



ORIGINAL RESEARCH PAPER

Psychiatry

IMPACT OF BUPRENORPHINE ON QUALITY OF LIFE, HORMONAL LEVELS AND SEXUAL FUNCTIONS IN POST/DODA USER ; A PROSPECTIVE STUDY FROM WESTERN RAJASTHAN

KEY WORDS:

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ABSTRACT

INTRODUCTION Buprenorphine is a new drug for maintenance therapy of opioid dependence. Aside from its role in harm reduction it may potentially enhances client's quality of life. This study aims to identify the impact of Buprenorphine as a substitution therapy on clients' quality of life,hormonal level and sexual life after 6 weeks in treatment .

Methods In this prospective study , 102 subjects from my private clinic were selected. The raw score from the WHO Quality of Life questionnaire (WHOQOL-BREF), at baseline and 6week of buprenorphine therapy were collected and converted to 0–100 scale form to give quality of life scores for four domains; physical, psychological, social, relationships and environment. Other variables of interest were socio-demography, age when joining therapy, age and duration of illicit ,drug use, sexual dysfunction were collected. Statistical analysis used the SPSS version 16.

RESULTS The results showed significant positive mean differences in all four domains with p values ≤ 0.001. The largest mean difference was for psychological domain, with mean improvement of 14.84 ± 20.88. Social domain showed the least improvement in WHOQOL scores (6.34 ± 18.80). On Beck depression inventory (BDI) there was significant difference after 6 week of therapy (p=.0008) .There was significant difference in levels of serum Testosterone, Estradiol and Prolactin . Serum AST(aspartate aminotransferase) decreased from 33.5 ± 8.2 to 29.1 ± 6.4 with p value of less than 0.0001.

CONCLUSIONS There was a significant improvement in the quality of life and sexual life of individuals who remained in the programme for 6 weeks.

INTRODUCTION

The word 'Opium' is derived from Greek, meaning 'Juice'. It is obtained from the milky exudate of the incised unripe fruit of the poppy plant *Papaver somniferum*. [1,2] The milky exudate when dried in air forms a brownish gummy mass which is then further dried and powdered to make opium which contains a number of alkaloids. In rural areas of western Rajasthan opium is consumed in social gatherings, marriages and even at condolence. Opium initiation ceremonies are held in various rural communities such as Vishnoi, Seervi, Jat, etc. and offerings are made to Lord Shiva[3,4]. The Western Rajasthan region is known for its traditional use of raw opium in the form of **amal** or **doda** [4].The ethnographic information suggests that opium use is in many ways integrated into the sociocultural fabric of the local community [5]. People of this region believe that it is aphrodisiac along with being a recreational drug and a good pain reliever.

Opium being a highly addictive substance and with severe and painful withdrawal syndrome is very difficult to get rid of once a person starts consuming it on daily basis. It also takes a huge toll over financial resources of a person as a few grams of opium cost thousands of rupees. Consequently, opium consumption is considered as an on-going stressor, not only for the individual, but for family members as well. The negative social consequences of opioid consumption accompanied by stressful life events may trigger psychological, biological and behavioural responses which interact to diminish the individual's ability to adapt, leading to emotional distress and thereby increasing the likelihood of psychological problems[6].

The interest of measuring quality of life has increased in the recent decades as it is seen as a tool for impact measurement in any intervention [7,8]. Particularly so in managing chronic diseases such as drug dependency, where one of the aims of treatment is to enhance the quality of life by reducing the impact of the disease [9]. Among the options for substitution therapy, methadone has been recognised as one of the most popular choices. In 2004, WHO had proposed for methadone as an essential medicine for the management of opioid dependence [10]. Methadone is a long acting synthetic opioid, previously used predominantly as pain reliever, but has found its role in opioid substitution therapy or specifically Methadone Maintenance Therapy (MMT) [11]. Methadone can be potentially lethal if the dose titration is not

accurate. Another emerging problem with methadone is testosterone suppression. The methadone-induced suppression of testosterone levels is mediated by the inhibition of hypothalamic GnRH production [12] as well as direct reduction of testicular testosterone secretion [13]. Buprenorphine is a new drug for maintenance therapy of opioid dependence. Unlike methadone, a pure agonist at the μ -opioid receptor, it is a mixed agonist-antagonist opioid with low intrinsic activity and high affinity at the μ opioid receptor and with no intrinsic activity, but high affinity, at the opioid receptor [14,15]. Buprenorphine has a good safety profile and a decreased abuse potential, and it suppresses opioid withdrawal, all of which make it very suitable for the maintenance therapy of heroin addicts. Additionally, it blocks the effects of concurrently administered opioids and thereby reduces the risk of relapse in buprenorphine-maintained patients [14,15]. The efficacy of buprenorphine in comparison with methadone in the therapy of opioid dependence has been firmly established [16]. Though many men start consuming opium as an aphrodisiac and as a medicine to increase the ejaculatory latency time, clinical studies have reported decreased sexual drive and performance in male heroin addicts [17].

There is paucity of studies regarding the impact on quality of life , hormonal levels ,sexual functions and mood status in Doda/Post user after substitution with buprenorphine . The aim of this study was to investigate the Quality of life , hypogonadism and sexual dysfunction in opiod dependent men receiving buprenorphine maintenance.

MATERIAL & METHODS

The study was carried out at a private psychiatric clinic during the period of July 2017 to July2018. Opium dependent patients coming to the clinic for the purpose of de-addiction were given Buprenorphine and naloxone combination as a substitute to opium . most of the patients came voluntarily while many others were referred by other hospitals. The inclusion criteria were that client must be registered with the deaddiction clinic and had completed the WHOQOL-BREF assessment at baseline and 6 weeks after enrolment in Buprenorphine substitution. Patients consuming substances other than opium, those suffering from any other significant psychiatric illness, patients suffering from Diabetes, hypertension and those suffering from any chronic neurological disorders were excluded from the study. Subjects who had not completed WHOQOL-BREF assessment at baseline

and 6 weeks and those who were terminated from the programme before 6 weeks of treatment, were also excluded from this study. The WHOQOL-BREF is a result of 10 years of development research on QOL and health care. It is a person centered, multilingual instrument for subjective assessment and is designed for generic use as a multidimensional profile, so enabling a wide range of diseases and conditions to be compared and it is a cross-culturally valid assessment of well-being, as reflected by its four domains - Physical, psychological, social and environmental [18,19,20,21,22]. Its Hindi version, The WHOQOL-Hindi appears to be a suitable instrument for comprehensively evaluating the QOL in health care settings in India. [18,19] The administration of WHOQOL-BREF at baseline to MMT clients was assisted by trained health personnel to ensure that clients fully understand the questionnaire. Subsequent assessments at 6 weeks. Social demographic data such as age at the time of enrolment gender, locality, marital status, employment and formal education were noted. Hormone assays Blood samples of all patients and all healthy controls were obtained directly before the daily morning dose of buprenorphine between 09:00 –11:00 h. Testosterone, LH, FSH, estradiol, and prolactin were assayed using an automated Immunoassay system (ADVIA Centaur XP Immunoassay System). The sensitivities for testosterone, estradiol, LH, FSH, and prolactin were 0.2 ng/ml (0.7 nmol/liter), 0.04 nmol/liter, 0.05 U/liter, 0.1 U/liter, and 0.16 ng/ml (3.4 nmol/liter), respectively. The interassay coefficients of variation were 11.8%, 7.0%, 6.7%, 5.5%, and 6.9%, respectively. The normal ranges of testosterone, estradiol, LH, FSH, and prolactin were determined to be 3.1–10 ng/ml (10.8–35 nmol/liter), 12–56 pg/ml (44–206 pmol/liter), 0.8–7.6 U/liter, 0.7–11.3 U/liter, and 2.5–17 ng/ml (53–360 nmol/liter). All samples were assayed for concentrations of testosterone, estradiol, LH, FSH, and prolactin in a single batch to reduce variability. Assessment of sexual activity and Sexual function was assessed using Arizona Sexual Experience Scale (ASEX) [25]. It is a five-item self-report inventory using a six-point Likert scale method. It evaluates sexual function in men and women, regardless of sexual orientation or relationship with a partner. It measures the quality of functioning in terms of five questions, each representing one domain: drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm and satisfaction from orgasm. These were selected as the domains because these were consistent with domains of sexual function described in the DSM-IV, International Classification of Diseases-10 (ICD-10) [23,25] and currently used inventories of sexual function. ASEX is interpreted based on a total score and/or assessment of scores on individual items with lower scores indicating better sexual functioning. A total score >19 on ASEX or a score >5 on any one item or a score >4 on any three items is associated with clinical sexual dysfunction. Reliability coefficients for internal consistency and test-retest forms are excellent, and initial favourable test results of concurrent, convergent and discriminative validity have been reported. The sensitivity of ASEX was found to be 80.8 per cent and specificity as 88.1 per cent [25]. In the current study, a Hindi translated version of ASEX was used. Depression was assessed using the Beck Depression Inventory (BDI). Suggested cut-off values of the BDI are: 0–10 no depression; 11–17 mild depression; 18–23 moderate depression; and 24 or higher severe depression [6].

Data analysis

The scoring from the WHOQOL-BREF (raw score) was transformed to the 0–100 scale scoring format, according to the guideline for the transformation of raw WHOQOL-BREF score, which is available from the WHOQOL Group [7]. The end result gave scores in the transformed 0–100 scale format for each of the four domains in quality of life; physical, psychological, social relationships and environment. The statistical analysis was done using the SPSS programme version 16.0. Students T-test was used to compare the quality of life scoring, difference in hormonal levels and sexual dysfunctions at 0 and 6 weeks.

Results

Table 1. Sociodemography characteristics of subjects

	Frequency	%
Gender		
Male	102	100.0
Age		

< 20	1	0.9
20 – 29	15	14.7
30 – 39	53	51.96
40 – 49	29	28.4
50 – 59	4	3.9
Overall mean = 34 ± 8.96		
Locality		
Rural	92	91.2
Urban	10	9.8
Marital status		
Single	14	13.7
Married	88	86.3
Employment status		
Unemployed	37	36.4
Part time employment	49	48
Full time employment	16	15.7
Educational level		
Primary	9	8.8
Matric	24	23.6
Post Matric	65	63.7
Graduation and above	4	3.9
Age starting opium use (years)		
15- 20	16	15.7
20– 25	35	34.3
25 – 30	40	39.3
> 30	11	10.7
Overall mean = 22 ± 4.65		
Previous attempt to Stop substance		
Yes	34	33.3
No	68	66.7

The socio-demography characteristics of subjects are listed in Table 1. All 102 subjects were male. The age of subjects when joining the deaddiction programme ranged from 21 to 55 years old with mean of 34 ± 8.96. 48 % of subjects have part time employment and most of them were working as a labourer. 86.3% were married and 91.2% were from rural background. 73.6% started using opium third decade. 66.7% of individuals never attempted to cut down the substance ever. Table 2 showing that daily use of opium (doda/post) 126±32 ranging from 40 to 320 gram per day. This was as per information given by patients. Average years of opium use were 9.8±4.6 ranging from 4 to 35 years.

Table 2. Characteristics of opium addicts

Characteristics	Average	Range
Daily dose of Opium (Post/Doda) gm/day	126±32	40-320
Daily dose of Buprenorphine(mg/day) at 6 weeks	9.2±4.8	4-16
Years of Use	9.8±4.6	4-35

TABLE 3. Depression scores, hormone analysis, and Enzymes status

	At day 0 (n = 102)	After 6 weeks of Buprenorphine (n = 92)		
Age	34 ± 8.96	33 ± 7.6	T= 0.8336	p= .4055
BDI score	20.5 ± 9.7	15.4 ± 11.2	T=3.3982	p=.0008
Testosterone (ng/ml)	2.6 ± 1.3	4.7 ± 1.2	T=11.6507	p=.0001
Estradiol (pmol/liter)	24 ± 9.5	29 ± 10	T=3.5702	p=0005
LH (U/liter)	3.7 ± 2.7	4.3 ± 1.6	T=1.8573	p=.0648
FSH (U/liter)	3.6 ± 2.7	4.0 ± 2.3	T=1.1047	p=.2707
Prolactin (ng/ml)	8.6 ± 3.5	4.9 ± 1.9	T=9.0112	p=.0001
GGT (U/liter)	34.0 ± 10.8	35.0 ± 18.0	T=.0308	p=.9755
ALT (U/liter)	33.1 ± 9.7	32.1 ± 6.5	T=.8341	p=.4052
AST (U/liter)	33.5 ± 8.2	29.1 ± 6.4	T=4.1344	p=.0001

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; GGT, γ-glutamyltransferase; Values are the mean ± SD. Significance was determined by ttest.

By the end of 6th week 90 % patients stuck to the buprenorphine

therapy. On Beck depression inventory (BDI) there was significant difference after 6 week of therapy (p=.0008). There was significant difference in levels of serum Testosterone, Estradiol and Prolactin. serum AST(aspartate aminotransferase) decreased from 33.5 ± 8.2 to 29.1 ± 6.4 with p value of less than 0.0001. there were no significant difference in the serum level of LH,FSH,ALT and GGT at the end of 6th week.

Table 4. WHOQOL scores

Domain	Baseline score (mean ± SD)	6 week score (mean ± SD)	Difference (mean ± SD)	T	p value
Physical	48.54 ± 13.65	64.11 ± 10.53	11.32 ± 15.68	-9.0688	<0.001*
Psychological	52.28 ± 16.87	64.43 ± 12.32	14.84 ± 20.88	-5.6759	<0.001*
Social	52.00 ± 19.83	63.43 ± 19.28	6.34 ± 18.80	-4.0616	0.001*
Environment	53.84 ± 11.49	66.36 ± 11.60	9.55 ± 15.30	-7.5161	<0.001*

According to table 3, Paired t-test was done on the WHOQOL score at baseline and 6 months after, for all four domains (Table 4). The results showed significant positive mean differences in all four domains with p values ≤ 0.001. The largest mean difference was for psychological domain, with mean improvement of 14.84 ± 20.88. Social domain showed the least improvement in WHOQOL scores (6.34 ± 18.80).

Table 5. Patients with sexual dysfunction on day zero and at 6th week

(Sexual dysfunction as per ASEX with cut-off of 5 taken as an indication of sexual dysfunction in each domain)

ASEX sexual dysfunction domain	On day 0 %(n)	After 6 weeks %(n)
Desire/drive**	88(86.27)	22(21.56)
Arousal**	79 (77.45)	12 (11.76)
Erection**	56 (54.49)	10 (9.8)
Ability to reach orgasm	34 (33.33)	22(21.56)
Satisfaction with orgasm**	86(84.31)	21 (20.58)

ASEX - Arizona Sexual Experience Scale, **p value <0.001

With a overall score of 19 or more ASEX defined sexual dysfunction was seen in 60.78 per cent patients in the opium user group. With a cut-off score of five used to define sexual dysfunction, among the domains, the highest frequency was seen for dysfunction for desire (86.27%), satisfaction with orgasm (84.31%) arousal (77.45%), followed by problems in erection (54.49%), and ability to reach orgasm was least affected (33.33%). In contrast, none of the participants fulfilled the overall definition of sexual dysfunction after 6 week of buprenorphine therapy. The prevalence of sexual dysfunction in each domain was also significantly except for the domain of ejaculation/ability to reach orgasm.

DISCUSSION

Opium consumption as part of social custom is exclusive to rural areas of western Rajasthan giving it the unenviable distinction of being home to the largest number of opium addicts in the world.[5]. The total number of registered addicts all over India was 80,809 in 1975, (Reports of Expert Committee Drug Abuse in India, 1976) [3]. According to Purohit et al (1988), 12.67% of adult males in villages of Rajasthan are opium dependent. In another study, 11.81% of adult males were opium dependent in village Joliyali in Jodhpur district [4]. Mathur et al carried out a study in 19 villages in Jodhpur district and concluded that 7.1% of adult males in villages of Rajasthan are opium dependent [26]. In this study all patients were male (n=102), almost half of them had part time job ,91% were from rural background and 86% were married. A one third of them never attempted to cut down or stop the usage of the substance (opium).A recent review on quality of life among opiate-dependent individuals showed that this subpopulation had lower quality of life in comparison to the general population and

the people with various medical illnesses [27]. Drug substitution therapy such as MMT, not only has its role in harm reduction, but it also has a beneficial impact on improving quality of life. This study has managed to show significant increasing trend of quality of life in all four domains measured; the physical, psychological, social relationships and environment within 6 weeks of therapy. The findings are similar to other significant studies. Nizam Baharom et al[24] showed significant improvement at 6 months for physical, psychological, environment and social relationships. Huong et al. showed similar trend for MMT clients who only had 3 to 6 months of therapy [28]. Padaiga et al [29].Recently, Xiao et al. demonstrated significant improvement of quality of life among MMT clients in China, as soon as 1 month of therapy [30]. Torrens et al. also showed marked increase in quality of life in the first year, followed by lesser but steady improvement for the next 3 years [31]. Our study has strengthened the notion that like methadone maintenance therapy buprenorphine replacement has positive effect on clients' quality of life invaluable role in short term. In his review, Maeyer et al. argued that the long term effect is still unclear [27] although we anticipate that the positive trend in improvement in quality of life will continue and plateau, to the level of perhaps general population. Further studies are needed to verify that the improvement of quality of life is sustained in the long run. Our findings showed that the most improved quality of life domain was psychological, followed by physical, environment and social relationships. Huong et al. and Padaiga et al. also showed that social relationship has the least improvement among clients in MMT programme which is replicated in our study.. In many parts of the world, opioid drug users are socially marginalised, so this might explain why it is harder for them to improve the social relationship quality by drug substitution therapy in a short run. Perhaps, the oral substitution programme should include more interventions on enhancing client's social and relationship skills. On a larger scale, the local community and the public should be encouraged to assimilate opioid dependent persons into the society. Serum testosterone, prolactin and estradiol levels were significantly high after 6 week of therapy which replicated the finding of Nizam Baharom et al.[24]. We found a significant improvement in sexual function after 6 weeks buprenorphine therapy. Initially 60.78 per cent individuals were having sexual dysfunction in all domains of ASEX scale which drastically reduced to none after buprenorphine therapy. Our study replicates the findings Nizam Baharom et al regarding sexual functions and hormonal levels after buprenorphine replacement therapy although the sample size was small(n=17), and duration of study was 6 months[24]. In our study we found statically significant different in BDI scores which reduced from 20.5± 9.7 to 15.4 ± 11.2 (p=.0008) which was inconsistent with the finding of Nizam Baharom et al. [24] So we can assume marked increase in quality of life, sexual functions & hormonal level after 6 weeks of buprenorphine therapy.

CONCLUSION :- Buprenorphine oral substitution therapy clients who completed 6 weeks of therapy showed significant improvement in the quality of life and sexual functions in this study. A certain non-pharmacotherapy interventions improving their quality of life should be included in the therapy. Interventions could also be aimed at strengthening client's social and relationship skills. The Buprenorphine oral substitution therapy has great prospects in the treatment of opioid addiction.

REFERENCES :-

- Jaffe JH, Martin WR. Opioid analgesics and antagonists. In: Gilman AG, Goodman LS, editors. The pharmacological basis of therapeutics. 8. New Jersey: Riverside; 1990. pp. 485-521. [Ref list]
- Nicholls L, Bragaw L, Ruetsch C: Opioid dependence treatment and guidelines. J Manag Care Pharm. 2010, 16 (1-b): S14-S21. PubMed/Google Scholar
- Purohit DR, Vyas BR, Limba PR. Opium de-addiction camp II. J Clin Psychiatry India. 1982;6:98-106.
- Purohit DR. Community approach to opium dependent subjects in rural area of Rajasthan. J Community Psychiatry. 1988;11:3-5.
- Ganguly KK, Sharma HK, Krishnamachari KA. An ethnographic account of opium consumers of Rajasthan (India): socio-medical perspective. Addiction. 1995;90(1):9-12. doi: 10.1111/j.1360-0443.1995.tb00998.x. [PubMed] [Cross Ref]
- Ruchi soni et al ,Psychiatric morbidity, quality of life and marital satisfaction among spouse of men with opioid dependence syndrome: a study from North India,http://www.ijmedicine.com/index.php/ijam/article/viewFile/580/537
- Fitzpatrick R, Fletcher A, Gore S, Jones D, Spiegelhalter D, Cox D: Quality of life measures in health care. I: Applications and issues in assessment. BMJ. 1992, 305:

- 1074-1077. 10.1136/bmj.305.6861.1074.PubMed CentralView ArticlePubMedGoogle Scholar
8. Quality of life and health: concepts, methods and applications. Edited by: Guggenmoos-Holzmann I, Bloomfield K, Brenner H, Flick U. 1995, Oxford: Blackwell ScienceGoogle Scholar
 9. Carr AJ, Gibson B, Robinson PG: Measuring quality of life: Is quality of life determined by expectations or experience?. *BMJ*. 2001, 322: 1240-1243. 10.1136/bmj.322.7296.1240.PubMed CentralView ArticlePubMedGoogle Scholar
 10. WHO: Proposal for the inclusion of Methadone in the WHO model list of essential medicines. 2004, Geneva: World Health Organization,http://www.who.int/substance_abuse/activities/methadone_essential_medicines.pdf,Google Scholar
 11. Ward J, Hall W, Mattick RP: Role of maintenance treatment in opioid dependence. *Lancet*. 1999, 353: 221-226. 10.1016/S0140-6736(98)05356-2.View ArticlePubMedGoogle Scholar
 12. Daniell HW 2002 Narcotic-induced hypogonadism during therapy for heroin addiction. *J Addict Dis* 21:47-53
 13. Singh HH, Purohit V, Ahluwalia BS 1982 Methadone blocks dopaminemediated release of gonadotropins in rat hypothalamus. *Neuroendocrinology* 34:347-352
 14. Chang KJ, Cooper BR, Hazum E, et al. Multiple opiate receptors: different regional distribution in brain and differential binding of opiates and opioid peptides. *Mol Pharmacol*. 1979;16:91-104. [PubMed]
 15. Walsh SL, Eissenberg T 2003 The clinical pharmacology of buprenorphine: extrapolating from the laboratory to the clinic. *Drug Alcohol Depend* 70(Suppl 2):S13-S27
 16. Sharifa Ezat W, Noor Azimah H, Rushidi R, Raminder K, Ruhani I: Compliance towards methadone maintenance therapy and its associated factors in Selangor primary care centers and Kuala Lumpur hospital. *Med J Malaysia*. 2009, 64: 65-70.PubMedGoogle Scholar
 17. Daniell HW 2002 Narcotic-induced hypogonadism during therapy for heroin addiction. *J Addict Dis* 21:47-53.
 18. Saxena S, Chandiramani K, Bhargava R. WHOQOL-Hindi: A questionnaire for assessing quality of life in health care settings in India. *World Health Organization Quality of Life*. *Natl Med J India*. 1998;11:160-5. [PubMed]
 19. Sathvik BS, Parthasarathi G, Narahari MG, Gurudev KC. An assessment of the quality of life in hemodialysis patients using the WHOQOL-BREF questionnaire. *Indian J Nephrol*. 2008;18:141-9.[PMC free article][PubMed]
 20. Pacian A, Kulik TB, Pacian J, Chrusciel P, Zolnierczuk-Kieliszek D, Jarosz MJ. Psychosocial aspect of quality of life of Polish women with breast cancer. *Ann Agric Environ Med*. 2012;19:509-12. [PubMed]
 21. Khosravi A, Ramezani MA, Toghianifar N, Rabiei K, Jahandideh M, Yousofi A. Association between hypertension and quality of life in a sample of Iranian adults. *Acta Cardiol*. 2010;65:425-30. [PubMed]
 22. de Oliveira PP, Sandrin CC, Batista PH, Marinheiro LP, Wender MC, Roisenberg F. Relationship between quality of life and vertebral fracture in older women living in Southern Brazil. *Rev Bras Ginecol Obstet*. 2011;33:231-7. [PubMed]
 23. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
 24. Nizam Baharom et al Improvement of quality of life following 6 months of methadone maintenance therapy in Malaysia Substance Abuse Treatment, Prevention, and Policy 2012:32 ,<https://doi.org/10.1186/1747-597X-7-32>
 25. McGahuey CA, Gelenberg AJ, Laukes CA, Moreno FA, Delgado PL, McKnight KM, et al. The Arizona Sexual Experience Scale (ASEX): reliability and validity. *J Sex Marital Ther* 2000; 26: 25-40.
 26. Mathur ML, Bansal RK, Dixit AK. Prevalence of opium consumption in rural population of a desert district, Jodhpur. *Indian J Public Health*. 1991;35(4):117-118. [PubMed]
 27. De Maeyer J, Vanderplasschen W, Broekaert E: Quality of life among opiate-dependent individuals: A review of the literature. *International Journal of Drug Policy*. 2010, 21: 364-380. 10.1016/j.drugpo.2010.01.011View ArticlePubMedGoogle Scholar
 28. Huong AGW, Ng CG, Amer SA: Quality of life assessment of opioid substance abusers on methadone maintenance therapy (MMT) in University Malaya Medical Centre. *ASEAN Journal of Psychiatry*. 2009, 10: 1-11. Google Scholar
 29. Padaiga Z, Subata E, Vanagas G: Outpatient methadone maintenance treatment program. Quality of life and health of opioid-dependent persons in Lithuania. *Medicina (Kaunas)*. 2007, 43: 235-241. Google Scholar
 30. Xiao L, Wu z, Luo W, Wei X: Quality of life of outpatients in Methadone Maintenance Treatment clinics. *J Acquir Immune Defic Syndr*. 2010, 53: S116-S120.PubMed CentralView ArticlePubMedGoogle Scholar
 31. Torrens M, Domingo-Salvany A, Alonso J, Castillo C, San L: Methadone and quality of life. *Lancet*. 1999, 353: 1101-View ArticlePubMedGoogle Scholar