TITLE: Oral methadone versus sublingual buprenorphine for acute opioid withdrawals: A triple-blind RCT

BACKGROUND. Oral methadone and sublingual buprenorphine have the best evidence of effectiveness, globally formanaging acute opioid withdrawals ('detoxification').In India, buprenorphine is used commonly owing to easier availability and local evidence of effectiveness, while methadone use is limited as long-term maintenance in a few centres. Hence, we conducted this randomized controlled trial (RCT)to compare the effectiveness of methadone and buprenorphine in the in-patient management of acute opioid withdrawals.

METHODS. Study setting:a tertiary-care drug dependence treatment centre. Study design: triple-blind, double-dummy,RCT. A total of 80 malepatients aged 18-60 years were included and were randomized immediately after hospitalization, written informed consent and baseline assessment into two groups: oral methadone (with sublingual placebo) and sublingual buprenorphine (with oral placebo).Those with comorbid other substance dependence(except nicotine) were excluded.Assessment modalities:a semi-structured questionnaire, WHO-ASSIST, MINI-SCREEN, Visual Analogue Scale (VAS)for craving, subjective opioid withdrawal scale (SOWS) and clinical opiate withdrawal scale (COWS). Assessments:twice-daily application of SOWS, COWS, VAS, side-effect checklist and treatment monitoring(till treatment completion or for 20 days). For additional confirmation of abstinence:urine Thin Layer Chromatography for opioidsat baseline, 7^{th} and 14^{th} day.Treatment: a flexible and tapering dosing regimen, whereby patients were eligible for additional dosage, over-and-above the fixed, once-a-day dose, in case of withdrawals.Primary outcome measure: proportion of patients completing the in-patient treatment.Secondary outcome measures: relief from opioid withdrawals and craving. The protocol was approved by the institute ethics committee and registered in the national clinical trial registry. SPSS V24.0 was used for the statistical analysis, based upon the principle of Intention-to-treat (using last observation carried forward).

RESULTS. A total of 40 patients each were randomized into either buprenorphine or methadone arm. There were no significant differences between both the arms in terms of their socio-demographic profile and substance use profile (both opioids and non-opioids). Primary opioid used was heroin in both the groups (n=38 in buprenorphine group and n=39 in methadone group; p=0.56). There were no significant differences between both the arms in the term of past history

of detoxification and agonist treatment.The cumulative mean dose (of the entire detoxification period) required in buprenorphine group was 20.16 mg (SD=5.81; range:1.60-29.60) while that of methadone was 127.75 mg (SD=25.56; range: 40.00–175.00). The mean durationof opioid agonist treatment (for detoxification) was almost alike in both the groups(buprenorphine: 8.93 days, S.D= 3.38 and methadone: 8.70 days, S.D. = 2.23; p=0.71).The treatment completion rates were also similar i.e. 32 (80.0%) in buprenorphine and 33 (82.5%) in methadone group (chi-square=0.08; p=0.77). However, at the end of treatment regimen, a significantly higher proportion of patients in buprenorphine group had withdrawals (as measured by COWS) (p=0.02) and higher scores on VAS (p=0.01).

CONCLUSION. Sublingual buprenorphine and oral methadone were equi-efficacious in terms of treatment completion rates for the management of acute opioid withdrawals amonghospitalized Indian men. However,for clinical parameters like craving and clinical objective withdrawalsscores themethadone groupperformed better. More studies on these linesare needed to replicate the finding.. Along with buprenorphine, now methadone can also be an effective option for the acute opioid withdrawal management inIndia.

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