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Tramadol vs. Buprenorphine for the Treatment of Opioid Dependence: A Comparative Study

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Abstract

Background: Tramadol is an atypical centrally acting synthetic analgesic and its o-demethylated metabolite, (+)-o-demethyltramadol (known as m1), has greater affinity for the mu-opioid receptor which makes it a candidate for opiate withdrawal treatment. , it appears to have low abuse potential and is a non-scheduled analgesic.

Aim and Objective: to compare the effects and relative clinical utility of Tramadol and Buprenorphine in the treatment of heroine withdrawal in opioid dependant patients.

Methods: Ina randomized open label parallel group design study, 70 patients with opioid dependence with daily heroine use equal to 1-10 mg, 10-20 mg, >20 mg methadone using stratified proportionate sampling were assigned into two treatment groups i.e. Tramadol and Buprenorphine. Flexible dosing schedule was followed and drug was titrated using (COWS) Clinical Opiate Withdrawal Scale and (CGI) Clinical Global Impression

Results: There was statistically significant difference between the two groups in patients with moderate level of addiction with 78% of Tramadol group and 57% of the Buprenorphine group completed detoxification at the end of 12 weeks. Whereas patients with severe level of addiction had to be maintained on buprenorphine and detoxification could not be completed with high dropout rate in tramadol group

Discussion: Tramadol has good efficacy in detoxification and relapse prevention in patients with moderate level of opioid dependence as compared to buprenorphine, Whereas Buprenorphine is better for maintenance treatment and is of higher clinical utility in severe level of opioid dependence where maintenance therapy is required.

Introduction

Many medications have been used over the past thirty years for the treatment of opioid withdrawal, including methadone, LAAM, propoxyphene, clonidine, parenteral buprenorphine, and, more recently, sublingual buprenorphine. Each has been found to have clinical strengths and limitations. Tramadol is an atypical centrally acting synthetic analgesic. In its parent form, tramadol exists as a racemic mixture of two active enantiomers which undergo hepatic biotransformation to form *N*- and *O*-demethylated compounds. The *O*-demethylated metabolite, (+)-*O*-demethyltramadol (known as M1), has greater affinity for the mu-opioid receptor than the parent compound and is responsible for tramadol's mu-opioid activity, and is primarily due to its binding to the micro receptor [1]. Despite this micro receptor activity, tramadol appears to have low abuse potential and was approved as an unscheduled analgesic in the USA in 1994 based largely on epidemiologic experience, and a number of animal and human [2-4] studies suggested, it had low abuse potential. The pharmacologic profile of tramadol makes it a candidate for opiate withdrawal treatment; Whereas Buprenorphine has high abuse potential.

Aims and objective

To compare the effects and relative clinical utility of tramadol [5-8] and buprenorphine [9,10] in the treatment of heroine withdrawal in opioid dependant patients.

Materials and Methods

- Randomized open label parallel group design study was done in a deaddiction unit of tertiary care hospital in India (Punjab)
- Inclusion criteria for this study were Male sex, heroin as drug of choice, current opioid physical dependence (i.e., withdrawal symptoms), and no current abuse of oral opioid analgesics.
- Exclusion criteria included female sex, major mental illness (e.g., schizophrenia), significant medical problem (e.g., history of seizure or hypertension), no other concurrent drug abuse, i.e. alcohol or benzodiazepine.
- 82 male Patient in the age group of 20 to 50 years that met inclusion criteria were categorized into three groups as mild, moderate and severe on the basis of amount of daily heroin use, i.e. <10 mg of methadone equivalent, 10-20mg methadone equivalent and >20 mg methadone equivalent.
- There were 35 patients who met the criteria for mild drug use, 32 for moderate and 15 that met the criteria for severe drug use. Among these patients were matched for sociodemographic characteristics and Proportionate Stratified Random sampling was done and patients were randomly assigned in two treatment groups (i.e. tramadol and buprenorphine) in each category.
- There were 12 dropouts leaving total no of patients to be 70: 30 in the mild group (15 each), 28 in the moderate group (14 each category), and 12 in severe group (6 in each category).
- Baseline investigations were done and after 8-12 hours of last heroine intake and treatment was initiated with 2 mg of

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buprenorphine and 100 mg of tramadol which was gradually increased as per patient's withdrawal symptoms.

- Flexible dosing schedule was followed and dose was titrated on the basis of objective and subjective evaluation using Clinical Opiate Withdrawal Scale (COWS) [11] and Clinical Global Impression (CGI) [12].
- Patients were detoxified in inpatient setting and followed with intensive outpatient treatment. Measurements using COWS and CGI were taken at every alternate week and patients were followed up for 12 weeks.

Results

In the mild group (1-10 mg methadone equivalent): out of 15 patients in each category patients, 8(53.33%) patients achieved early full remission and 5(33.33%) early partial remission in tramadol group and 36%, 46.66% respectively in the buprenorphine group . Moderate (10-20mg methadone equivalent): out of 14 patients in the tramadol group: early full remission was achieved by 5 (35.71) and partial remission by 6 (42.85%) summed up to 78.57%, whereas in buprenorphine group, 3 (21.42%) patients achieved full remission and 5(53.17%) partial remission amounting to total of 57.14% remission. Difference in the two was due to high relapse rate in buprenorphine group after detoxification i.e. 28.57%. Severe (>20 mg methadone) only 16.6% of patients could be sustained in tramadol group whereas 66.66% patients were maintained on buprenorphine at the end of 12 weeks. Tramadol-treated patients had higher average withdrawal symptoms when compared to the buprenorphine group and a greater reduction in withdrawal symptoms over time. In the tramadol group, average COWS maximum at week1 was 36 and in buprenorphine it was 24 ($p=0.001$) whereas at week 12 COWS max was 3 in tramadol and 8 in buprenorphine ($p<0.05$) (Figure 1) showing gradual reduction of withdrawal symptoms in tramadol group and no increase in withdrawal symptoms after drug cessation as compared to sudden decline in withdrawal symptoms in buprenorphine group which was followed by higher withdrawal symptoms on tapering the dose or after cessation of the drug (Figures 2 and 3) (Table 1).

Conclusion

- Tramadol appears to have comparable clinical efficacy as buprenorphine for treatment of patients with low levels of opioid dependence [5,13]

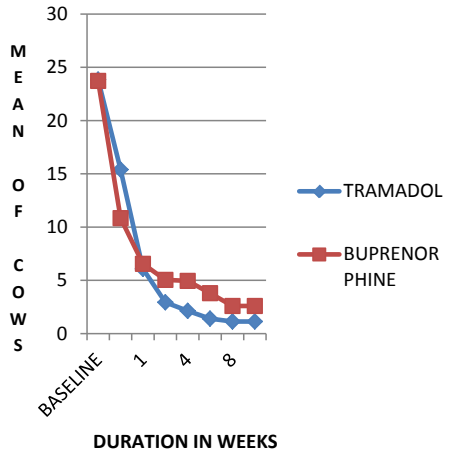

Figure 1: showing gradual reduction of withdrawal symptoms in tramadol group compared to sudden decline in withdrawal symptoms in buprenorphine group.

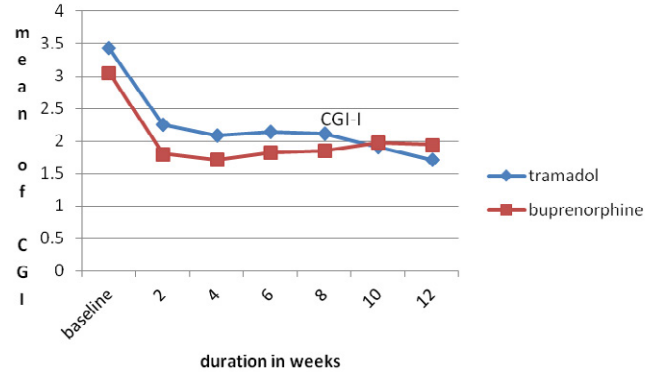

Figure 2: showing comparison of mean score of clinical global impression scale in two groups.

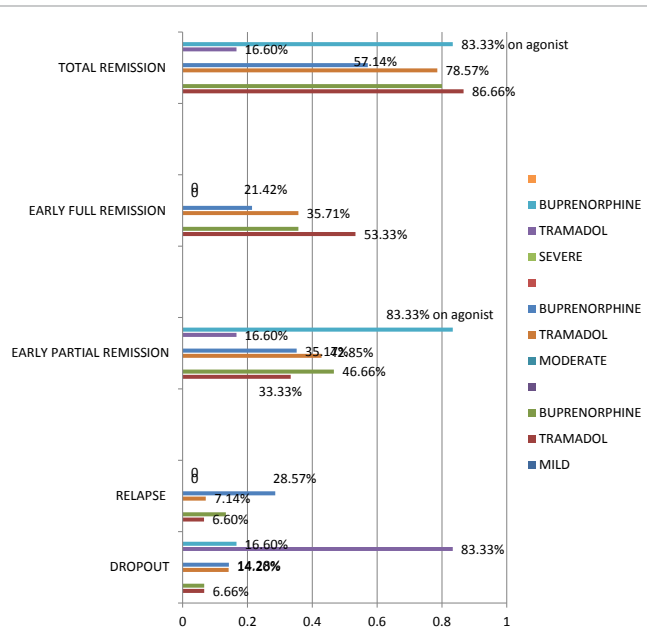

Figure 3: Bar graph showing clinical outcome of patients treated with tramadol and buprenorphine with mild, moderate and severe level of addiction.

CGI	Tramadol		Buprenorphine			
Moderate group	MEAN	SD	MEAN	SD	t	P
Baseline CGI-S	10.26	25.11	10.33	25.08	-0.56	0.5
2 weeks CGI-I	9.20	25.40	8.66	25.55	3.22	0.006*
12 weeks CGI-I	8.066	25.72	9.133	25.45	-2.41	0.02*

Table 1: T test: CGI scores of moderate level of addiction group.

- Patients with moderate level of dependence; tramadol has more efficacy in detoxification and relapse prevention with minimum abuse potential.
- Patients with severe and persistent form of addiction are more likely to have co occurring psychiatric morbidity and typically require long term comprehensive treatment and in such patient's induction and maintenance on buprenorphine may be more effective than detoxification for engaging and retaining patients in Comprehensive Outpatient addiction treatment.
- Detoxification with flexible dose schedule and tailoring the

treatment according to individual has better outcomes as compared to fixed dose rapid or ultra-rapid detoxification [14].

Summary /Discussion

- Tramadol has good efficacy [5,6,13] in detoxification and relapse prevention in patients with moderate level of opioid dependence as compared to buprenorphine [15].
- Whereas Buprenorphine is better for maintenance treatment and is of higher clinical utility in severe level of opioid dependence where maintenance therapy is required [10,12].
- These findings, if reproduced in larger studies with stronger research designs, have potentially great implications for the management of opioid withdrawal in both the inpatient and outpatient setting.

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