

Is the availability of buprenorphine/naloxone therapy for opioid-dependent inmates a necessity?

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ABSTRACT

Agonist therapy (OAT) programs in combination with a psychosocial approach are the most effective way to prevent relapse in opioid-dependent patients. These programs reduce morbidity and risk behaviours for HIV transmission and other infections, improve quality of life and retention in treatment, and have a positive impact on antisocial behaviour. They are therefore very useful for prisoners with a history of opiate use. OATs based on buprenorphine/naloxone (B/N), along with others using methadone, are currently available in Spain. Diversified treatment offers an alternative treatment for opioid dependence that is more personalized and tailored to the patient's characteristics. As regards effectiveness, both drugs are very similar, but B/N shows a better safety profile and fewer drug-drug interactions and can be dispensed in pharmacies once the patient is released, which can assist with the patient's social reintegration. B/N treatment is more expensive than methadone.

It is advisable to have different modes of OAT. These should be prescribed according to the characteristics and needs of each case, without incarceration impeding the right to drug treatment, which should be similar to that performed outside prison.

Key words: Substance-Related Disorders; Opioid-Related Disorders; Opium / Agonism; Substance Abuse Treatment Centers; Buprenorphine; Naloxone; Prisons; Spain.

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INTRODUCTION

The number of opioid – dependent people in Spain is estimated at a total of 100.000-150.000 individuals. This figure reaches 1.200.000-1.500.000 people in Europe. In 2007, 50% of treatment implementation featured heroin as the main substance of abuse, and 650.000 European opioid-dependent patients were subject to opioid agonist therapy (OAT) substitution programs¹. Substitutive treatment in combination with psychosocial care is the main therapeutic option for heroin consumers in Europe²⁻³. After the introduction of buprenorphine in Cyprus's medication stock in 2007, this type of therapy is available in all EU Member States, as well as in Croatia and Norway. Northern and eastern European countries feature a reduced availability of these therapeutic strategies.

The most commonly used agonists in substitution treatments are methadone (MT) and buprenorphine alone or in combination with naloxone (B/N). In Spain, commercial distribution of the B/N combination started in 2006, but its use is still reduced, which does not seem to be due only to the lack of experience with this therapy. The aim of this report is to assess the advantages and disadvantages of substances used in OAT, as well as to review the situation of parity between treatment in prison and therapy outside the prison realm.

OAT TREATMENT

It is sometimes believed that substance abuse is a manifestation of moral weakness, without taking into consideration that physiopathology of addiction is

affected by genetic factors which make certain individuals more prone to addiction⁴. It is also usually disregarded that extended drug consumption leads to brain alterations⁵ which modify the reward pathways⁶ and produce an intense desire of drug consumption known as *craving*, consequently leading to reiteration in consumption or relapse⁷⁻⁸.

OAT treatment, along with psychosocial approach, is the most effective way to prevent relapse in heroin consumers¹⁻².

1. OAT advantages

OATs not only diminish the use of opioids and have a positive impact on patient behavior⁹⁻¹⁰, but they also decrease morbidity and risk behavior for HIV and other infections' transmission. In addition to this, they improve quality of life and treatment adherence^{8,11-12}. These programs are important not only from a healthcare point of view, but also from a socio-political one, since they contribute to reduce illegal substance abuse, delinquency and criminality¹³.

Opioid dependent patients feature morbidity, both from infections related to consumption, acute intoxication ("drug overdose"), and other causes such as traffic accidents associated to drug abuse. Regarding this, OATs present ideal results, especially as far as injectable drug consumption and consumption related risk behavior are concerned¹⁵. As a matter of fact, it is estimated that opioid-dependent patients who are not subject to OAT therapy feature a risk 6 times higher of HIV infection than those who are under treatment¹⁶. For the most part, OATs reduce opioid consumption, both injectable and non-injectable, along with the number of consumers with several sexual partners and the use of sex in exchange for drugs or money¹⁷. Actually, decrease in endogenous drug abuse and other risk behavior patterns has led to a reduction, both in Spain and in other countries, of HIV and HCV prevalence amongst prison population, as well as amongst non-convict population¹⁷⁻¹⁸. OATs also help to decrease mortality rates. Regarding this, an estimate reports that patients under OAT treatment feature a rate three or four times lower than prison inmates who are not subject to this sort of treatment.

On the other hand, the average yearly cost in Spain per patient under triple antiretroviral treatment was estimated at 8.100 euros in 2011²⁰, while the yearly cost per OAT patients under MT or B/N therapy was estimated at 1.041 euros (MT) and 1.050 euros (B/N) in 2010²¹. Through comparison between the different treatment's yearly costs, the economical, human and

healthcare benefit of HIV infection prevention becomes apparent.

Concerning criminality, it is commonly accepted that OATs decrease its rates, for they reduce opioid consumption, which is intimately related to recidivism²²⁻²³. In a study carried out in the UK, comparison between opioid-dependent individual's penalties two years prior to and after their specific treatment depicted that the number of penalties had been reduced by 26%. This did not depend on whether patients began their treatment willingly, as a consequence of a court warrant issued regarding the patient or as a requirement for probation²⁴. OATs are, therefore, also beneficial from a social point of view. It is possible that, taking only into account their impact on criminality prevention, excluding different revenue, OATs are cost-effective interventions. By means of reducing delinquency, police, court and prison costs are reduced as well²⁵⁻²⁶. In the US, a report features that for each dollar invested in treatment, the costs regarding drug-related crimes, including theft, and the court systems costs decrease 4 to 7 dollars. This figure could reach 12 dollars if healthcare cost reduction was to be taken into consideration.

2. OATs in prisons

There is a significant opioid-dependent patient prevalence among prison inmate population, for it is common that illegal drug consumers commit criminal offence, especially against property^{9,27-28}. In Spain, the last National Drug Policy Report (PND in Spanish)²⁹, estimated that a total number of 34.827 drug-dependent prison inmates in 89 prison facilities were subject to drug-dependence treatment: 7.431 in outpatient treatment programs, 8.768 in modular programs and 18.628 in MT maintenance programs.

Our country has attested that opioid-dependent individuals commit more frequent and serious offence than cocaine consumers³⁰⁻³¹. The Proteus Study reports a 19% of court procedure prevalence among patients under OAT.

Spain is one of the countries with the highest OAT implementation rates in prisons³². The priority concerns of the PND Plan of Action for the period starting from 2009 until 2012³³ and the main aims of the 2009-2016 National Strategy on Drugs³⁴ include ensuring integral attention for drug-dependent prison inmates regardless of the treatment modality.

Moreover, a high percentage of prison inmates incarcerated for drug-related crime and who have not been subject to treatment during their imprisonment, lapse back into drug consumption after their release

²⁵. This has been related to a high risk of overdose and death during the first weeks and months after release ^{29, 35-36}. OAT programs carried out in prisons reduce the risk of heroin consumption during the period immediately following discharge ³⁶. Due to this, coordination with community OAT maintenance program services becomes extremely relevant, for it prevents treatment interruption.

3. OATs: equal access, quality and diversification both amongst the community and within prisons.

OATs are provided more and more frequently in prisons. The continuity of this sort of therapy after incarceration is approved by 26 European countries but is not implemented in five of them. 21 of these countries provide treatment from the start upon arrival in prison¹.

Intravenous drug consumption (UDI in Spanish) and some infections related to endovenous abuse, as well as HIV infection, are much more prevalent amongst prison inmates than amongst the community ³⁷⁻³⁸. As a result of this, and especially due to the fact that incarcerated population has the same right to healthcare as the population without freedom deprivation, the same therapy modalities which are offered to opioid-dependent patients outside prison must be offered to prison inmates ³⁹, as it has been regarded by the WHO for years ⁴⁰. The EU Council of Ministers considers that healthcare within prisons must reach the same levels as healthcare provided to the community, with special emphasis on treating psychiatric disorders ⁴¹ and transmissible disease, HIV infection in particular. It has been considered that prison healthcare must rely upon a similar budget as primary healthcare aimed at the general population. Nevertheless, if we take into consideration the higher risk of suffering certain diseases, such as mental disorders and others, amongst prison inmates, this budget should probably be larger ⁴¹. The WHO even recommends that prison healthcare services work together with the national healthcare services and the Ministry of Health, in order to ensure that prisons provide the same healthcare standard as hospitals ⁴². Despite this fact, prison healthcare services in Spain have not been integrated, except for the basque services, into the autonomous healthcare services, causing possible service malfunction ⁴³ and equity problems as far as healthcare resources are concerned.

There are many countries which still have not implemented OAT therapy programs in prisons, despite it being a therapeutic option widespread outside

prisons ³². This service discrepancy between the community and incarcerated population contradicts, as it has already been stated, the WHO and the EU recommendations, and is both ethic and therapeutically hardly legitimate. Quality healthcare must provide a series of services which include all therapeutic options regarded by the scientific community.

SUBSTANCES COMMONLY USED IN OAT: MT AND BUPRENORPHINE OR B/N.

OATs have mainly used MT as opioid agonist because it is the substance with more therapeutic experience, although an estimate portrays that 25% of the cases in which it is used certain circumstances (drug interactions, pathology history, etc.) make the use of B/N more suitable ⁴⁴.

In October 2002, the US Food and Drug Agency (FDA) approved the use of B/N sublingual tablets in OATs excluding traditional programs ⁴⁵. B/N is prescribed in the US by general physicians without any sort of additional training ⁴⁶. Moreover, B/N has been successfully used in "harm control" programs in New York City, aimed at handling withdrawal amongst marginalized population ⁴⁷. In the EU, healthcare authorities approved its use for opioid-dependence treatment in 2006. Two years later, it was commercially distributed in Spain with the same aim and it is included in the Social Security's pharmaceutical provision ⁴⁸. In France, MT and buprenorphine have been used in OAT programs since 1996, but currently 60% of all patients have been prescribed buprenorphine treatment ⁴⁹⁻⁵⁰. The review by Auriacombe et al ⁵⁰ describes how its use became widespread. In 1995, the French Drug Agency approved its use and its commercial distribution started in February 1996. General physicians could prescribe buprenorphine, while only doctors working in clinics authorized to provide drug abuse treatment could prescribe MT. The easier use of buprenorphine, along with its complete economic reimburse due to the fact that opioid-dependence is considered a chronic disease, resulted in 10 times more opioid-dependent patients being treated with buprenorphine than with MT. From 1995 to 1999, OAT programs (80% with buprenorphine, 20% with MT) increased by 95%, while death incidence caused by overdose decreased by 79%. During this same period, death risk attributed to MT treatment was 10 times higher than the one attributed to the use of buprenorphine. Despite the fact that 20% of buprenorphine stock ended up in the illegal market, there were only rare overdose cases, usually related to sedative

consumption. Moreover, buprenorphine is also used in France to treat opioid-dependent pregnant women, resulting in withdrawal syndromes amongst neonates which are less frequent, less severe and shorter than those reported amongst infants whose mothers were subject to MT therapy⁵⁰.

Other European countries, such as Sweden, Finland, the Czech Republic and Latvia feature more OAT programs with buprenorphine. Nevertheless, its use in Spain is less extended. In our country, the "Patient Care Quality" survey, by means of which 91 doctors (16 of them within the prison healthcare services) who attended opioid-dependent patients were interviewed, featured that 100% of interviewees considered availability of all treatment modalities of vital importance, in such a way that these different therapies could be used attending to patient's needs. Diversified and individual treatment availability has also been proposed as one of the courses of action by experts participating in the "Treatment Systems and Drug-dependence care Lecture", set up by the Parliament (Cortes Generales) through the Joint Commission constituted to deal with Drug Issues⁵¹.

Both MT and buprenorphine feature in the WHO's essential drug list for its use in OAT. Once their efficacy has been agreed upon, it becomes important to highlight that some patients manifest predilection towards one or other treatment option. This leads to an increase in treatment compliance and adherence, and therefore to a greater efficacy^{17,53-57}. Full availability of drugs which have proven their efficacy in opioid-dependence therapy offers, as it has been previously stated, alternatives regarding treatment which can better attend individual needs and feature a higher possibility to adapt to patient's characteristics⁵⁸. Despite the fact that, without any doubt, MT therapy will continue to be widely implemented, there is a group of patients for which the use of B/N is the most appropriate option⁵⁹.

4. Use of MT and B/N in prison

In France OATs with MT or with B/N can be put into practice with patients who have already initiated treatment prior to their incarceration, although before 2002 the only drug used to start OAT in prison was buprenorphine, for MT could only be prescribed by physicians specifically authorized to do so⁵⁰. In the US, in 2009, 55% of prison facilities offered OATs with MT and 14% offered treatment with buprenorphine⁴⁴. In Spain, OAT with MT has become progressively widespread since 1992 and represents today a therapeutic option completely integrated into prison

healthcare. Conversely, OATs with B/N are highly limited in prisons, presumably because of economic issues, despite it being supported by the Social Security system. Nevertheless, both the *European Network of Drug Services in Prison* (ENDSP) and the Spanish prison policy emphasize that drugs financed by the Social Security and attainable for the general population must also be available for the incarcerated population⁴³.

Literature concerning OATs with B/N in prisons includes some experience in the field. Thus, in a study carried out with 45 prison inmates in Puerto Rico who participated in a B/N daily program 6 months prior to their release⁶⁰, with whom the continuation of their treatment amongst the community was coordinated, the 30 days prior to incarceration were compared to the 30 days following their release. The number of days in which former inmates consumed heroin (median 30 vs 8 days; $p=0,01$) and cocaine (median 2,5 vs 0 days; $p=0,04$), along with the number of criminal acts ($p=0,06$) decreased more significantly amongst patients who completed treatment. Additionally, a study carried out in a New York prison facility in 2009 which compared OAT with buprenorphine to OAT with MT, reported a higher rate of adherence to treatment during incarceration amongst patients under OAT with buprenorphine. Furthermore, patients under treatment with buprenorphine featured more continuity in treatment after their release⁶¹. It has also been monitored that amongst patients who after their release are subject to treatment with buprenorphine, the adherence rate (38%) and the number of opioid withdrawal weeks (6,2) are similar to those amongst patients in the community who have not been imprisoned (46% and 5,9 weeks)^{32,62}. In Spanish prison facilities, the first B/N use experience to be acknowledged was carried out in the Albolote prison (Granada), where it was put into practice during the last detoxification phases of patients under treatment with MT⁶³, aimed at alleviating opioid deprivation withdrawal syndrome. MT withdrawal with B/N featured good results amongst 86% of patients (12 out of 14), a figure similar to data gathered amongst the community regarding the use of buprenorphine with the same aim⁶⁴⁻⁶⁵. Furthermore, patients manifested a high satisfaction rate and no significant adverse reactions were reported⁶³.

DIFFERENCES BETWEEN MT AND B/N USE.

There are several comparative studies confronting buprenorphine vs methadone, but their results are so-

metimes contradictory, for they include different doses, induction periods, etc. Originally, buprenorphine trials (without naloxone) which compared 2-16 mg doses to 20-90 mg MT doses⁶⁶⁻⁷⁰ did not report any difference regarding consumption decrease and program adherence time, although they seemed to indicate the need for high buprenorphine doses to ensure success.

The first clinical trial with sublingual absorbency buprenorphine was carried out by Uehlinger et al in 3 Swiss community health centers⁷¹. It involved 58 patients selected at random who were prescribed buprenorphine (4-16mg dose/day) or MT (30-120mg/day). There were no differences between both groups as far as illegal opioid consumption decrease is concerned, but there was a higher adherence amongst MT patients, which the authors of the study attributed to the low buprenorphine doses. Suboptimal doses and slow induction have been attributed to the lower retention of buprenorphine⁷²⁻⁷³. Conversely, comparison between 65mg/day MT doses and 12mg/day buprenorphine doses portrays no difference regarding neither adherence nor illegal opioid consumption⁷⁴. Hence, buprenorphine doses play an important role as far as adherence and *craving* reduction are concerned. A recent meta-analysis⁷⁵ concludes that medium (8-15mg/day) and high (over 16mg/day) buprenorphine doses are effective concerning heroin consumption reduction when compared to placebo, but is less effective than MT, especially if MT is prescribed with adequate doses between 60-120 mg/day. Consequently, the authors advocate buprenorphine use mainly when high MT doses cannot be prescribed due to patient refusal or other causes, or due to a lack of MT tolerability.

Additionally, other studies depict differences regarding quality of life, which seem to improve more positively amongst patients treated with B/N than amongst MT patients⁷⁶. B/N use seems also better than MT therapy as far as security is concerned, for it features lower overdose^{36,50,77-79} and QT interval prolongation⁸⁰⁻⁸⁴ risks. As regards the interaction profile, B/N is globally better than MT⁸⁵ and it can be prescribed without causing withdrawal syndrome amongst HIV infected patients when combined with non-nucleoside reverse transcriptase inhibitors (NNRTI), such as efavirenz or nevirapine⁸⁶. In conclusion, B/N is a drug that features less complications than MT, clonidine or lofexidine, when aiming to achieve ambulatory detoxification^{63,87}.

CONCLUSION

MT and B/N are both adequate drugs for OAT. There is enough experience as far as both are concerned. Choosing one or the other depends on the opioid-dependent patient's condition and characteristics. Diversified treatment offers a treatment alternative which adapts better to the patient and can therefore improve the healthcare quality provided.

B/N is an option with an efficacy similar to MT, somewhat more expensive, but safer, with a better interaction profile, less stigmatized and with the possibility of being distributed by pharmacists once patients are released, which might enhance social reintegration. Due to all this, and especially because it features in the Social Security drug provision, it should be available for patients who request it and for whom healthcare professionals consider it more suitable regarding the patient's individual characteristics, as it currently occurs outside prisons.

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