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Does buprenorphine maintenance improve the quality of life of opioid users?

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***Background & objectives*: The quality of life (QOL) of substance abusers is known to be severely impaired. Information on impact of opioid maintenance treatment on the QOL of opioid dependent subjects though available from the developed countries, is lacking from India. This study was carried out to assess the impact of buprenorphine maintenance treatment on the quality of life (QOL) of opioid dependent subjects at nine months follow up.**

***Methods*: Based on specified inclusion criteria a total of 231 subjects were recruited from five participating centres across India. They received sublingual buprenorphine as a directly observed therapy along with brief psychosocial intervention (provided in groups of 8-10 subjects) after intake in to the study. The WHOQOL-BREF scale domain scores obtained at baseline were compared to domain scores at nine months follow up.**

***Results*: At nine months follow up, among the 64.1 per cent retained in buprenorphine maintenance, there was a significant (P<0.001) decline in opioid use from 24.9 ± 10.1 days at baseline to 1.7 ± 4.7 days at nine months follow up and improvements in score of the four WHOQOL-BREF domains (Physical, Psychological, Social relationships and Environment).**

***Interpretation & conclusions*: The results showed the beneficial effects of buprenorphine maintenance treatment in improving the QOL of opioid-dependent subjects at nine month follow up. These results point towards the need for an expanded nation-wide provision of buprenorphine maintenance treatment as a harm reduction strategy for the opioid dependent population.**

Key words Buprenorphine maintenance - India - opioid users - quality of life

Defined in various ways[1] the concept of quality of life (QOL) helps to evaluate social and clinical interventions, treatment side effects, disease impact over time[2], treatment efficacy[3] and/or drug-addiction maintenance programmes[4,5], as also comparing the QOL outcomes with different opioid substitution agents[6,7].

The rates of dissatisfaction with life are higher among opioid dependent persons as compared to the general population[8]. The QOL is severely impaired

among substance users[5,9] and opioid dependent subjects[10]. Majority of studies on the impact of treatment for opioid dependence on quality of life are from the developed countries[11,12]. The available options for detoxification and long term treatment of opioid dependence include agnosists [methadone, buprenorphine, L-alpha acetyl methanol (LAAM)], antagonists (*e.g.*, naltrexone) and non-opioid agents (*e.g.*, alpha-2 adrenergic)[13]. Methadone and buprenorphine are recognized as effective agonists for maintenance treatment[14]. In India, at present only buprenorphine is available and data are emerging on its effectiveness among opioid users in community based settings[15], but there are no studies on its effect on the QOL.

QOL can be measured by a variety of generic and disease-specific instruments[16]. The World Health Organization Quality of Life scale (WHOQOL and its shorter version WHOQOL-BREF) was developed as cross-cultural tool for intervention studies in health care settings and a Hindi version is available[17].

Under a UNODC (United Nations Office on Drugs and Crime), Regional Office for South Asia (ROSA) funded project to develop treatment protocol guidelines for buprenorphine prescription for use in Asian countries, a sub-component of the project studied oral substitution with buprenorphine at different sites in India. This communication reports on the WHOQOL-BREF related outcome among opioid dependent subjects participating in the study in India. The objective was to study the hypotheses whether buprenorphine maintenance treatment (BMT) improves QOL in Indian drug dependents and whether the beneficial effects would remain at nine months among those receiving BMT.

Material & Methods

Setting: The study was carried out during 2005-2007. National Drug Dependence Treatment Centre, All India Institute of Medical Sciences (NDDTC, AIIMS), New Delhi conducted this study at five centres across India. There were two centres in Delhi *viz*. NDDTC, AIIMS and SHARAN and three centres from the three eastern region States of India [CALSAM (Kolkata) in West Bengal, SASO (Imphal) in Manipur and Presbyterian Hospital (Aizawal) in Mizoram]. Mizoram and Manipur came under the high prevalence States for HIV prevalence[18] and intravenous drug use (IDU) which is the route of HIV transmission[19]. Each participating centre was catering to a catchment area for its work on drug abuse through an outreach clinic.

Sampling: The *a priori* determined total number of subjects to be included was 45 at each centre which was decided on the basis of available clinical resources and literature[20] showing that with this sample size the probability of a clinically relevant treatment effect of improvement at nine months retention from about 60-70 per cent would be 95 per cent (at two-tailed=0·05). The first 45 opioid users who fulfilled the inclusion and exclusion criteria and provided an informed consent were included providing a final total sample of 231 subjects. There were 48 users at AIIMS, 46 at SHARAN, 45 at CALSAM, 47 at SASO and 45 at Presbyterian Hospital.

Study design: This was a single arm intervention study with a 'pre-post design'. After recruitment and provision of written consent, and contact details of subject, the baseline assessment was carried out. Follow up assessments were scheduled for 3 and 6 and 9 months after intake and could occur up to two weeks after the date.

Participant recruitment: Prospective subjects were identified from catchment area by informing community leaders, snowball, contacting cases already registered at the centres, drop-outs, peer outreach by ex-drug users, visits to drug using congregation sites, *etc*. The opioid users were brought to the outreach clinic in each centre to begin the intake process. Eligibility criteria included: *(i)* a minimum age of 18 yr; *(ii)* self-report of illicit drug use in the past 30 days; *(iii)* at least five years of opioid use; *(iv)* two or more failed abstinence attempts; *(v)* dependence on opioids as per ICD-10 criteria; *(vi)* willingness to take buprenorphine to participate in the study; and *(vii)* residing in catchment area. Diagnoses of substance dependence were made by the medical doctor. Subjects were excluded if they did not meet the inclusion criteria or if they had serious medical conditions like acute respiratory failure, acute hepatic disease, delirium tremens, current dependence on alcohol; female users who were pregnant or breastfeeding; known hypersensitivity to buprenorphine; presence of major psychiatric illness or physical illness due to which subject were unable to cooperate for interview.

Dosage: The subjects were put on buprenorphine (as directly observed therapy) in an individualized flexible dosing schedule. The clinician made dose adjustments

based on reported continued opioid use, craving, any withdrawal symptoms. In general, buprenorphine doses in the range 2-12 mg/day were required for stabilization. All subjects received their daily dosage at the centre (at one centre they received take-home doses for one day for Sunday).

Psycho-social intervention was delivered by the social worker to all subjects in groups of 8-10 each. Two sessions of one hour each, on psychosocial intervention, were undertaken in the first three months. The sessions focussed on reducing high risk behaviour, enhancing motivation, increasing adherence to medication, developing strategies to cut down and prevent relapse, promoting self efficacy, optimism, lifestyle changes and rehabilitation as well as avoiding substitution with other drugs such as alcohol. Efforts were made to involve family members and retain patients in treatment by making home visits.

An author-constructed simple questionnaire was used to assess standard socio-demographic information, including age, gender, education level, employment status, and marital status and information on pattern of drug use. The WHO Quality of Life brief version (WHOQOL-BREF - Hindi)[17] was used at baseline and at follow ups. WHOQOL-BREF is a 26-item shorter version of the WHOQOL-100 which correlates at 0.9 with the WHOQOL-100 with good discriminant validity, content validity and test-retest reliability[21]. The questionnaire includes two items on overall quality of life and general health, while the remaining 24 items measure four domains of quality of life: *(i)* physical (7 items); *(ii)* psychological (6 items); *(iii)* social relationships (3 items); and *(iv)* environment (8 items). It enquires about quality of life in the 'last 2 weeks', and is easily administered. Each item is rated on a 5-point (0-5) scale and the domain scores (within a 0-100 range) are calculated with 100 denoting the highest achievable score. The scale has been reported to be useful for clinics with high patient load as it takes only 5-8 min to complete[22].

Urine testing of subjects on maintenance treatment allowing verification of self-reported recent opioid use was conducted at one centre only due to budget constraints. The study protocol was approved by the ethics committee of the AIIMS, New Delhi.

Statistical analysis: The investigators at each participating centre were responsible for local coordination, data collection and transfer to the coordinating centre. All data received were checked for completeness. All analyses were undertaken using the SPSS for Windows statistical package (SPSS version 11.0 license code from South Asia Customer no.200293). Quality of life was taken as an outcome variable. The descriptive variables such as mean, median, standard deviations and 95% confidence intervals were obtained. The difference between the means was calculated by using `t' test. The four domain scores denoted the users' perception of QOL in each domain which scaled in positive direction *i.e.* higher scores denoted a higher QOL. The standard deviation (SD), the measure of dispersion around the mean was also calculated. Inter-domain correlation coefficients between the four domains were calculated. All statistical tests were two-tailed. Correlational analysis was done using Spearman's rho. Repeated-measures analysis of variance was used to determine the extent and direction of change in quality of life domain scores from baseline to 9 month follow up.

Results

The socio-demographic characteristics of the study sample are presented in Table I. Of the 231 subjects, 219 were male (94.8%; the 5.2% females came from Manipur and Mizopram) aged 35.3 ± 10.0 yr, married (53.7%), educated up to high school (31.6%), and unemployed (39.4%) using heroin [91.8%; dextropropoxyphene (spasmaproxyvon) in 8.2%] by chasing (47.6%) as well as injectable route (43.7%).

The mean age at first drug use was 22.1 ± 8.1 yr and mean duration of use was 8.4 ± 5.1 yr. The mean days opioid used was 24.9 ± 10.1 during the past one month at baseline which reduced significantly to 1.7 ± 4.7 days (P<0.001) at nine months. The mean dose for buprenorphine maintenance was 5.9 ± 2.4 mg at baseline and 3.7 ± 2.5 mg at nine months follow up. No serious adverse events were reported as attributable to buprenorphine during the course of the study.

The 12 women had a mean age of 27 ± 5.0 yr; 8 women were aged 21-30 yr; 6 women were (divorced/separated); 9 had completed high school; 7 were unemployed. All women were dependent heroin users and had been injecting heroin by the intravenous route daily before entering treatment. Follow up information for three women only was available at nine months.

For the total sample, the retention rates were 79.2 per cent at 3 months, 70.6 per cent at 6 months, and 64.1 per cent at 9 months. A comparison of socio-demographics of dropouts vs those retained in study showed no significant differences. For women,

Table I. Socio-demographics of the sample

Variable	N=231	N (%)
Sex	Male	219 (94.8)
	Female	12 (5.2)
Age (yr)	Up to 20	7 (3.0)
Mean age 35.3 ± 10.0	21-30	78 (33.8)
	31-40	87 (37.7)
	41-50	44 (19.0)
	51 and above	15 (6.5)
Marital status	Single/unmarried	79 (34.2)
	Married	124 (53.7)
	Married but single	28 (12.1)
Education	Illiterate	60 (26.0)
	5 yr schooling	33 (14.3)
	8 yr schooling	36 (15.6)
	High school	73 (31.6)
	College	29 (12.6)
Employment	Unemployed	91 (39.4)
	Employed	62 (26.8)
	Self employed	73 (31.6)
	Student	4 (1.7)
	Others (house person/pensioner)	1 (0.4)
Primary drug	Heroin	212 (91.8)
	Other opiates	19 (8.2)
Route of administration	Chasing	110 (47.6)
	Intravenous	101 (43.7)
	Smoking	18 (7.8)
	Intramuscular	2 (0.9)

completed follow up data at three, six and nine months were available for only seven (58.3%), four (33.3%) and three women (25%), respectively. The dropout was not associated with age, gender, marital status or educational status.

The subjects experienced substantial impairment in the QOL-BREF scores at baseline. The domain specific QOL scores showed significant improvements at three month follow up which continued to improve till nine months. The physical domain score increased significantly from 50.3 ± 14.4 at baseline to 61.3 ± 13.3 at nine months (P<0.001). Similarly the social relationship scores increased significantly (P<0.001) from 45.8 ± 21.3 at baseline to 56.2 ± 17.9; psychological domain scores 43.6 ± 18.2 to 57.9 ± 16.3 and environment domain scores 42.3 ± 18.7 to 54.3 ± 14.1 nine months follow up (Table II).

At nine months, a weak correlation with QOL domain scores was observed with the mean current dose of the subjects which was 3.7 ± 2.5 mg of buprenorphine. The internal consistency between the four domains of the WHOQOL-BREF was found to be excellent (Cronbach's α=0.89) among opioid dependent subjects. The inter-domain correlations were found to be positive and significant between all pairs of the four domains using two tailed test at P<0.01 (Pearson coefficient varied between + 0.62 to + 0.71 between the domain pairs).

Discussion

The present multi-centric study in community settings was a formal assessment of quality of life among opioid using subjects on buprenorphine maintenance. The quality of life of opioid dependent subjects significantly improved at nine months follow-up compared to baseline.

In the study, a total of 64.1 per cent subjects could be retained at nine months, most dropouts occurred during the first three months in treatment. A meta analysis suggests a correlation between daily dose buprenorphine and outcome[14] and treatment dropout being greater if a patient is undertreated with buprenorphine[23]. In the study, as a flexible dosing schedule with a daily modal dose of 6 mg (range 1-14 mg) of buprenorphine was prescribed. It may be argued that the dosing regimen prescribed falls well within the clinical guidelines[24] and may not be attributed to the dropout. The early dropout probably indicates a low motivation for treatment as no other baseline variables were found to be significantly associated. Preliminary information on the reason for dropouts at 3 months of treatment indicated 'left the area', 'did not like/want treatment', and 'returned to heroin use'.

The WHOQOL-BREF scale is a multidisciplinary tool that has been used for depressive patients[25], cases of dual diagnoses[26]; HIV/AIDS cases[27] and alcohol users[28] in India.We heave earlier demonstrated that buprenorphine is safe and highly effective in the treatment of opioid dependence in Indian settings[15]. The significant improvement in QOL scores visible at three months continued to show a significant increase till the nine month follow up. This highlights the benefits of maintenance treatment for opioid dependent subjects.

Table II. QOL domain scores at baseline and 3 follow up points

WHOQOL-Bref Domains	Baseline Mean ± SD (95% CI)	3 Month follow up Mean ± SD (95% CI)	6 Month follow up Mean ± SD (95% CI)	9 Month follow up Mean ± SD (95% CI)	F & P values (df=3)
	N=231	N=183	N=163	N=148	
Physical domain	50.3 ± 14.4, (48.4 - 52.2)	59.39 ± 15.1 (57.2 - 61.6)	60.80 ± 13.9 (58.6 - 62.9)	61.3 ± 13.3, (59.1 - 63.5)	F=26.9, *P*<.0001
Social relationship domain	45.8 ± 21.3 (43.0 - 48.6)	52.50 ± 16.4 (50.1 - 54.9)	54.14 ± 16.8 (51.5 - 56.7)	56.2 ± 17.9, (53.3 - 59.2)	F=11.79, *P*<.0001
Psychological domain	43.6 ± 18.2 (41.2 - 45.9)	53.87 ± 17.4 (51.3 - 56.4)	55.60 ± 16.9 (53.0 - 58.2)	57.9 ± 16.3, (55.3 - 60.6)	F=26.85, *P*<.0001
Environment domain	42.3 ± 18.7 (39.8 - 44.7)	50.79 ± 13.7 (48.7 - 52.8)	51.19 ± 14.8 (48.9 - 53.5)	54.3 ± 14.1, (51.9 - 56.6)	F=21.27, *P*<.0001

At baseline, greater impairment in psychological and environment domain scores was observed and the environment domain scores were the lowest. Highest improvements were observed in the physical health domain scores at nine month follow up which reflect lower prevalence of physical dysfunction.

The results of this study reinforce the need to further examine the meaning of QOL assessments of opioid users. First, improvements in the physical QOL domain may have resulted from physical recovery as a consequence of agonist maintenance programme itself. Second, differences in the magnitudes of the score changes across the four domains might reflect the sensitivities of different domains as well as the effects of intervention programme. Finally, a meaningful interpretation of changes in QOL scores is usually difficult, because the statistical significance of changes in QOL scores implies little about the clinical significance. Additional studies investigating the relationship are required.

Evidence suggests that adding standard psychosocial support to maintenance treatment significantly improves results in terms of reducing problems associated with drug use[29]; treatment outcome and retention[30] which translate to better life quality. In this study though the psychosocial intervention was on a low intensity model it was observed to be protective against relapse as a significant decline in the mean number of days any opioid was used (during the past one month) at nine months compared to baseline was demonstrated.

The representation of females in the present study was low (5%). This under-representation of females at drug treatment services represents underutilization of facilities as well as a lower prevalence. Several barriers to formal treatment among women have been reported[31] which the treatment professionals need to consider when promoting substance use treatment services.

The limitations of the study are that it was a single arm study with urine testing of subjects on maintenance treatment for verification of self-reported recent opioid use being conducted only at one centre. The psychosocial intervention delivered was also minimal.

In conclusion, using buprenorphine as a maintenance agent to treat opiate dependence showed a positive effect on quality of life of drug users. The findings add to the worldwide evidence base on buprenorphine treatment and the WHO QOL assessment among opioid users from India. The results may be useful to policy makers, programme administrators and evaluators as benchmark for scaling up of maintenance programme in the country to serve drug-dependent individuals.

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References

1. 'Quality of Life and Well-being'. Available from: *http://www.scotland.gov.uk/Publications/2006/01/13110743/0*, accessed on June 2, 2008.
2. Koch T. Life quality vs the 'quality of life': Assumptions and underlying prospective quality of life instruments in health care planning. *Soc Sci Med* 2000; *51* : 419-27.

3. Smith K, Larson MJ. Quality of life assessments by adult substance abusers receiving publicly funded treatment in Massachusetts. *Am J Drug Alcohol Abuse* 2003; *29* : 323-35.
4. Giacomuzzi SM, Riemer Y, Ertl M, Kemmler G, Rossler H, Hinterhuber H, *et al*. Buprenorphine versus methadone maintenance treatment in an ambulant setting: a health-related quality of life assessment. *Addiction* 2003; *98* : 693-702.
5. Winklbaur B, Jagsch R, Ebner N, Thau K, Fischer G. Quality of life in patients receiving opioid maintenance therapy. A comparative study of slow-release morphine versus methadone treatment. *Eur Addict Res* 2008; *14* : 99-105.
6. Maremmani I, Pani PP, Pacini M, Perugi G. Substance use and quality of life over 12 months among buprenorphine maintenance-treated and methadone maintenance-treated heroin-addicted patients. *J Subst Abuse Treat* 2007; *33* : 91-8.
7. Ponizovsky AM, Grinshpoon A. Quality of Life Among Heroin Users on Buprenorphine versus Methadone Maintenance. *Am J Drug Alcohol Abuse* 2007; *33* : 631-42.
8. Luty J, Arokiadass SM. Satisfaction with life and opioid dependence. *Subst Abuse Treat Prev Policy* 2008; *3* : 2.
9. Senbanjo R, Wolff K, Marshall J. Excessive alcohol consumption is associated with reduced quality of life among methadone patients. *Addiction* 2007; *102* : 257-63.
10. Habrat B, Chmielewska K, Baran-Furga H, Keszycka B, Taracha E. Subjective Quality of Life in opiate-dependent patients before admission after six months and one-year participation in methadone program. *Przegl Lek* 2002; *59* : 351-4.
11. Torrens M, Domingo-Salvany A, Alonso J, Castillo C, San L. Methadone and quality of life. *Lancet* 1999; *353* : 1101.
12. Ventegodt S, Merrick J. Psychoactive drugs and quality of life. *Scientific World J* 2003; 3 : 694-706.
13. Veilleux JC, Colvin PJ, Anderson J, York C, Heinz AJ. A review of opioid dependence treatment: Pharmacological and psychosocial interventions to treat opioid addiction. *Clin Psychol Rev* 2010; *30* : 155-66.
14. Amato L, Davoli MA, Perucci C, Ferri M, Faggiano FP, Mattick R. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. *J Subst Abuse Treat* 2005; *8* : 321-9.
15. Mohan D, Dhawan A, Chopra A, Sethi H. A 24 week outcome following buprenorphine maintenance among opiate users in India. *J Subst Use* 2006; *11* : 409-15.
16. Vanagas G, Padaiga Z, Subata E. Drug addiction maintenance treatment and quality of life measurements. *Medicinia (Kaunas)* 2004; *40* : 833-41.
17. Saxena S, Chandiramani K, Bhargava R. WHOQOL-Hindi: A questionnaire for assessing quality of life in health care settings in India. *Natl Med J India* 1998; *11* : 160-5.
18. National AIDS Control Organization (NACO). *HIV/AIDS Epidemiological Surveillance & Estimation Report for the year 2005.* New Delhi: Ministry of Health and Family Welfare; 2006.
19. Chandrasekaran P, Dallabetta G, Loo V, Rao S, Gayle H, Alexander A. Containing HIV/AIDS in India: the unfinished agenda. *Lancet Infect Dis* 2006; *6* : 508-21.
20. Soyka M, Zingg C, Koller G, Kuefner H. Retention rate and substance use in methadone and buprenorphine maintenance therapy and predictor of outcome: results from a randomized study. *Int J Neuropsychopharmacol* 2008; *11* : 641-53.
21. Skevington SM, Lotfy M, O'Connell KA. WHOQOL Group. The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL Group. *Qual Life Res* 2004; *13* : 299-310.
22. Testa MA, Simonson DC. Measuring quality of life in hypertensive patients with diabetes. *Postgraduate Med J* 1998; *64* : 50-8.
23. Mattick RP, Ali R, White J, O'Brien S, Wolk S, Danz C. Buprenorphine versus methadone maintenance therapy: A randomized double-blind trial with 405 opioid-dependent patients. *Addiction* 2003; *98* : 441-52.
24. Lintzeris N, Clark N, Muhleisen P, Ritter A, Ali R, Bell J, *et al*. Clinic guideline: buprenorphine treatment of heroin dependence. Available from: *http://www.ahrn.net/library_upload/uploadfile/file2447.pdf*.
25. Painuly N, Sharan P, Mattoo SK. Antecedents, concomitants and consequences of anger attacks in depression. *Psychiatry Res* 2007; *153* : 39-45.
26. Singh J, Mattoo SK, Sharan P, Basu D. Quality of life and its correlates in patients with dual diagnosis of bipolar affective disorder and substance dependence. *Bipolar Disorders* 2005; *7* : 187-91.
27. Wig N, Lekshmi R, Pal H, Ahuja V, Mittal CM. The impact of HIV/AIDS on the quality of life: A cross sectional study in north India. *Indian J Med Sci* 2006; *60* : 3-12.
28. Pal H, Yadav D, Mehta S, Mohan I. A comparison of brief intervention versus simple advice for alcohol use disorders in a north India community based sample followed for 3 months. *Alcohol Alcohol* 2007; *42* : 328-32.
29. Hesse M, Pedersen MU. Easy-access services in low-threshold opiate agonist maintenance. *Int J Mental Health Addict* 2006; *6* : 316-24.
30. Leonardi C, Hanna N, Laurenzi P, Fagetti R; I.D.A.C. Group. Multi-centre observational study of buprenorphine use in 32 Italian drug addiction centres. *Drug Alcohol Depend* 2008; *94* : 125-32.
31. Copeland J. A qualitative study of barriers to formal treatment among women who self-managed change in addictive behaviours. *J Subst Abuse Treat* 1997; *14* : 183-90.

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