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Methadone-treated Patients After Switching to Buprenorphine in Residential Therapeutic Communities: An Addiction-specific Assessment of Quality of Life

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Summary

Background: evaluating the addiction-related quality of life of a sample of opiate-dependent patients in treatment with buprenorphine in therapeutic communities after a switch from methadone. Design and participants: observational (descriptive), open longitudinal prospective study ('before-after' design); a non-probabilistic consecutive sampling procedure was used. After their admission to five therapeutic communities, a sample of patients in treatment with methadone switched to buprenorphine induction (Subutex^{R}). When considered appropriate, a gradual reduction in buprenorphine dose was begun, so as to bring it down to 0 mg within 16 weeks. The patients met DSM-IV-TR criteria for Opiate Dependence, were adults and had signed an informed consent release. All the patients were evaluated at three times; baseline assessment (Mo), after one month of treatment (M1) and after three months (M2). The study protocol was approved by the Andalusian Regional Committee for Clinical Trials, and was conducted in accordance with the Declaration of Helsinki. Measurements: The Objective Opiate Withdrawal Scale (OOWS), the Subjective Opiate Withdrawal Scale (SOWS), the Health Related Quality of Life for Drug Abusers Test (HRQoLDA Test), the General Health Questionnaire (GHQ-28), the Opiate Treatment Index (OTI) and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN). Results: A total of 119 patients met the selection criteria. Of these, 46 subjects transferred from methadone to buprenorphine, while the remaining 73 decided to stay on their methadone maintenance treatment. A statistically significant increase was observed in scores on the quality of life scale after one month of treatment with buprenorphine (from 0.62 to 0.99; $p<0.05$) and at three months (from 0.43 to 0.77; $p<0.05$). One month after the start of treatment, statistically significant improvements were observed in "general state of health" (from 10.7 to 4.3; $p<0.05$), in "severity of dependence" (11.7 to 4.1; $p<0.05$) and in "psychological adjustment" (from 7.5 to 3.7; $p<0.05$). At the three-month assessment, statistically significant differences were again observed in the same variables, except for "psychological adjustment". Conclusions: the patients who were in treatment with methadone after their admission to a therapeutic community and switched to buprenorphine were able to experience ongoing improvement in their quality of life.

Key Words: Buprenorphine; Quality of Life; QOL; Addiction; Therapeutic Community

1. Introduction

In spite of a rising incidence of cases of cocaine abuse and dependence, opiate dependence continues to be the most prevalent addictive disorder treated in specific drug addiction services in our catchment area. Methadone maintenance programmes (MMPs), whose efficacy and effectiveness have been widely documented [44], continue to be the main option for this group of patients. The results of these programmes are, however, subject to variation, depending on factors such as: a) patients' clinical characteristics at time of treatment admission, and b) a variety of process indicators [9,30,31,34,40]. One of these factors is given by the heterogeneous prognostic profile of patients who begin the programme. The availability of various different opiate substitutes, such as methadone, buprenorphine and diacetylmorphine, allows each of these programmes to be matched to certain patient subgroups. In this way, relative programme effectiveness could be improved for each patient 'typology'– a

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refinement that would enhance the overall effectiveness of the service [32].

Buprenorphine is a partial m-opioid receptor agonist for the treatment of patients with opiate dependence; there is solid evidence of its effectiveness [23,24,25,26,38]. At the present time it is commonly used and standardized in many countries. It is not, however, marketed in Spain because the National Health System has not yet come to a decision on its financing. Our only experience with it therefore belongs to research contexts [2,3,36]. Clinical research has not yet provided sufficient evidence of the patient profile that best responds to treatment with buprenorphine compared to patients on methadone [4]. Randomized clinical trials that have compared the effectiveness of these two pharmaceuticals suggest that, at equivalent doses, they are equally effective in terms of retention in the programme and in reducing heroin consumption [4,25]. However, both accumulated clinical experience and data from studies performed with observational-type designs, show some situations in which treatment with buprenorphine is advisable [28] (e.g., appearance of side-effects with methadone, fast metabolizers, pharmacological interactions, development of anti-methadone antibodies, rejection of effective doses, prejudice towards the methadone programme associated with poor compliance, perception of the buprenorphine programme as less stigmatizing, expectations and curiosity about a new opiate, easier withdrawal from the methadone programme by taking buprenorphine).With reference to this last point, buprenorphine may be a useful substance in assisting methadone maintenance patients who wish to terminate that kind of maintenance therapy [6].On the other hand, most of the studies on the effectiveness of buprenorphine treatment have been carried out in an outpatient setting, employing classical outcome indicators such as reduction in heroin use, increased retention rate or reduction in severity of addiction. Therapeutic communities have traditionally been considered drug-free-oriented residential programmes and, even if they have recently begun incorporating methadone therapy [7,46], studies that have evaluated the usefulness of buprenorphine in these residential resources are still a rarity [10]. We think that it is of interest to evaluate the usefulness of buprenorphine in the treatment of opiate addicts in therapeutic communities, as in our catchment area; therapeutic communities are not a last-in-line or last-resort service, but provide an extra link in a wide network of coordinated services.Another point in question is the concept of quality of life, which, compared to traditional outcome indicators, is becoming more widely recognized as a fundamental variable in drug abuse programme evaluation, due to the wealth of information it provides [41,42]. Although there are different operative definitions of the health-related quality of life concept, most authors consider that it deals with a subjective perception of a patient's level of physical, emotional and social functioning and well-being, as well as its repercussions on daily life activities [8]. Although several articles evaluating the impact of methadone treatment on the quality of life of these patients have already been published [5,37,41,42], there is still little available evidence on buprenorphine treatment [14,15]. All of these publications used general health-related quality of life scales. We have been working on the design and validation of a quality of life scale based on the bi-axial addiction model of Edwards et al. [12] that is specific to a drug addict population [29]. The aim of this study is to evaluate the effectiveness of buprenorphine in terms of addiction-related quality of life in a sample of patients after they have taken the decision to switch from methadone in a therapeutic community.

2. Methods

2.1 Sampling design and procedures

This has been an observational (descriptive), open prospective longitudinal study ('before-after' design). A non-probabilistic consecutive sampling procedure was used. Subjects who met the criteria for selection were eligible and signed the informed consent release. Study protocol ethics approval was granted by the Andalusian Regional Committee on Clinical Trials and the study was conducted in accordance with the Declaration of Helsinki.

2.2 Clinical setting

The study was carried out at five public residential therapeutic communities (TCs) belonging to the Andalusian Regional Drug Abuse Programme in southern Spain. These TCs are members of a coordinated service network, so the patients who are admitted to them come from specific public outpatient drug addiction service centres. When a patient is released from a TC, he/she can continue treatment provided by the referral outpatient clinic, or may be referred to daycare centres. Patients on methadone can be admitted to Andalusian TCs. At admission, the general clinical profile is defined by: a) continuous use of heroin in spite of treatment with methadone, b) the concomitant presence of one or more other addictions (especially cocaine, alcohol and/or benzodiazepine abuse), c) whether patients show any form of psychiatric comorbidity (regardless of its degree of severity) and d) whether they are difficult to handle in an outpatient regime. At the TCs, these patients have two therapeutic options: a) clinical stabilization and maintenance with methadone throughout the time they remain in residence, followed by continuing treatment with this opiate afterwards as an outpatient; b) clinical stabilization and gradual methadone dose reduction until complete withdrawal before therapeutic release. This second group is the target group selected to permit the assessment of the effects of switching from methadone

to buprenorphine.

2.3 Subjects

Buprenorphine treatment was offered to all the patients who were on methadone at a dose equal to or less than 80 mg/day admitted to the TC, and who were clinically assessed as being able to begin a gradual dose reduction of this opiate during their time of residence at the TC. Patients were maintained on their current methadone dose for 1 week, during which time they were assessed against the eligibility criteria. All patients were subjected to medical, psychological and social assessment by the usual clinical procedures during the TC admission phase. The opinions and wishes of the methadone users were taken into consideration in this assessment. Those patients who were on methadone doses equal to or less than 40 mg/day were eligible for direct admission to buprenorphine induction. If the methadone dose was between 40 and 80 mg/day, the patient went through a prior flexible individualized reduction stage until the dose was no more than 40 mg/day.

Inclusion criteria for the study were: a) diagnosed as "Opioid Dependence on Agonist Therapy" ("In a Controlled Environment") by DSM-IV-TR criteria, and currently in a methadone treatment programme at his/her referral centre, b) taking a maximum daily dose of methadone of 40 mg/day for one week before induction to buprenorphine, c) the characteristic of being a patient who is going to start or is currently in the methadone treatment programme's "tapering off/withdrawal stage", as assessed by clinical judgment and d) signed informed consent release. Exclusion criteria were: a) subjects with pending judicial sentences or with a pending sentence due to be executed in the following 6 months, b) pregnant or nursing women and c) methadone doses over 80 mg/day. We considered the following criteria for definition of opioid agonist treatment stages: 1. Induction Stage: Period comprising the first month of treatment; the time necessary to get down to the adequate dose and achieve minimum medical and psychosocial stabilization. 2. Stabilization/Maintenance Stage: Beginning after the first month of treatment and lasting for an indefinite period. From the pharmacological perspective, once the therapeutic opioid dose has been established, it is maintained with little modification. In their health-care and psychosocial facets, certain therapeutic goals, depending on patient needs and possibilities, are covered. 3. Tapering off/withdrawal Stage: begins with the decision that withdrawal from opioid treatment is to be the final goal (usually because of therapeutic or voluntary discharge).

2.4 Induction procedure

The principles of buprenorphine treatment (induction, maintenance, tapering off/withdrawal, recording of adverse effects, interactions, etc.) were organized following the criteria proposed by the Australian Department of Health Clinical Guidelines for Buprenorphine Treatment of Heroin Dependence (27). Buprenorphine (Subutex^{R}) was administered in 2 and 8-mg sublingual tablets.

Patients who decided to switch from methadone to buprenorphine were fully informed twice: a) before signing the informed consent release and b) days before the first buprenorphine dose was administered. As stated in the informed consent release, the patients could, at any time, ask anything they wanted to know about the medication and about withdrawal from treatment. The first day of induction to buprenorphine began 24 hours after the last methadone tablet was taken. At that time, the patient was asked to wait until the moment when he/she would report withdrawal discomfort. This process was personally supervised by the medical and nursing staff, who periodically recorded the symptoms using the Handelsman et al. [18] *Subjective Opiate Withdrawal Scale* (SOWS) and *Objective Opiate Withdrawal Scale* (OOWS). Patients could participate in any of the therapeutic community activities and receive psychological assistance during this time. The latest records in the SOWS and OOWS, evaluated before administering the first buprenorphine dose, were encoded for statistical analysis. An hour after taking it, the response was evaluated, again using these scales. Symptomatic medication including NSAIDs, clonidine or benzodiazepines were available for withdrawal symptoms as required. During the first five days of induction, withdrawal symptoms before/after taking sublingual buprenorphine were evaluated. The dosing schedule was flexible, with doses modified according to patient response.

2.5 Reduction procedure and follow-up

Patients went daily to the TC infirmary to receive buprenorphine. The psychosocial intervention model accompanying pharmacological treatment with buprenorphine followed the same pattern used in the methadone tapering off/withdrawal stage.

After induction, the patient received an individualized dose which was maintained for a time varying between 1 and 4 months**.** When considered appropriate, and in agreement with the patient, gradual reduction was begun (no more than 2 mg/week) to reduce the buprenorphine dose to 0 mg within 16 weeks. For assessment purposes, the maximum duration of the programme for each patient was 3 months, from the moment treatment began. After baseline assessment (before buprenorphine induction), follow-up interviews were given one month and three months after the beginning of treatment.

2.6 Outcome measures

The Objective Opiate Withdrawal Scale (OOWS) (18) is a scale evaluating the presence and severity of objective opiate withdrawal symptoms through the observation

of 13 physical signs. A clinician rates the symptoms as being absent (0) or present (1). The maximum score is therefore 13.

The Subjective Opiate Withdrawal Scale (SOWS) [18] is a 16-item checklist that measures the presence of subjective symptoms of opiate withdrawal. Patients rate each item on a scale ranging from 0 (none at all) to 4 (extremely high); scores therefore vary between 0 and 64.The purpose of the Health Related Quality of Life for Drug Abusers Test (HRQoLDA Test) [29] is to assess how addiction to substances affects a person's daily life by evaluating physical/psychological health and social functioning. It is a quality of life instrument specific to drug abuse and is based on the bi-axial concept of addiction as defined by Edwards et al. [12]. According to this concept, addiction can be defined along two axes – the first, substance "dependence" itself, and the second, "problems" (medical, psychological and social) that result from substance use. The HRQoLDA Test is a self-administered scale comprising 22 items coded on a 5-point Lickert-type scale. Low scores on this scale show a poorer quality of life and high scores a higher quality. The Opiate Treatment Index (OTI) [11] is a semi-structured clinical interview, whose purpose is to evaluate the severity of problems related to drug abuse. It consists of six subscales, the total scores on which make it possible to assess the severity of each of these problems. Each of the subscales can be applied independently. In this study, the scale given was for "General State of Health", which evaluates general medical condition and injection, neurological, cardiorespiratory, genital-urinary, muscular-skeletal and gastrointestinal problems. Low scores on this scale indicate a good state of health. We used the Spanish version of the OTI adapted to and validated in our environment [17].The General Health Questionnaire (GHQ-28) [16] is a symptom scale that estimates psychological adjustment or distress. The items on the subscales refer to subjective somatic symptoms associated with anxiety and depression, as well as difficulties in relating and adjusting to social and family roles. Low scores on this scale represent a good level of psychological adjustment. On the other hand, GHQ-28 enables "probable psychiatric cases" to be screened. We used the general cut-off point (total score of 5 or over) for this.Severity of opiate dependence was measured using Section 12 of the clinical interview, Schedules for Clinical Assessment in Neuropsychiatry (SCAN) [45]. The CATEGO-5 System is a software application that generates a clinical diagnosis from interview scores according to ICD-10 criteria. It also gives severity scores for a certain disorder (in this case, Substance Dependence), and these go to make up the Definition Index (DI). This parameter is the one we used as our indicator for severity of dependence.Finally, using a Data Collection Notebook (DCN), sociodemographic variables, variables on recent drug use and history of substance abuse, prior treatments, and biochemical and serological parameters were all recorded.

3. Results

3.1 Sample description

A total of 119 patients met the selection criteria during the recruiting stage. Of these, 46 subjects (38.7%) chose to switch from methadone to buprenorphine, while the remaining 73 (61.3%) decided to remain on their methadone maintenance programme. This group did not participate in the study, but baseline information was recorded for comparative purposes.

93.5% of the patients that began the buprenorphine treatment were males; their mean age was 36.9 years (SD: 6.8). As observed in Table 1a-b, most of them had not completed primary school, their employment level was very low and almost half of them had a criminal record. The sociodemographic profiles in the two groups is similar. The only statistically significant difference found is for the variable "level of education". Among the patients in the buprenorphine group, the mean period that had passed since their initial use of opiates and cocaine was over 15 years. These periods are longer than those observed in methadone patients, even if the differences do not reach statistical significance. In the group that stayed on methadone, there was more use of cocaine in the month prior to admission. Only small differences were detected in the case of other substances. The mean number of prior treatments was 1.3 for all patients, whether they began with buprenorphine or stayed on methadone. On the other hand, the mean time they had stayed in the last MMP before the time of the interview was almost double for those on buprenorphine. In spite of this difference, there was no statistical significance. The total time they stayed on MMP was, again, higher than for those who started with buprenorphine, but in this case too the difference was not statistically significant. As can be seen in Table 1, the mean methadone dose at the time of admission to the therapeutic community was considerably higher in the group that stayed in the MMP. The prevalence of HIV infection was low in the buprenorphine group (6.5%), and almost three times higher in the group that stayed on methadone (17.3%), although there was no statistical significance. The prevalence of HBV and HCV infection was also higher in the methadone group, as can be seen in Table 1. There were no significant differences between the groups with respect to the type of drug they had been taking. Assessment of patients' physical health was carried out using the OTI health scale. As shown in Table 1, health scores were similar for all groups in all of the subscales. In overall terms, if we consider the total score on the state of health scale, the severity of the various problems listed in the OTI was slightly lower than in the buprenorphine group. The mental health profile differs in the two groups. As observed in Table 1, the profile of psychopathological severity is more severe in the patients who continued on methadone treatment. In this group higher general scores are observed in the GHQ-28 scale

Table 1a. Demographic and clinical characteristics

	With switch toBuprenorphine (N=46)	Staying on Methadone (N=73)	p
Demographic			
Age	36.9 ±6.8)	34.3 ±:6.3)	NS
Sex (Males)	43 (93.5%)	52 (100%)	NS
Education			
Primary/no education	26 (68.4%)	55 (75.3%)	
Professional training	10 (26.3%)	8 (11%)	
Secondary or higher	2 (5.2%)	10 (13.7%)	<0.05
Employment (unemployed)	30 (65.2%)	46 (63%)	NS
Living with drug-using relatives	10 (21.7%)	16 (22.5%)	NS
Police record	22 (48.9%)	41 (57.7%)	NS
Clinics and therapeutics			
Years of abuse			
Opiates	15.3± 6.5	14.7±7.0	NS
Cocaine	15.7± 6.7	14.2±6.9	NS
Alcohol	23.7±17.3	19.8 ± 6.9	NS
Cannabis	22.2±7.1	21.1 ± 14.7	NS
Days of abuse in the last month			
Opiates	7.8±11.2	11.7±13.4	NS
Cocaine	8.3±11.5	15.5±13.5	<0.05
Alcohol	10.6±12.8	12.4±14.1	NS
Cannabis	8.3±11.5	12.9±14.5	NS
Prior methadone treatment			
Nº previous treatments	1.3±1.3	1.3±1.6	NS
Months on current treatment	42.3±40.5	27.1±34.5	NS
Months on previous treatments	16.6±32.7	25.4±35.8	NS
Months on all treatments	62.3±55.9	54.2±50.0	NS
Methadone dose at TC entry	46.6±22.0	53.5±18.4	NS
Prevalence of			
HIV +	3 (6.5%)	9 (17.3%)	NS
Hepatitis B	9 (19.6%)	8 (15.4%)	NS
Hepatitis C	24 (52.2%)	28 (53.8%)	NS
Current treatment with:			
None	19 (41.3%)	20(38.5%)	NS
Benzodiazepines	18 (39.1%)	14 (26.9%)	NS
Antipsychotics	1 (2.2%)	6 (11.5%)	NS
Antidepressants	8 (17.4%)	8 (15.4%)	NS
Antiretroviral	2 (4.3%)	6 (11.5%)	NS
Tuberculostatics	2 (4.3%)	1 (1.9%)	NS

Table 1b. Clinical characteristics			
	With switch to Buprenorphine (N=46)	Staying on Methadone (N=73)	p
OTI-Health Scale			
General Scale	3.5±2	4.27±1.9	NS
Problems related to injection	0.26±0.8	0.15±0.5	NS
Neurological scale	2.33±1.9	2.35±1.3	NS
Cardio-respiratory scale	1.41±1.6	1.9±1.9	NS
Genital-urinary scale	0.52±0.6	0.6±0.6	NS
Muscular-skeletal scale	0.78±0.8	0.94±0.9	NS
Gastrointestinal scale	1.63±1.2	1.73±1.4	NS
Total store on the "State of health" scale	10.6±6.4	11.9±5.1	NS
Psychological Adjustment			
Psychosomatic symptoms	2.5±2.4	2.84±2.1	NS
Anxiety/Distress	2.7±2.6	3.9±2.3	<0.05
Social Dysfunction	2.5±2.7	2.9±2.4	NS
Depression	2±2.4	3.2±2.7	<0.05
Severity of general psychopathology	9.7±8.3	12.7±7.7	<0.05
Prevalence of probable psychiatric cases	26 (63%)	42 (80.8%)	<0.05
Quality of life related to total health score	0.4±0.6)	0.3±0.6)	NS

and the percentage of patients classified as "probable psychiatric cases" is higher. Statistical differences are found between the groups in the "anxiety/distress" and "depression" scales. There are slightly better scores for quality of life in the buprenorphine treatment group.

The average dose of buprenorphine used during the treatment period was 4.8 mg/day (S.D.: 1.02).

3.2 One-month follow-up (M1)

After one month of treatment with buprenorphine, 93.5% of the original sample (43 patients) were still on it. The three patients who abandoned the study during this period did so voluntarily after having remained an average of 3.7 days in buprenorphine treatment. In other words, they were subjects who had failed to complete the induction phase set to last the first week. Table 2 shows the statistics found by comparing the two assessment times (M0-M1). As can be seen from the four variables analyzed, statistically significant clinical improvement was observed in the patients. The Hedges g statistic was used to interpret clinical significance. This follows the interpretation of the Cohen D statistic, according to which an effect is considered "small" if the figures are between 0 and 0.2, as a "medium-low" change if they are between 0.3 and 0.5 and as "moderate to high" if they are between 0.6 and 0.7. When a figure of 0.8 or higher is observed, the change is considered "high". As a result, and as shown in Table 2, the effect of the variations noted (all were improvements) between the two assessment times may be considered "moderate" for "psychological adjustment" and "quality of life", and "high" for "severity of dependence" and "general state of health".

The GHQ-28 subscales measure different dimensions of psychopathological adjustment. Although a considerable degree of general improvement is observed in Subscale A ("psychosomatic symptoms") and Subscale B ("anxiety/distress") between the two times, this variation is not statistically significant (Table 3). Conversely, in Subscales C ("social dysfunction") and D ("depression") statistically significant differences were observed between the two assessment times. The magnitudes of the effects recorded on the "depression" subscale should be noted carefully.

Table 2. Assessment of the results for variables after one month of treatment

	Comparison M0 – MPA (Mean and SD)	Diff in means	95% C.I. I. Low – W. High	p	Effect Size (Hedges g)
Severity of dependence (SCAN) (n=36)	11.72 (3.4) - 4.1 (2)	7.61	6.36 – 8.86	<0.05	2.7
Psychological adjustment (GHQ-28) (n=43)	7.58 (8.2) - 3.74 (4.4)	3.84	1.19 – 6.49	<0.05	0.57
General state of health (OTI) (n=43)	10.77 (6.5) - 4.37 (4.5)	6.4	4.38 – 8.41	<0.05	1.13
Quality of life related to health (TECVASP) (n=43)	0.62 (0.6) - 0.99 (0.6)	-0.37	-0.57 – -0.17	<0.05	0.58

Table 3. Comparison of GHQ-28 subscales

	Comparison M0 – MPA (Mean and SD)	Diff in means	95% C.I. I. Low – W. High	p	Effect Size (Hedges g)
Psychosomatic symptoms (n=43)	1.88 (2.4) – 1.37 (1.9)	0.51	-0.27 – 1.29	NS	0.24
Anxiety/distress (n=43)	2.1 (2.4) – 1.35 (1.8)	0.72	-0.1 – 1.54	NS	0.34
Social dysfunction (n=43)	1.84 (2.5) – 0.7 (1.3)	1.14	0.31 – 1.97	<0.05	0.57
Depression (n=43)	1.79 (2.6) – 0.3 (0.7)	1.49	0.7 – 2.28	<0.05	0.8

Table 5. Assessment of variables after three months of treatment

	Comparison M0 – MPA (Mean and SD)	Diff in means	95% C.I. I. Low – W. High	p	Effect Size (Hedges g)
Severity of dependence (SCAN) (n=21)	11.3 (3.9) – 3.65 (2.2)	6.45	2.77 – 10.13	<0.05	2.4
Psychological adjustment (GHQ-28) (n=21)	8.62 (8.6) – 5.5 (6.5)	3.1	-1.75 – 7.94	NS	0.4
General state of health (OTI) (n=20)	11.25 (7.2) – 4.8 (3.7)	7.65	5.58 – 9.72	<0.05	1.1
Quality of life related to health (TECVASP) (n=21)	0.43 (0.6) – 0.77 (0.5)	-0.34	-0.64 – 0.03	<0.05	0.58

3.3 (Three-month follow-up) (M2)

Three months after starting the treatment, another assessment was made with the remaining patients (comparison M0-M2). These represented 45.7% of those who began (21 patients). Between the one-month and three-month assessments (M1-M2), 14 subjects were released after having completed buprenorphine treatment, 6 left the TC and were switched back to methadone and 2 subjects were withdrawn for disciplinary reasons. The results of this new assessment are shown in Table 4. It may be seen that the scores show improvement in all the variables evaluated ("severity of dependence", psychological adjustment", "general state of health" and

Table 5. Assessment of GHQ-28 Subscales at three months

	Comparison M0 – MPA (Mean and SD)	Diff in means	95% C.I. I. Low – W. High	p	Effect Size (Hedges g)
Psychosomatic symptoms (n=21)	1.95 (2.4) – 1.9 (2.5)	0.05	-1.35 – 1.45	NS	0.02
Anxiety/ distress (n=21)	2.29 (2.5) – 1.81 (2.2)	0.48	-0.95 – 1.9	NS	0.2
Social dysfunction (n=21)	2.24 (2.8) – 0.81 (1.4)	1.43	-0.16 – 3.02	NS	0.64
Depression (n=21)	2,14 (2.8) – 1 (1.9)	1.14	-0.18 – 2.46	NS	0.46

"quality of life"); the improvements noted in "severity of dependence" and "general state of health" were the same as those found in the first follow-up assessment. GHQ-28 subscale changes observed are not statistically significant. However, considering the clinical importance of the variations observed, it should be noted that these patients experienced "moderate" improvements (Table 5) on Subscales C ("social dysfunction") and D ("depression"). Of the 21 subjects evaluated in the M2 follow-up, 20 concluded the treatment with buprenorphine and were released from treatment within the 16-week withdrawal period, while 1 subject was released for disciplinary reasons.

4. Discussion

Addiction to substances is a chronic condition of relapse. The health-related quality of life is a clinical parameter which is being used more and more in evaluating outcomes in this field, since, compared to traditional indicators, it provides relevant information on the impact of treatment on a level of general patient functioning [5,37,41,42]. The data from our work contribute new evidence on the effectiveness of treatment with buprenorphine measured in terms of health-related quality of life.

In this sense, we have observed that both at one month and at three months of treatment with buprenorphine, the level of patients' quality of life had risen. Although one study has found similar results in evaluating the quality of life in patients on treatment with buprenorphine [14,15] and another reported the usefulness of this partial agonist in facilitating admission to therapeutic communities [10], our work is the first to combine these two characteristics. On one hand, it provides the first evidence that we know of on the effectiveness of this opiate measured in terms of quality of life in a therapeutic community. On the other, we have for the first time employed a scale for the health-related quality of life that is specific to a population of drug addicts. General scales measure the patient's subjective perception of his/her "disease" and its repercussions on the general level of functioning. These general scales come up against problems when they are applied to drug abusers, as they are oriented to the physical concept of "disease". The HRQoLDA Test proposes that the concept of "disease" be replaced by that of "disorder" (addictive disorder) made operational by the bi-axial addiction model. Another strong point in our work is the use of the Hedges g statistic as an estimator of the effect size, that is, the magnitude of the difference that is recorded between the base-line time and at each of the follow-up assessments for a specific variable. In this sense, the clinical distinction between a "statistically significant difference" and a "relevant clinical improvement" should be borne in mind. From the perspective of clinical epidemiology, both conditions are desirable [35]. Although the criteria for considering an improvement "clinically relevant" are relative and based on knowledge of the indicator assessed, the Hedges g statistic provides an additional criterion for clinical interpretation of outcomes. Concerning the other outcome variables studied ("severity of dependence", "psychological adjustment" and "general state of health") we have observed an improvement at both one and three months of treatment. The magnitude of change at both follow-up times is greater for "severity of dependence" and "general state of health". This can be explained as a direct consequence of intervention in the therapeutic community, as the patient remains abstinent and receives adequate medical attention. The severity of psychopathological symptoms has fallen significantly at one month of treatment; this is especially noticeable for symptoms of depression. Although a further decrease is observed at three months, it is less noticeable. Data on these complementary variables abound in a tendency observed with other types of treatment that aim to improve the psychophysical health conditions that accompany a reduction in drug abuse. Working from the paradigm of harm reduction, apart from abstinence from substance abuse, an improvement in quality of life and in physical and mental health problems constitutes a basic treatment goal. It can be observed that all of these variables behave in the same way during follow-up. On one hand, an improvement at one and again at three months of treatment was verified, but the magnitude of this improvement was

greater in the first follow-up assessment and more moderate in the second. This tendency in outcomes, called the "hit-bottom effect" by Apsler and Harding [1], is common in most longitudinal opiate addiction treatment follow-up studies. According to this phenomenon, when the subject is in an active heroin abuse situation, the most likely outcome is that the variable level of severity of the problems that are related to abuse will tend to gradually increase. This gradual increase will motivate the baseline treatment demand, and the patient's initial levels of severity are likely to be relatively high. From this point onward, these levels undergo significant reduction, especially during the first month, partly due to decreased consumption. During follow-up, the figures could continue to improve somewhat, but, predictably, to a lesser degree, with variations depending on the circumstances. These falls in severity might be influenced by the 'regression to the mean' phenomenon, which cannot be monitored in studies on a single group such as this. This same phenomenon has been observed by Giacomuzzi et al. [14,15], who evaluated quality of life in a sample of 29 patients in buprenorphine treatment for three years.

Generally speaking, the sample in which we have observed these outcomes has a medium-low addiction severity profile compared to the patients who decided to stay on MMP. More specifically, the patients who chose to switch to buprenorphine showed lower baseline levels of cocaine abuse and psychopathological severity. These differences in severity profiles have also been observed in comparative studies on the long-term outcome effects of methadone and buprenorphine maintenance treatments on quality of life [14,15]. Although there is no consensus on a definite clinical profile [4], it does seem clear that treatment with methadone will continue to be the first-line alternative therapy for **a** majority of opiate-dependent patients, especially for those with higher levels of heroin use and greater heroin-related problems. This is at least partly determined by the different pharmacological profile of the two opioids (partial agonist vs. complete agonist)[13]. More studies are now needed to identify the characteristics of the subgroups of patients that best respond to methadone or buprenorphine [39,43]. As described in "Patients and Methods", treatment with buprenorphine was offered to all of the patients who were admitted to the TC with a dose equal to or less than 80 mg/day. Of the 119 patients who met the selection criteria, 46 accepted buprenorphine treatment and the remaining 73 rejected it. It is, therefore, a self-selection process. Almost all of the subjects who rejected buprenorphine explained their decision in terms of their uncertainty and fear towards a pharmaceutical unknown to them. This is understandable, since it should be borne in mind that sublingual buprenorphine treatment (Subutex^{R}) is not yet marketed in our country and this study is experimental. These patien**ts**, who have the worst kind of addiction severity profile, are the most suspicious of the benefits that buprenorphine could bring them. In Spain, it has still not been decided whether the National Health Service should finance buprenorphine; nor is it available for treatment at private centres because of the strict legislation regulating it. Fortunately, this is not true of methadone treatments.

4.1 Limitations

Our work has two main limitations. The first is the small size of the sample – a factor that makes outcomes statistically less powerful and less representative; besides this, as in all observational designs without a control group, we cannot provide any guarantee that the improvements in quality of life were not due to factors other than buprenorphine. More specifically, we cannot be sure that they would not have appeared in other patients who were admitted to the TC but did not receive buprenorphine. Secondly, the 73 patients who decided to stay on their MMP were not evaluated at one and three months because the study lacked the required funding. In this sense, we cannot discard the possibility that in this group an improvement in quality of life might have been similar, lower or higher with respect to the group that switched to buprenorphine.

5. Conclusions

The patients in treatment with methadone who, after admission to a therapeutic community, switched to buprenorphine, were able to experience ongoing improvement in their quality of life. The results of this study argue in favour of buprenorphine treatment programmes being extended to drug-dependent populations with an appropriate profile.

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Contributors

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Conflict of Interest

There are no conflicts of interests. This study was done without any pressure from the Pharmaceutical Industry or Government political interests. The authors of this work declare their desire for buprenorphine treatment to be made definitively available in Spain with the same level of equality and accessibility as methadone treatments.

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