

# EARLY DROPOUT AFTER ONE MONTH OF BUPRENORPHINE/NALOXONE MAINTENANCE THERAPY

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## Summary

**Introduction.** Suboxone (Buprenorphine/naloxone) is a drug used in opiate substitution therapy. In Hungary, it was introduced in November 2007. Suboxone is a product for sublingual administration containing the partial p-receptor agonist buprenorphine and antagonist naloxone in a 4:1 ratio.

**Aim.** Objectives of our study were to monitor and evaluate the psychosocial changes after one month of Suboxone treatment.

**Material and methods.** 6 outpatient centres participated in the study; 3 from Budapest and 3 from smaller cities in Hungary. At these centres, all patients entering Suboxone maintenance therapy between November 2007 and March 2008, totalling 80 persons (55 males, 35 females, mean age = 30,2 years, SD=5,48) were included in the study sample. During the 6-month period of treatment, data were collected 4 times; when entering treatment, 1 month, 3 months, and 6 months after entering treatment. Applied measure was the Addiction Severity Index.

**Results.** Nearly fourth of the total of 80 heroin dependent patients (18 persons, 22.5%) dropped out of treatment during the first month (the majority, 12 persons [15%] during the first week) or chose methadone substitution instead. During the first month of treatment significant positive changes were observed in all studied psychological and behavioural dimensions and proved to be stable throughout the studied period.

**Conclusions.** According to the experience with Suboxone treatment, it is a well tolerable and successfully applicable drug in the substitution therapy of opiate addicts. A critical phase seems to be the first one or two weeks of treatment. Dropout rate is high during this early period, whereas after a successful conversion patients presumably remain in therapy for a long period. At the beginning of administration special emphasis must be put on informing patients, especially concerning withdrawal symptoms that might be present during the first week, which highly contributes to better retention in treatment.

Key words: psychosocial changes, buprenorphine, naloxone, heroin substitution, maintenance therapy, dropout

Out of all drug patients entering treatment in Hungary in 2008, 17% used opiates, typically injected heroin (Hungarian National Focal Point, 2009). The aim of agonist maintenance treatments is to reduce public health risks related to intravenous heroin use; infections (mainly HIV and hepatitis C), criminality, overdose, and to increase life quality, physical and mental health of patients (World Health Organization, 2009). Besides the widespread methadone maintenance treatment in Hungary (677 patients received such treatment in 2008; Hungarian National Focal Point, 2009), in 2007 the need arose for the introduction of a sublingual product (Suboxone) containing buprenorphine and naloxone in a 4:1 ratio. The reasons were its clinical advantages compared to methadone due to its favourable characteristics when applied in

treatment; less euphoric and sedative effects, good tolerability, no unwanted side effects (overdose) (Amass et al., 2004; Kakko et al., 2007; Kleber, 2007; Orman & Keating, 2009a, 2009b), and the fact that intravenous heroin use significantly decreases during the maintenance treatment (Mammen & Bell, 2009). Suboxone, besides its application in substitution maintenance programs, is effectively adaptable in the preparation of patients for abstinence-oriented programs, hence effectively applicable for the aim of detoxification as well (Amass et al., 2004; Johnson & McCagh, 2000; Van den Brink & Haasen, 2006)

At the same time, there are only a few studies on the efficacy of Suboxone treatment even in the international scope. Objectives of our study were monitoring and evaluating the effect of Suboxone treatment parallel with

the introduction of the product in Hungary. Besides exploring dropout ratio and the dimensions influencing it, we also intended to study the changes occurring in the course of treatment.

## MATERIAL AND METHODS

### Sample

All opiate dependent patients entering Suboxone maintenance treatment therapy between November 2007 and March 2008 in Hungary were included in the study sample. Suboxone therapy was provided at six treatment centres during this period:

1. Nyíró Gyula Hospital Drug Outpatient and Prevention Centre, Budapest
2. Soroksár Addiction Treatment Centre, Budapest
3. Blue Point Drug Counseling and Outpatient Centre, Budapest
4. INDIT Foundation Baranya County Drug Outpatient Centre, Pécs
5. BMKT Pándy K. Hospital, Drug Outpatient Centre, Gyula
6. Dr. Farkasinszky Terézia Drug Outpatient Centre, Szeged

During the study period 80 opiate dependent patients were involved in Suboxone treatment. Before entering the treatment, all patients received detailed information on Suboxone therapy. 68.8% (55 persons) of the study sample were male, while 31.2% (25 persons) were female. Mean age was 30.2 years (sd=5.48 years, with an age range of 18-45 years).

### TREATMENT PROTOCOL

The treatment was carried out according to the guidelines of the Suboxone Therapy Protocol. The appropriate dose and dosage was defined by the doctors responsible for the treatment, these parameters were not influenced by the present study. The applied dosage was between 6 and 32 mg (mean dose: 19.3 mg; SD=5.3 mg) however, most of the patients (87.5%) received 16-24 mg buprenorphine per day. During the first 30 days of treatment patients were obliged to attend the treatment centres daily. For two weeks after the first month visit on every second or third day, and after this period weekly visits were required.

### Measures

During the study, besides the necessary laboratory examinations, HIV and HCV tests, we have assessed the severity of addiction, prevalence of comorbid psychiatric disorders and other parameters regarding the patients' psychosocial status.

### Addiction severity

Extent of dependence was measured with the Addiction Severity Index (ASI). Hungarian experiences with the measure of McLellan and colleagues (McLellan et al., 1992) show satisfactory results concerning validity and reliability of the applied measure (Gerevich, Bacskai, Ko, & Rozsa, 2005; Rácz, Pogány, & Máthé-Árvay, 2002).

### Craving

The extent of craving was assessed by the Heroin Craving Questionnaire of Tiffany et al. (Schuster, Greenwald, Johanson, & Heishman, 1995; Tiffany, Fields, Singleton, Haertzen, & Henningfield, 1995). The scale consists of five subscales; (1) Desire to Use Heroin; (2) Intentions and Plans to Use Heroin; (3) Anticipation of Positive Outcome; (4) Relief from Withdrawal or Dysphoria; (5) Lack of Control over Use. Reliability indices of the scale are satisfactory (Cronbach's  $\alpha$  for the entire scale is .962; while for the subscales: .907; .892; .857; .782; and .815 respectively).

### Well-being

The short version of the WHO well-being questionnaire was applied (Bech, Gudex, & Johansen, 1996; Susánszky, Konkoly Thege, Stauder, & Kopp, 2006). Reliability of the scale is satisfactory (Cronbach's  $\alpha$ =0.782).

### Procedure

Changes in the measured dimensions during treatment were studied in a prospective design.

In the first month of treatment, data on patients were collected 2 times; right before entering treatment ( $T_0$ ) and 1 month after ( $T_1$ ). Patients entering Suboxone maintenance treatment therapy between November 2007 and March 2008 became part of the study sample. Regarding the 6-month follow-up period, data collection ended on 30th October, 2008.

## RESULTS

In the study period 80 opiate dependent persons entered Suboxone therapy in one of the six treatment centres. 18 persons (22.5%) dropped out of treatment within one month. Highest dropout rate was present in the first week; 12 persons (15%) left the treatment during this period.

Changes in the specific dimensions were analyzed by means of paired sample t-tests, by comparing the mean values of consecutive points of data collection. In all seven profiles of ASI a favourable transition could be observed after the first month of treatment. There was a significant improvement in all assessed dimensions during the first month of treatment ( $p < 0.001$ )

Similarly, there was a significant improvement in the well-being dimension during the first month and no further changes occurred in the following months.

Dimension of craving showed a pattern similar to the abovementioned dimensions. The total scores of the scale, like all of its subscales indicated significant ( $p < 0.001$ ) decrease in craving during the first month, while no further changes occurred in the course of treatment (tab. 1).

Factors possibly influencing retention in treatment were introduced to a stepwise method linear regression analysis. Number of weeks in treatment was considered to be the outcome variable while values of all measured dimensions at the point of entering the treatment were included as potential predictor variables. As a result of the analysis three variables remained in the model. Retention

Table 1. Means and standard deviations of craving dimensions, and changes between points of data collection

	T <sub>0</sub>		T <sub>1</sub>		T <sub>2</sub>		T <sub>3</sub>
	N <sub>0</sub>	N <sub>1</sub>	N <sub>1</sub>	N <sub>2</sub>	N <sub>2</sub>	N <sub>3</sub>	N <sub>3</sub>
N	16	61		49		30	
Heroin Craving (I)	210.4(63.03)	196.0(61.69)	99.5 (56.41)	97.0 (54.40)	93.1 (50.28)	90.2 (45.11)	93.8 (46.86)
T		10.130***		0.517		-0.614	
Desire to use heroin	39.9 (17.33)	34.5 (15.32)	15.7 (11.21)	15.1 (10.79)	14.0 (10.54)	13.9 (10.52)	15.0 (9.22)
t		8.215***		0.693		-0.863	
Intentions & plans	36.9 (13.33)	36.6 (14.77)	16.4 (11.81)	15.9 (11.53)	14.8 (9.07)	14.0 (8.72)	15.3 (9.26)
t		9.089***		0.704		-0.948	
Anticip. of pos. outc.	44.4 (15.17)	39.8 (13.72)	20.3 (12.94)	19.1 (12.11)	18.8 (12.98)	17.8 (11.63)	20.0 (10.60)
T		9.550***		0.183		-1.26	
Relief from withdr.	48.9 (12.47)	45.4 (11.57)	25.6 (12.29)	25.8 (12.20)	24.8 (13.58)	23.8 (11.33)	22.4 (10.98)
t		11.129***		0.502		0.95	
Lack of control	40.4 (13.84)	39.7 (12.76)	21.5 (13.61)	21.0 (13.17)	20.7 (10.98)	20.8 (10.30)	21.1 (11.80)
t		8.286***		0.16		-0.197	

\* =  $p < 0.1$ , \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$

in treatment is best predicted by higher perceived stress on the PSS ( $P = 0.335$ ;  $p = 0.008$ ), lower childhood hyperactivity ( $P = -0.339$ ;  $p = 0.009$ ), and less favourable legal status assessed with ASI ( $P = 0.264$ ;  $p = 0.040$ ). Model explains 24.7% variance (Adjusted  $R^2 = 0.203$ ) of the outcome variable (number of weeks in treatment).

## DISCUSSION

In the course of the present study 80 opiate dependent persons entered Suboxone treatment. 22.5% (18 persons) dropped out after one month of treatment. In this time almost in all studied psychological and psychosocial characteristics positive changes were experienced (except for the Employment/Support dimension of the ASI, where primarily only a tendency of improvement could be observed, but during later phases of treatment a significant improvement was measured). Predictors of retention in treatment were a higher level of perceived stress, lower childhood hyperactivity and more legal problems. Our further analysis suggest that initial higher stress level is also in tight connection with depressive symptoms, however, depression did not appear in the model as a predictor variable because its effect was mediated by the perceived stress. The relationship between stress, depression and opiate dependency is well known (Strain, 2002), just as the tendency of decreasing depressive symptoms in the course of maintenance treatment (Nunes, Sullivan, & Levin, 2004).

When summarizing our experiences, we emphasize the promising results of Suboxone treatment, although at the same time we highlight the 60% dropout rate of patients, in case of whom other types of treatment, for example methadone maintenance treatment or abstinence-oriented therapy, should be applied (Kakko et al., 2007; Kleber, 2007; Whitley et al., 2007). Furthermore, it

must be underlined that 37.5% (18 persons) of the total of 48 patients characterized by early exit from treatment (before six months) dropped out in the first month of therapy, which for the majority of treatments, is a critical phase for patients. During this interval presence of withdrawal symptoms of various extents can be expected, which may be the reason for a very early dropout (in the first week) of 12 persons. This result inevitably shows that the initial period, the first one or two weeks of Suboxone buprenorphine, characterized by a stronger  $\mu$ -opiate receptor affinity, gradually expels heroin from the binding sites, while at the same time, due to its partial agonist effect, withdrawal symptoms cannot be totally eliminated. Appropriate support provided for the patients, thorough information on the unpleasant symptoms and especially on their transient nature, seems to be crucial in helping patients through this critical phase and thus in increasing the probability of long-term retention in treatment.

These results show, that pharmacological treatment alone is not enough for opiate-dependent patients. A motivation enhancement therapy or motivational interview (Hettema, Steele, Miller, 2005, Guydish et al., 2010, Magill et al., 2010, Grenard et al., 2006) is a crucial element of their treatment. For the first part, they object the early dropout, while during later phases they support retention. Retention (Walker, 2009, Vigezzi et al., 2009) is a non-specific factor related to treatment effectiveness. Unplanned discharge management (Crévecoeur-MacPhail et al., 2010) is also an important factor to keep patients in treatment. Another factor affecting retention is the long term community care (McKay, 2009).

Similar researches might be conducted on bigger population. Also, to avoid unplanned discharge, it would be important – besides boosting motivation – to monitor patients' psychosocial functions.

## Limitations

The research was done amongst the patients of only a few treatment centres, which indicates that it would be advisable to repeat research in other similar facilities. The one month period of the follow-up time should be extended to six months, ideally to one year, to harvest more precise results from the later stages of the therapy, the changes of the patients' state and also the extent of retention. □

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