions about the addictive potential of opioids and the appropriate dose needed to relieve pain have led to inadequate pain control, especially in burned patients. However, the use of opioids in hospitalized patients does not cause drug addiction, and the effective opioid dose should be determined based on the patient's response, not on the basis of a pre-defined concept of what the effective dose should be.

Tramadol - Tramadol is a centrally effective analgesic that has an opioid agonist effect and also has strong monoamine reuptake properties similar to many antidepressants and makes it look valuable in the treatment of neuropathic pain.

Anticonvulsants: useful for patients with neuropathic pain because these agents block calcium or sodium tension channels, thereby suppressing spontaneous neuronal discharge and therefore play an important role in the treatment of less sensitive neuropathic pain.

Carbamazepine: an anticonvulsant used to treat epilepsy and neuropathic pain. It stabilizes the inactivated state of voltage-dependent sodium channels, which makes the affected cell less excitable until the drug is removed. Carbamazepine is also a GABA receptor agonist. These mechanisms may contribute to its effectiveness in neuropathic pain and bipolar disorder.

Neuroleptics: sometimes they may be useful in patients with refractory neuropathic pain and may be more useful in patients with pronounced excitation or psychotic symptoms.

Haloperidol: This is a neuroleptic drug and its therapeutic effect appears to be due to blockage of dopaminergic receptors in mesolimbic regions. However, the long duration of action is not suitable for continuous infusion. It is not associated with the risk of cardiovascular depression and is also effective in delirium.

Goals and goals

The purpose of this study is to feel pain in patients with burns who feel better with the nurse when changing the dressing (a very stressful procedure to be performed daily) using a combination of tramadol, carbamazepine and haloperidol. The goal is to show the daily effect of tramadol, carbamazepine and haloperidol on vital signs during the first seven days: systolic, diastolic blood pressure and pulse; time to sleep; pain intensity based on the pain rating scale; Patient behavior was assessed by observational pain results during dressing change

PATIENTS AND METHODS:

This is a prospective cohort study held in the plastic surgery department of Jinnah Hospital Lahore for one year duration from March 2019 to March 2020,

Admission Criteria

The study included patients with the age group of 12–45 years, the percentage of burns 15–40%, the degree of burn: deep 2nd and 3rd degree.

Exclusion criteria

Patients with a history of renal impairment, hepatic impairment and history of hypertension were excluded from the study. All patients in our study received Tramadol (Tramal) 200 mg-300 mg daily in 50 ml saline infused with a 5 mg-10 mg syringe per hour for 12 hours. The dose was doubled during wound cleansing and dressing changes, carbamazepine (Tegral) 100 mg - 200 mg p.o. every 12 hours, Haloperidol (Haldol) (0.05-0.15 mg / kg (5 mg-10 mg po) from All patients were followed for 7 days and monitored for pain using a pain rating scale that depends on description of patient pain during change dressing and behavior monitoring using an observational pain rating scale (Table 1, Figure 1)

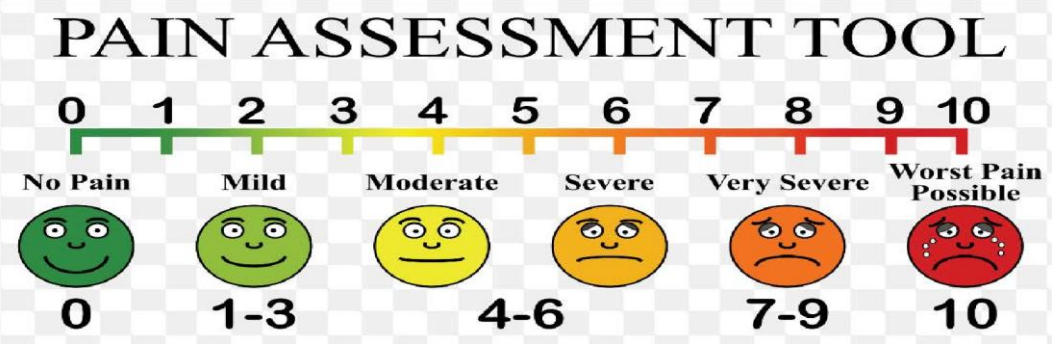

Figure 1 Pain Assessment Scale

Table 1 Observational pain assessment scale

Score	0	1	2
Restlessness	Calm, cooperative	Slight restlessness	Very restless, agitated
Muscle tension	Relaxed	Slight tenseness	Extreme tenseness
Facial expression	No frowning, or grimacing, composed	Slight frowning or grimacing	Constant frowning or grimacing
Vocalization	Normal tone, no sound	Groans moans, cries out in pain	Cries out, Shortness of breath
Wound guarding	No negative response to wound	Reaching gently touching the wound	Grabbing vigorously at the wound

Other parameters, including blood pressure, were monitored; pulse and sleep time. Data was collected from employees who changed their daily clothes and those who monitor vital signs and sleep. The data was then collected in the form of a table in paper form, and then entered electronically and analyzed using SPSS-PC version 23.0. Descriptive analysis of data using graphical and tabular analysis was performed by calculating the median, average and confidence intervals for each variable. The significance of differences between the scalar variables was tested using the paired Student's t-test, while the non-parametric data, the differences were tested using the Wilcoxon labeled pair sequence test when the symmetric and character test were used when the differences are asymmetrical.

RESULTS:

Blood pressure: The average daily systolic and diastolic blood pressure of 30 patients were calculated over the treatment period (Fig. 2).

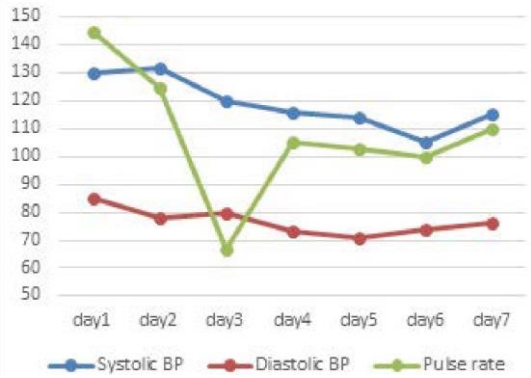

Figure 2 Hemodynamic status of 30 burn patients in the first seven days

Pulse: The average daily pulse of 30 patients was calculated during the treatment period (Fig. 2). Table 2 shows the importance of pulse rate, systolic and diastolic blood pressure between the first and seventh days of treatment.

Table 2 Significance of differences in blood pressure and heart rate between the first and seventh day

Variable		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Systolic day1-Systolic day7	14.762	14.703	3.209	8.069	21.455	4.601	20	0.000
Pair 2	Diastolic day1-Diastolic day7	8.905	10.178	2.221	4.272	13.538	4.009	20	0.001
Pair 3	Heartrate day1-Heartrate day7	31.481	15.073	2.901	25.519	37.444	10.853	26	0.000

On the second day of treatment, 19 out of 30 patients increased their sleep time to an average of 6-7 hours a day (mean: 0.63, 95% CI 0.45 to 0.81).

Pain intensity: tramadol, carbamazepine and haloperidol were measured during seven days of treatment and pain score (Table 3).

Table 3 Daily number of patients stratified by severity of pain

Variables	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Worst pain	17	0	0	0	0	0	0
Very severe pain	4	10	2	0	0	0	0
Sever pain	9	7	4	1	1	1	1
Moderate pain	0	7	12	15	15	12	12
Mild pain	0	6	9	5	5	4	5
No pain	0	0	3	9	9	13	12

The median total pain score of 30 burn patients dropped from 9 to 1 over seven days with subsequent daily decreases for the first four days, followed by a decrease each day (Fig. 3, Table 4). It was found that subsequent daily differences between pain points are asymmetrical. The sign test showed a significant decrease in pain results on all consecutive days before the sixth day, exact validity of 2 tails using binomial distribution p <0.39; The sign test also showed a significant decrease between days 1 and 7 (test statistics Z-5 295, 2-sided asymptotic significance p = 0.000).

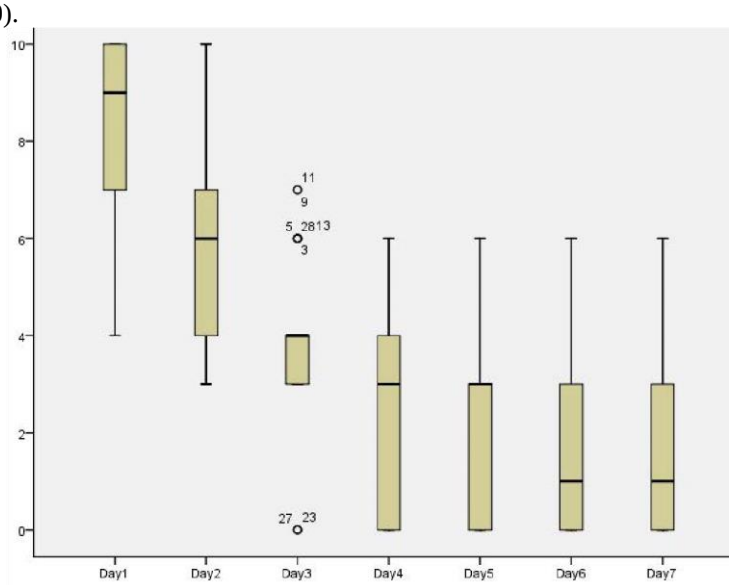

Figure 3 Box plots showing daily total pain scores in 30 burn patients over seven days

Table 4 Descriptive Statistics of total pain scores for 30 burn patients over seven days

Variables	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Day 1	30	8.3	1.968	4	10	6.75	9	10.0
Day 2	30	5.83	2.451	3	10	4.00	6	7.0
Day 3	30	3.77	1.813	0	7	3.00	4	4.5
Day 4	30	2.50	1.676	0	6	0.00	3	4.0
Day 5	30	2.07	1.639	0	6	0.00	3	3.0
Day 6	30	1.53	1.634	0	6	0.00	1	3.0
Day 7	30	1.57	1.612	0	6	0.00	1	3.0

Patient behavior: According to the observational pain rating scale, patient behavior changed dramatically over the seven-day treatment period; Eighteen patients (mean 0.6; 95% CI: 0.43-0.75) were more calm, cooperative, relaxed, with a normal tone, without crying and having an adverse reaction after touching the wound (Table 1). The median sum of all individual behavioral results of 30 burn patients decreased from 10 to 3 over seven days with subsequent daily decreases for the first 3 days followed by a decrease of two days (Table 5). Further daily differences between the total behavioral results were symmetrical for the first 3 days, and then asymmetrical (Fig. 4).

Table 5 Descriptive statistics: daily total behavior scores

Variables	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Day 1	30	9.43	1.104	6	10	9.00	10	10
Day 2	30	7.03	1.752	4	10	6.00	7	8
Day 3	30	5.23	1.612	2	10	4.75	5	6
Day 4	30	4.27	1.617	0	7	3.75	5	5
Day 5	30	3.53	1.408	0	6	3.00	4	4
Day 6	30	3.3	1.466	0	5	2.75	4	4
Day 7	30	2.7	0.535	0	5	1.75	3	4

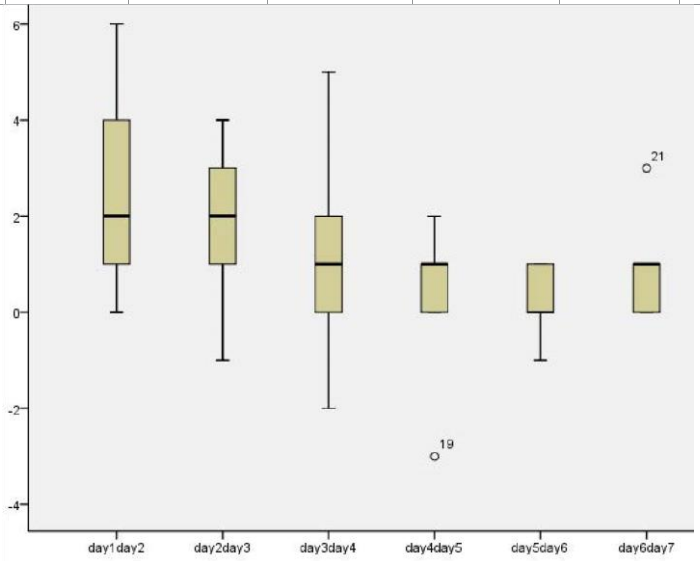

Figure 4 Box plots of consecutive daily differences in total behavior scores for 30 burn patients

Wilcoxon and the character test showed a significant decrease in pain scores on all consecutive days of the first week [Z test statistics (according to positive ranges): -4.411 (1st-2nd day), - 4.552 (2nd-3rd day), - 3.270 (3 - 4 day), -3 439 (4-5 day), -2.333 (5 - 6 day), - 3 900 (6 to 7 days); Bilateral asymptotic significance: p = 0.000, 0.000, 0.001, 0.001, 0.02, 0.000 respectively]. The sign test showed similar results [exact significance of 2 tails (binomial distribution used): p = 0.000 (day 1 to 2), 0.000 (day 3 to day 4), 0.000 (day 4 to day 5), 0.039 (5 Place until the 6th day))), 0.000 (from the 6th to the 7th day); Test statistics Z -4,725 (2-3 day), 2-sided asymptotic significance p = 0.000].

DISCUSSION:

During the acute phase of injury, burn patients should rely on a series of painful procedures that cause intense physical and psychological stress, including initial wound cleansing, daily dressing changes, exercise therapy, and placement[5-6]. For various reasons, adequate control of pain and anxiety associated with these procedures is particularly difficult due to many factors such as severe but brief pain; risk of complications with deep sedation; long-term effects of deep sedation; frequent periods of hunger interrupt the nutritional needs of patients with burns; discussion about who should do deep sedation. Poorly controlled pain can interfere with performing an effective or safe procedure, and increased anxiety can affect patient compliance and contribute to behavioral morbidity such as post-traumatic stress disorder, as well as increase sympathetic tension; On the other hand, wound healing and immune function are associated with pain and may contribute to long-term hospitalization[7-8]. The level of pain is not only a physical feature of the stimulus, because pain can be influenced by past experiences, suggestions, emotions (especially anxiety) and the simultaneous activation of other sensory methods. Rest and sleep help the body maintain homeostasis, restore energy levels, and reduce stress and anxiety. For the first time, research was conducted on the use of this combination of drugs in the treatment of pain in burn patients, previously single drugs were used in burn patients. Current research confirms the view on multiple drug management (balanced multimodal analgesia), the size of the sample in the current study is relatively small, and comparisons with other studies cannot be reliably established[9-10]. However, it aims to give preference to this combination of drugs that gives positive results to all patients with 4 study goals:

Vital signs: the average change in systolic blood pressure decreased significantly during the first 3 days of treatment and then reached a constant level from day 4 to day 7; the mean change in diastolic blood pressure gradually decreased over the first three days of treatment and then reached a steady level from day 4 to day 7. The average change in pulse rate is 60 b / min on the first day (Fig. 1).) on the third day, reaching a stable level between 100–110 b / min during the last 4 days of treatment. We believe that this reduces the intensity of pain and associated stress as a result of treatment with our combination of drugs[11-12].

Sleep time: On the second day of treatment, sleep time was increased to 6-7 hours a day in 19/30 patients, and their sleep was deep and comfortable. We believe that as a result of treatment with our combination of drugs, this reduces pain and stress.
Severity of pain: The overall pain assessment showed daily decreases suggesting both background pain and procedural pain (Fig. 3, Table 4). Despite the asymmetries of consecutive daily differences in total pain results, the sign test showed that all were statistically significant; the decrease is clinically significant because the overall pain score increases from 9 to 1 from day 7 to day 7. This decrease is mainly associated with the effect of the combination of drugs used. In general, deep pain after a second or third degree burn is not expected to decrease to such a degree without taking any medication[13-14]. Burn patients have a higher level of treatment-related anxiety, and because these levels may increase over time, waiting for at least daily wound care can increase the patient's pain, which can increase anxiety. This reaction may explain the need for an analgesic effect on daily burn dressing changes. Depression also plays a similar role in the treatment of pain. Pain causes depression, and depression improves pain perception.

The intensity of background pain after dressing is always greater than the pain before changing the dressing. Failure to attend hospital treatment increased the risk of post-traumatic stress disorder and increased treatment as a result of inadequate pain relief in burn patients.

Although the problem of pain caused by untreated burns was well defined 20 years ago and despite the call for pain, it is the highest research priority in the care of burns due to its harmful effect on patients and those who care for no more than 15 years burn pain remains constant challenge. Recent publications indicate unacceptably high pain results (average: 7/10). This is surprising given the wide utility of the guides to promote pain management and a guidelines-based approach. In addition, unlike the gradually decreasing surgical pain, the pain caused by burns is very variable and may increase over time until the patient suffers before recovery[15]. The result is that burns and cuts from the World

Health Organization assess pain from burns and is often impractical. These factors cause us to establish our own protocol in our burn team to solve this problem with these effective, affordable and available drugs.

CONCLUSION:

Treatment with tramadol infusion in combination with carbamazepine and haloperidol orally is effective in managing background pain as well as in decreasing stress and anxiety in burn patients during daily change dressing and debridement which is a very painful and stressful procedure. It is effective during the first seven days of burn in achieving hemodynamic stability, increasing the duration of sleep, decreasing pain severity and improving behavior.

REFERENCES:

1. Nesbit, Suzanne, Ilene Browner, and Stuart A. Grossman. "Cancer-Related Pain." In *Abeloff's Clinical Oncology*, pp. 581-592. Content Repository Only!, 2020.
2. Davison, Sara N. "Clinical pharmacology considerations in pain management in patients with advanced kidney failure." *Clinical Journal of the American Society of Nephrology* 14, no. 6 (2019): 917-931.
3. Toński, Michał, Joanna Dołżonek, Piotr Stepnowski, and Anna Białk-Bielińska. "Hydrolytic stability of selected pharmaceuticals and their transformation products." *Chemosphere* 236 (2019): 124236.
4. Miller, Andrew C., Abbas M. Khan, Alberto A. Castro Bigalli, Kerry A. Sewell, Alexandra R. King, Shadi Ghadermarzi, Yuxuan Mao, and Shahriar Zehtabchi. "Neuroleptanalgesia for acute abdominal pain: a systematic review." *Journal of Pain Research* 12 (2019): 787.
5. Robbins, Miriam R. "Pharmacologic Management of Patients with Neurologic Disorders." In *Contemporary Dental Pharmacology*, pp. 69-84. Springer, Cham, 2019.
6. Nemergut, Greta, and Jennifer Sandra. "Neuroleptics (Typical/Atypical Antipsychotics)." In *Pain*, pp. 255-260. Springer, Cham, 2019.
7. Czernicki, Michal, Sreekumar Kunnumpurath, William Park, Anamika Kunnumpurath, Gopal Kodumudi, Jing Tao, Vijay Kodumudi, Nalini Vadivelu, and Richard D. Urman. "Perioperative Pain Management in the Critically Ill Patient." *Current pain and headache reports* 23, no. 5 (2019): 34.
8. Monteith, Scott, and Tasha Glenn. "A comparison of potential psychiatric drug interactions from six drug interaction database programs." *Psychiatry research* 275 (2019): 366-372.
9. Lonchampt, Sophie, Fabienne Gerber, Jean-Michel Aubry, Jules Desmeules, Markus Kosel, and Marie Besson. "Pain interventions in adults with intellectual disability: A scoping review and pharmacological considerations." *European Journal of Pain* 24, no. 5 (2020): 875-885.
10. Jokanovic, Natali, Noha Ferrah, Janaka J. Lovell, Carolina Weller, Lyndal Bugeja, J. Simon Bell, and Joseph E. Ibrahim. "A review of coronial investigations into medication-related deaths in residential aged care." *Research in Social and Administrative Pharmacy* 15, no. 4 (2019): 410-416.
11. Shobhana, A. "Drug Interactions of Chronic Neuropsychiatric Drugs in Neuro-critical Care." *Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine* 23, no. Suppl 2 (2019): S157.
12. Shobhana, A. "Drug Interactions of Chronic Neuropsychiatric Drugs in Neuro-critical Care." *Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine* 23, no. Suppl 2 (2019): S157.
13. Lunenburg, Carin Adriana Theodora Catharina, Alexander Sebastian Hauser, Kazi Ishtiak-Ahmed, and Christiane Gasse. "Primary Care Prescription Drug Use and Related Actionable Drug-Gene Interactions in the Danish Population." *Clinical and Translational Science* (2020).
14. Kratz, Torsten, and Albert Diefenbacher. "Psychopharmacological Treatment in Older People: Avoiding Drug Interactions and Polypharmacy." *Deutsches Ärzteblatt International* 116, no. 29-30 (2019): 508.
15. Alkholany, Mahmoud, and Jonathan Rajan. "Antidpressants and antipsychotics: anaesthetic implications." *Anaesthesia & Intensive Care Medicine* (2020).