

THE EFFECT OF BUPRENORPHINE THERAPY ON DEPRESSIVE SYMPTOMATOLOGY IN HEROIN ADDICTS

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Abstract: According to the World Health Organization, heroin addiction is one of the most widespread diseases, right behind cardiovascular and malignant diseases.

Heroin addicts have a large number of comorbid somatic and psychological disorders, among which depressive states occupy a significant place.

It is known that on the territory of North Macedonia, two substitutes are used in the treatment of heroin addiction: methadone, which is an opioid agonist, and buprenorphine, which is an opioid agonist and antagonist.

Of particular importance is the effect of buprenorphine on kappa receptors, which have a major impact on mood and sexual functioning.

So the goal of this research is to see the effectiveness of buprenorphine therapy on depression in heroin addicts.

Materials and methods: In this prospective study, which was conducted at the Day Hospital for Addictions at the Psychiatric Hospital Skopje, 20 heroin addicts undergoing treatment with buprenorphine therapy were evaluated before treatment after three months and after six months of treatment.

The study used a questionnaire to collect sociodemographic data (gender, age, education, marital status, employment) specifically designed for the study. Depression scores were determined using the Hamilton Depression Rating Scale. Data were analyzed by descriptive method and by Student's t test. Statistical significance was considered $p < 0.05$.

According to the data obtained, after three months of treatment with buprenorphine we had a decrease the score of depression but without statistical significance $p = 0,43$, while after six month of treatment we had a decrease with statistical significance $p = 0,034$. However, in 5% of the respondents the score of depression was still high.

Conclusion The results obtained in our study indicated that buprenorphine therapy affects the reduction of depressive symptomatology in heroin addicts. So, when we have a high depression score in patients, antidepressants should not be used immediately, but buprenorphine should be allowed to take effect first.

If there is no improvement, then move on to the second step, including antidepressant therapy.

Keywords: heroin addicts, buprenorphine therapy, depression

1. INTRODUCTION

According to the World Health Organization, heroin addiction is one of the most widespread diseases, right behind cardiovascular and malignant diseases. It is known that heroin addiction is not only a medical problem, but also a social with the presence of a large number of deviant conditions, so its treatment is complex (Cindy F et al, 2024; Cornelia H et al, 2024). Opioid substitution treatment is required in parallel with psychotherapy treatment.

A large number of comorbid somatic conditions are present in heroin addicts (Skin and Soft Tissue infections, Cardiac complication, Pulmonary complication, Hepatitis B.C, HIV infection, Sexually (transmitted diseases) as well as comorbid psychiatric disorders. Anxiety disorders some studies found rates as high as 9,2 percent; personality disorders across studies range from 34,8 percent to 68 percent; other psychiatric disorders such as schizophrenia are relatively rare (prevalence to 2%) among which depressive states occupy a significant place. Some studies of mood disorders in opioid dependent patients report a high prevalence of depression as high as 53,9 percent (Alice D. et al, 2024; Bente W et al, 2023).

It is known that on the territory of the Republic of North Macedonia, two substitutes are used for the treatment of opiate addiction: methadone, which is an opioid agonist, and buprenorphine, which is an opioid agonist and antagonist.

Of particular importance is the effect of buprenorphine on kappa receptors, which have a major impact on mood and sexual functioning (Gatti F et al, 2020).

In some preclinical studies, the opioid drug buprenorphine has been shown to alter responses to emotional stimuli, exhibiting effects similar to antidepressants and anxiolytics (Jake-Schoffman D. E et al, 2023).

Several clinical studies suggest that symptoms of depression may be reduced in heroin patients treated with buprenorphine therapy, as a result of increasing serotonin levels (Sarah V. et al 2023; Bente .W et al,2023) So the **AIM** of this research is to see the effectiveness of buprenorphine therapy on depression in heroin addicts.

2. MATERIAL AND METHODS

The prospective study was conducted at the Day Hospital for Addiction Treatment, part of the Psychiatric Hospital Skopje. 20 male heroin addicts, middle-aged $\pm 24,3$ years who entering in treatment with buprenorphine therapy, were evaluated and depressive symptomatology was also monitored.

Inclusion criteria in the study were the presence of heroin addiction with depressive symptomatology, while exclusion criteria were the existence of other psychological and somatic comorbid conditions.

Before the start of the study, all participating patients signed written consent. All the patients were treated with 20mg -32mg/day doses of buprenorphine therapy.

The patients were evaluated before treatment, after three months and after six months of treatment.

The study used a questionnaire to collect sociodemographic data (age, years of education, marital status, employment) specifically designed for the study. Depression scores were determined using the Hamilton Depression Rating Scale. Consisting of 21 questionnaire. The obtained scores on the scale are ranked in 4 levels (score <8 indicates no depressive symptomatology, and a score >8 indicates depressive symptomatology).

Data were analyzed by descriptive method, by Student's t test and Spearman's correlation. Statistical significance was considered $p \leq 0.05$.

3. RESULTS

In our study we got the results who report that only 40% of patients living with partner, 75% was employment and only 10% have more than 12 years of education Tabl.1

Table.1. Sociodemographic characteristic of examination group.

perimeter	category	N	%
Live with partner	yes	8	40
	no	12	60
employment	yes	15	75
	no	5	25
Years of education	>12	2	10
	≤ 12	18	90

Source : Own research by the authors Spasovska, A. and Janicevic, D.

In the table 2 were present the score of Hamilton Rating Scale before treatment with buprenorphine therapy after tree and after six month of treatment

Table 2. The score od HM0- Hamilton Rating Scale score before the treatment, HM3- Hamilton Rating Scale score after 3 month treatment, and HM6- Hamilton Rating Scale after 6 months of treatment

HMRS	N	Mean	Std. Deviation	Median	Minimum	Maximum
HM0	20	22,17	2,981	20,1	16	26
HM3	20	18,66	1,225	21,5	13	24
HM6	20	10,53	1,314	11	7	16

Source : Own research by the authors Spasovska, A. and Janicevic, D.

We got not statistical significant results between HMRS score before treatment and after tree month of treatment with buprenorphine therapy but we got a statically significate result after six mount of treatment $p=0,034$ table 3 .

Table 3. Hamilton Rating Scale score before and after treatment with buprenorphine therapy

HM score	T test	P level
HM0 – HM3	0,48	0,43
HM0 – HM6	1,92	0,034

Source Own research by the authors Spasovska, A. and Janicevic, D.

Also in our study we got the correlation between buprenorphine therapy and some sociodemographic characteristic (living with partners, years of education, unemployment) but the correlation was insignificant table 4.

Table 4. The correlation between effects of buprenorphine therapy and sociodemographic characteristic

correlation	partner	education	employment
Spearman's	-0,132	-0,122	-0,049
P level	0,365	0,435	0,87

Source: Own research by the authors Spasovska, A. and Janicevic, D.

4. DISCUSSION

According to the data obtained, after three months of treatment with buprenorphine we had a decrease the score of depression but without statistical significance $p=0,43$ while after six month of treatment we had a decrease with statistical significance $p=0,034$. However, in 5% of the respondents the score of depression was still high. The results obtained in our study correlate with the results from another, that indicate an antidepressant effect of Buprenorphine as a result so its effect on kappa opioid receptors (Gatti F et al,2020)

We should also mention that such a good therapeutic effect is also due to the high doses of buprenorphine that were applied at the beginning of the treatment.

But the results in our study don't correlate with another studies of these field (Cornelia H et al,2024; İpek B et al 2023).

This bad result is most likely due to treatment with an inadequate dose (low), irregular intake of therapy which leads to the use of other psychoactive substances and abandonment of treatment.

However, in our study, we found that only in 5% of the subjects, despite the adequate dose of Buprenorphine, we did not obtain the desired score on the depression scale.

In such cases, guided by data from other studies, it is necessary to switch to the use of antidepressants. The SSRi antidepressants (Sertraline, Paroxetine) shown the best effect. (Bente W et al,2023; Corinne N et al ,2024).

According to some research, depression is most common in people who live alone and are unemployed (Cindy F et al,2024; Cornelia H. et al, 2024).

Also in our study we got the correlation between Buprenorphine therapy and some sociodemographic characteristic (living with partners years of education unemployment) but the correlation was insignificant (table4.)

However, in our study we did not have a high percentage of people living alone who were unemployed, and most of them were well-educated, and what is very important, they were all placed on adequate (high) doses. Which according to a large number of studies, is a major prerequisite for the antidepressant effect of buprenorphine therapy. (Sarah V et al,2023; Miha L et al,2025)

5. CONCLUSION

The results obtained in our study indicated that buprenorphine therapy affects the reduction of depressive symptomatology in heroin addicts. So, when we have a depression score in patients, antidepressants should not be used immediately, but buprenorphine should be allowed to take effect first.

If there is no improvement, then move on to the second step, including antidepressant therapy.

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