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Original Research

Comparison of Clonidine Hydrochloride and Buprenorphine-Naloxone in opioid withdrawal

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ABSTRACT:

Background: Since detoxification lessens the intensity of opioid withdrawal symptoms and increases patient motivation for continued maintenance therapy, it is the initial step in treating opioid addiction. The present study was conducted to compare Clonidine Hydrochloride and Buprenorphine-Naloxone in opioid withdrawal. **Materials & Methods:** 56 patients seeking treatment for opiate dependence of both genderswere divided into two groups of 28 each. Group I received 100 mg clonidine orally for 10 days in the dose range of 50-200 µg/day in divided doses and group II received 2mg of buprenorphine and 0.5 mg of naloxone sublingually in the dose of 2.0/0.5 mg/day (1 tab.) to 8.0/2.0 mg/ day (4 tab.) in two equal doses. Efficacy of drugs was assessed using clinical opiate withdrawal scale (COWS). **Results:** Education was illiterate in 4 and 7, middle in 15 and 11 and upto secondary level in 9 and 10 in group I and II respectively. Employment status was employed19 and 20 and un-employed9 and 8 in group I and II respectively. Marital status was married11 and 13, unmarried13 and 9 and divorced4 and 6 in group I and II respectively. The average COWS scores on day 1 was 11.3 and 11.4, on day 2 was 23.6 and 23.1, on day 3 was 15.2 and 11.1, on day 4 was 10.3 and 5.2, on day 5 was 5.8 and 2.1 and on day 6 was 2.4 and 0.42 in group I and II respectively. Average craving using VAS on day1 was 87.4 and 89.5, on day 2 was 66.2 and 48.5, on day 3 was 41.7 and 23.1, on day 4 was 20.5 and 5.8 and on day 5 was 7.2 and 1.9 in group I and II respectively. **Conclusion:** During the first few days of detoxification, buprenorphine-naloxone administration proved more effective in lowering the signs and symptoms of opioid withdrawal and in managing the urge for the drug of abuse.

Keywords: clonidine, naloxone, opiate

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INTRODUCTION

The consumption of opiate preparations involves the use of drugs derived from opium or synthetic analogs that act on opioid receptors in the brain.[1] These drugs can be used medically for pain relief or recreationally for their euphoric effects. However, they carry a high risk of addiction, overdose, and various health complications. Natural opiates are derived directly from the opium poppy, including morphine and codeine.[2]Semi-synthetic opioids are modified versions of natural opiates, such as heroin, oxycodone, hydrocodone, and hydromorphone. synthetic opioids are completely man-made, including fentanyl, methadone, tramadol, and buprenorphine.[3]

Since detoxification lessens the intensity of opioid withdrawal symptoms and increases patient motivation for continued maintenance therapy, it is the initial step in treating opioid addiction.[4] One α2 agonist that reduces noradrenergic hyperactivity and lowers the dysphoric state associated with opiate withdrawal is clonidine. Contrary to opioid drugs, which cause tolerance and dependency, clonidine does not cause orthostatic hypotension, a side effect that is dose-related.[5] Buprenorphine functions as an antagonist at the kappa receptor and a partial agonist at the mu-receptor.It has been discovered that buprenorphine's antagonistic activity accounts for its application in opioid addiction maintenance and detoxification. Because buprenorphine is a partial agonist, its agonist activity is capped, improving its safety profile and lowering its risk.[6]The present study was conducted to compare Clonidine Hydrochloride and Buprenorphine-Naloxone in opioid withdrawal.

MATERIALS & METHODS

The present study was conducted on 56 patients seeking treatment for opiate dependenceof both

genders. All were informed regarding the study and their written consent was obtained.
Data such as name, age, gender etc. was recorded. A thorough clinical examination was done. Baseline blood investigations including hepatitis and HIV were carried out for all subjects. Patients were divided into two groups of 28 each.Group I received 100 mg clonidine orally for 10 days in the dose range of 50-200 µg/day in divided dosesand group II received 2mg of buprenorphine and 0.5 mg of naloxone sublingually in the dose of 2.0/0.5 mg/day (1 tab.) to 8.0/2.0 mg/ day (4 tab.) in two equal doses. Efficacy of drugs was assessed using clinical opiate withdrawal scale (COWS). Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Parameters	Variables	Group I (28)	Group II (28)	P value
Education	Illiterate	4	7	0.75
	Middle	15	11	
	Secondary	9	10	
Employment status	Employed	19	20	0.05
	Un-employed	9	8	
Marital status	Married	11	13	0.21
	Unmarried	13	9	
	Divorced	4	6	

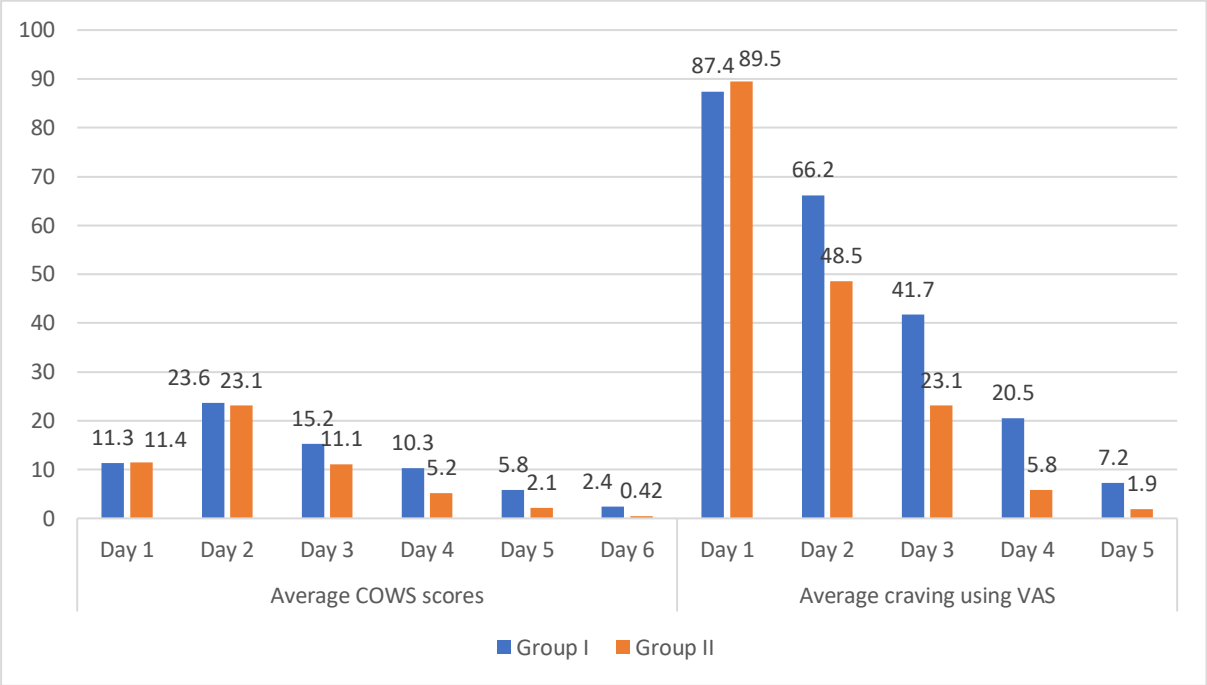
Table I shows that education was illiterate in 4 and 7, middle in 15 and 11 and upto secondary level in 9 and 10 in group I and II respectively. Employment status was employed 19 and 20 and un-employed9 and 8in group I and II respectively. Marital status was married11 and 13, unmarried13 and 9 and divorced4 and 6in group I and II respectively. The difference was non- significant (P> 0.05).

Table II Assessment of parameters

Parameters	Variables	Group I	Group II	P value
Average COWS scores	Day 1	11.3	11.4	0.05
	Day 2	23.6	23.1	
	Day 3	15.2	11.1	
	Day 4	10.3	5.2	
	Day 5	5.8	2.1	
	Day 6	2.4	0.42	
Average craving using VAS	Day 1	87.4	89.5	0.02
	Day2	66.2	48.5	
	Day3	41.7	23.1	
	Day4	20.5	5.8	
	Day5	7.2	1.9	

Table II shows that average COWS scores on day 1 was 11.3 and 11.4, on day 2 was 23.6 and 23.1, on day 3 was 15.2 and 11.1, on day 4 was 10.3 and 5.2, on day 5 was 5.8 and 2.1 and on day 6 was 2.4 and 0.42 in group I and II respectively. Average craving using VAS onday1 was 87.4 and 89.5, on day 2 was 66.2 and 48.5, on day 3 was 41.7 and 23.1, on day 4 was 20.5 and 5.8 and on day 5 was 7.2 and 1.9in group I and II respectively.The difference was significant (P< 0.05).

Graph I Assessment of parameters



DISCUSSION

Opiates bind to opioid receptors in the brain, spinal cord, and other parts of the body, reducing the perception of pain and producing feelings of euphoria.[7] They also slow down the activity of the central nervous system, which can lead to respiratory depression.Common side effects are Drowsiness, constipation, nausea, vomiting, dizziness, and euphoria.[8]Severe side effects arerespiratory depression, bradycardia (slow heart rate), hypotension (low blood pressure), confusion, and potential for overdose.Given the terrible effects of opioid dependence, the development of effective treatment is crucial, and a safe detoxification process is still a necessary first step.[9]The present study was conducted to compare Clonidine Hydrochloride and Buprenorphine-Naloxone in opioid withdrawal.

We found that education was illiterate in 4 and 7, middle in 15 and 11 and upto secondary level in 9 and 10 in group I and II respectively. Employment status was employed19 and 20 and un-employed9 and 8 in group I and II respectively. Marital status was married11 and 13, unmarried13 and 9 and divorced4 and 6 in group I and II respectively. Hussain et al[10] in their study fifty- four (54) treatment seeking subjects, 15-50 years of age, fulfilling DSM-1V TR (American Psychiatric association`s Mental Disorders-1V text revision) criteria for opioid dependence were included and randomized into two groups. The groups received either clonidine hydrochloride (Group A) or buprenorphine- naloxone (Bup-Nax) (Group B) for the duration of 10 days. The efficacy of the two drugs in controlling the opioid withdrawal was evaluated by Clinical Opioid Withdrawal Scale (COWS) and their effect on the desire for the abused substance was measured by Visual Analogue Scale (VAS). The safety of the two drugs was measured by taking the side effect profile of the two compared drugs into consideration. There was significant difference of COWS-score between the two groups which was evident from day 3 (14.85 ± 3.43 vs. 11.67 ± 2.40)and continued till day 6 (2.56± 1.40 vs. 0.30 ± 0.61, $p<0.005$), for Group A and group Brespectively. The effect of two drugs in controlling the cravingfor the abused substance also showed significant differencefrom day 2 (66.30 ± 10.80 vs. 47.40 ± 12.90, $p<0.005$) till day 5(7.78 ± 6.41 vs. 1.85 ± 6.22, $p<0.005$), for Group A and GroupB respectively.

We found that average COWS scores on day 1 was 11.3 and 11.4, on day 2 was 23.6 and 23.1, on day 3 was 15.2 and 11.1, on day 4 was 10.3 and 5.2, on day 5 was 5.8 and 2.1 and on day 6 was 2.4 and 0.42 in group I and II respectively. Average craving using VASon day1 was 87.4 and 89.5, on day 2 was 66.2and 48.5, on day 3 was 41.7 and 23.1, on day 4 was 20.5 and 5.8 and on day 5 was 7.2 and 1.9 in group I and II respectively. Nigam et al[11] in their study clinical efficacy of buprenorphine in controlling withdrawal symptoms was compared against clonidine among 44 opiate dependent males. Subjective and objective withdrawal symptoms were assessed by withdrawal rating scales daily for 10 days. The subjects were randomly assigned to fixed dose schedule of either buprenorphine (0.6-1.2 mg per day, sublingually) or clonidine (0.3-0.9 mg per day, oral) for 10 days. Buprenorphine was found superior to clonidine in alleviating most of the subjective and objective opiate withdrawal symptoms. Subjective symptoms declined earlier among the subjects receiving buprenorphine. No untoward side-effects of buprenorphine were noticed.

The shortcoming of the study is small sample size.

CONCLUSION

Authors found that during the first few days of detoxification, buprenorphine-naloxone administration proved more effective in lowering the signs and symptoms of opioid withdrawal and in managing the urge for the drug of abuse.

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