DEI DIPARTIMENTI E DEI SERVIZI DELLE DIPENDENZE

Convegno Regionale FeDerSerD Sardegna

14 GIUGNO 2016

DELLE DIPENDENZE IN SARDEGNA

tra crisi e bisogni come i Ser.D si ripensano

Sala Convegni Mistral 2 Hotel Oristano

*"Farmaci **sostitutivi:** diversione e misuso"*

ASLNuoro

SERVIZIO DIPENDENZE

R. CICALO'

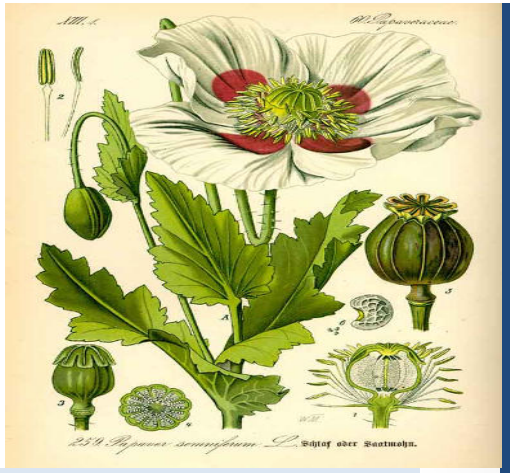
“ FARMACO”

“Droga” ***“Veleno”***

farmaco può indurre nel nostro organismo effetti dannosi simili a quelli che si hanno assumendo veleni e sostanze tossiche.

Ma soprattutto ***“ promessa” -“aspettativa di salute”***; promessa che non è sempre rispettata soprattutto quando manca la chiara partecipazione mentale e fisica del paziente alla cura stessa

La malattia ha spinto l'uomo a seguire il suo istinto di sopravvivenza cercando rimedi naturali



Una delle sostanze presenti era il papavero da oppio, quindi la morfina che ancora oggi viene utilizzata a distanza di millenni come farmaco antalgico tra i più potenti ma anche i più economici a nostra disposizione.

Ma è proprio la morfina, con le sue caratteristiche e le sue possibilità di utilizzo a mostrarci la molteplicità dell'azione dei farmaci. Da ciò deriva che il controllo sui farmaci e del loro utilizzo e quindi dell'appropriatezza, dell'indicazione clinica, impiega molti anni per evidenziare i pericoli che possono scaturire dall'abuso di farmaci

Fig. 5 - Le prime utilizzazioni terapeutiche dell'amfetamina

Fig. 4 - Utilizzazione dell'eroina all'inizio del XX secolo

- Così sostanze ora proibite venivano liberamente utilizzate in Europa un secolo fa. Agli inizi del XIX sec l'eroina veniva utilizzata per pennellature delle gengive dei lattanti nel periodo della dentizione, oppure come farmaco antiasmatico. L'amfetamina, veniva usata come spry nasale nel raffreddore dei bambini o nei piloti dei caccia durante le guerre.

- Gli ambiti di cura nel campo delle Dipendenze sono stati fortemente caratterizzati dall'uso dei farmaci sostitutivi degli oppiacei che hanno avuto un ruolo nel ridurre i danni associati alla dipendenza da oppiacei (overdose, infezioni, atti criminali…)

ADR (adverse drug reaction):

OVERDOSE somministrazione di una quantità di medicinale, singola o cumulativa, **superiore alla massima dose raccomandata** secondo le informazioni autorizzate del prodotto

OFF-LABEL il medicinale è usato **intenzionalmente** per finalità mediche **non in accordo** con le informazioni autorizzate del prodotto

ABUSO intenzionale uso eccessivo del medicinale, sporadico o persistente, accompagnato da effetti dannosi fisici o psicologici

ERRORE TERAPEUTICO il medicinale è usato **non intenzionalmente** ed **in modo inappropriato non in accordo** con le informazioni autorizzate del prodotto

Ma ADR può essere…

- conseguenza di due fenomeni che caratterizzano la prescrizione, la somministrazione e l'assunzione della terapia sostitutiva con oppioidi di sintesi:

Misuso :

1) assunzione della terapia per via diversa da quella abituale (ev, im. x os)

2) inosservanza della posologia e/o delle modalità di prescrizione

3) inosservanza da parte del paziente delle indicazioni fornite dal sanitario circa le modalità di custodia del farmaco

Diversione :

si intende per es. la non-assunzione del farmaco da parte del paziente a cui è stato prescritto e la possibilità di vendita o cessione dello stesso ad altri

L'American Society for Medicine identifica negli USA le principali motivazioni al misuso e diversione:

- ***Diversione:***
- pressione dei pari (condivisione che può essere favorita da dosaggi eccessivamente alti o da affidi particolarmente protratti)
- aiutare amici o parenti
- necessità di denaro per debiti, per spese di vita o per acquisto di altre sostanze preferite

- ***Misuso***
- abitudini (storia di uso ev)
- contenere sintomi di astinenza, presenza di craving per oppiacei
- raggiungere maggiori effetti gratificanti (più energia, più euforia)
- ridurre effetti negativi (dolore, ansia, depressione)

MISUSO

DIVERSIONE

- l'automedicazione
- le caratteristiche del farmaco prescritto
- Le caratteristiche del paziente, la sua storia clinica, la sua compliance al trattamento,la relazione terapeutica costruita dentro il servizio.

- correlata sia alle caratteristiche del farmaco quanto alla " disponibilità" dello stesso da parte del paziente ossia alla sua libera gestione

- Conseguenze dirette del misuso e della diversione sono situazioni quali overdose, decessi, infezioni, ed in definitiva il non raggiungimento dello scopo terapeutico per il quale tale terapia è stata prescritta.
- Tali condizioni si verificano per tutti i tipi di farmaci. Casi di misuso del paracetamolo (acetaminofene) soprattutto in età pediatrica hanno suggerito una serie di misure per prevenire errori terapeutici : diversificazione del colore dei blister a seconda del dosaggio, l'apposizione di immagini specifiche: bambino che gattona, ragazzo con il pallone sottobraccio, adulto che legge…

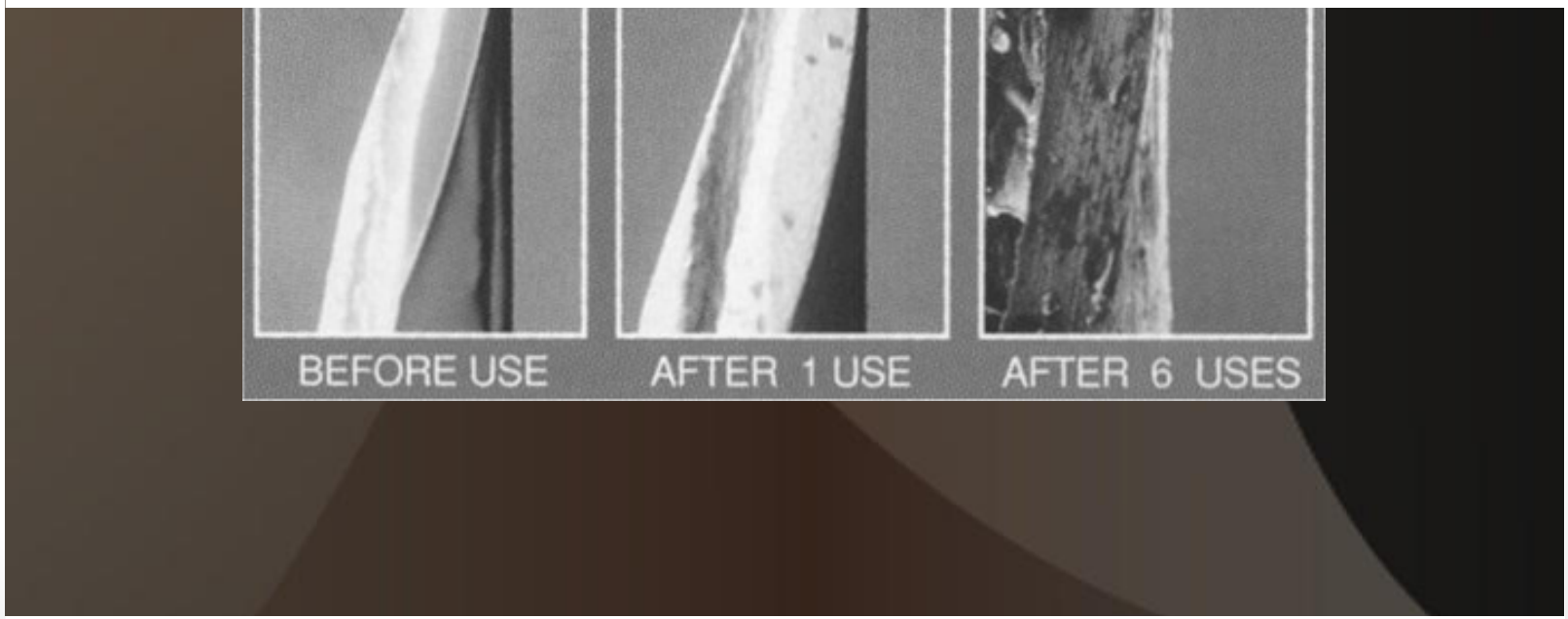
Da uno studio americano *"Substance use and mental health services administration-2013"*

- emerge che le classi di farmaci più comunemente oggetto di misuso sono:

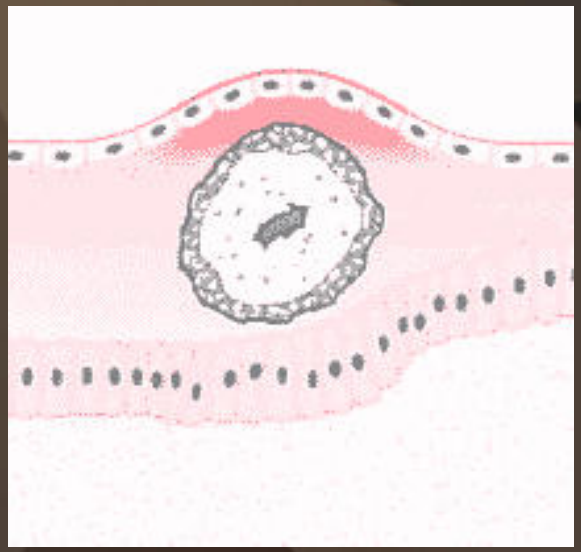
- Antiallergici 25%
- Antidolorifici 22%
- Antibiotici 21%

- Nella popolazione TD il misuso si verifica con le terapie a base di MTD o BPF, di BDZ e di analgesici

Nei Tossicodipendenti conseguenze più frequenti del misuso sono le infezioni



Nei Tossicodipendenti
conseguenze più frequenti del misuso sono le infezioni

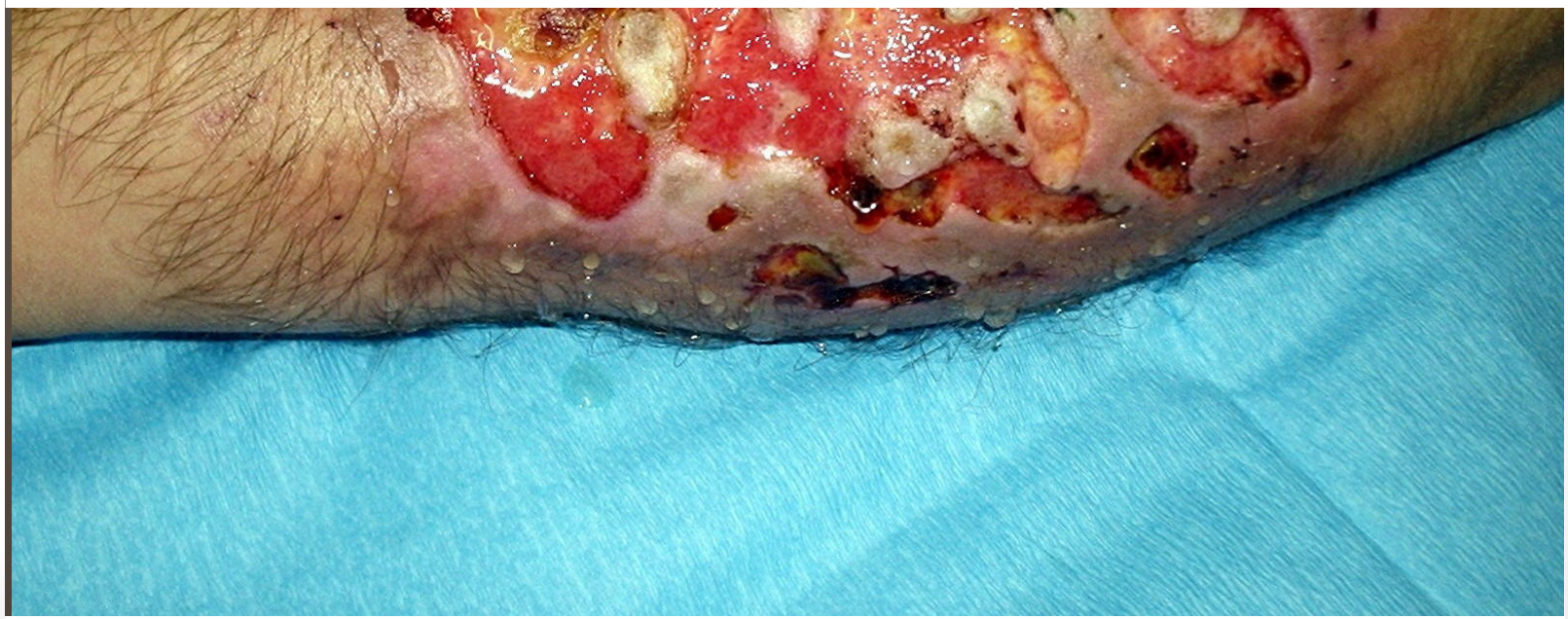


Ascesso i. localizzata con area colliquata
Staphylococcus aureus (MRSA),
streptococchi orali (S. milleri)

Nei Tossicodipendenti conseguenze più frequenti del misuso sono le infezioni

Ascesso esteriorizzato conseguente ad iniezione di buprenorfina

Nei Tossicodipendenti
conseguenze più frequenti del misuso sono le infezioni



Nei Tossicodipendenti
conseguenze più frequenti del misuso sono le infezioni

FIGURE 7: Extensive necrosis secondary to cocaine injection (courtesy Dr. Milton Viana, Belo Horizonte)

Nei Tossicodipendenti conseguenze più frequenti del misuso sono le infezioni

Ulcera conseguente ad iniezione di morfina orale disciolta

Desomorfina
Krokodil

Injection practices are likely to cause puffy hands syndrome, but buprenorphine misuse should not be considered as a significant risk factor.

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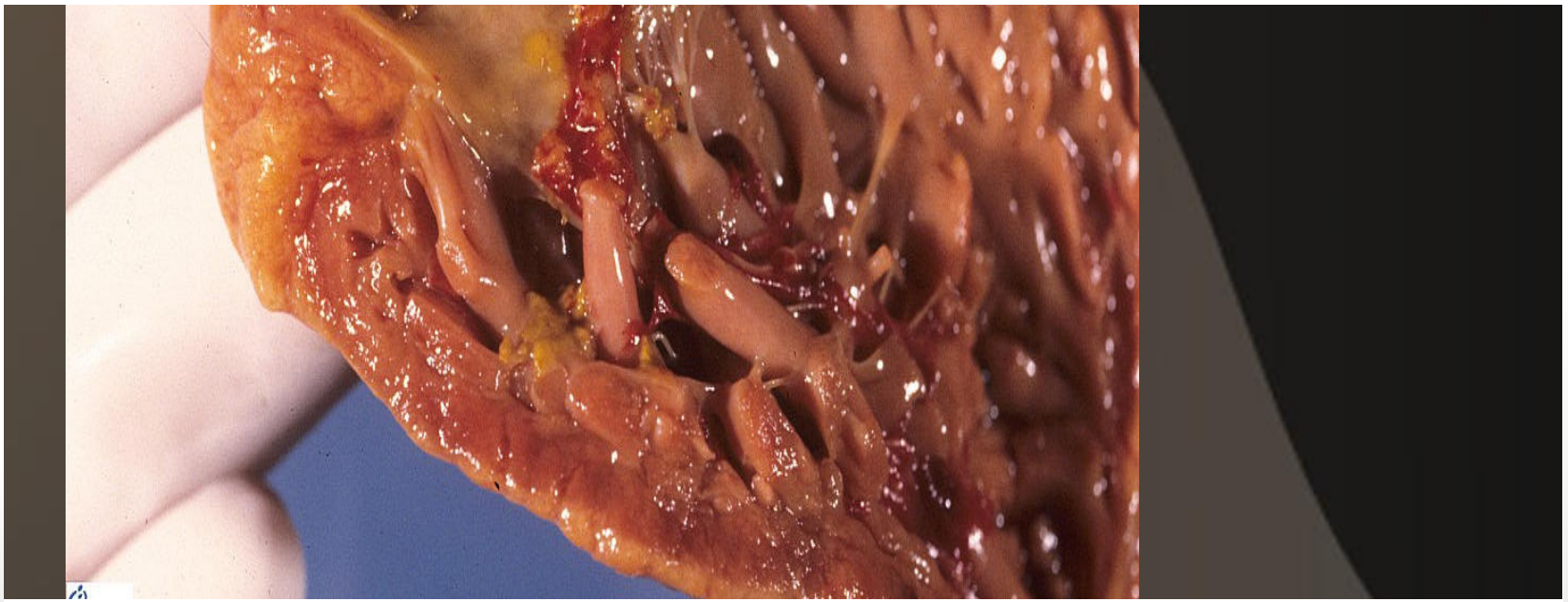

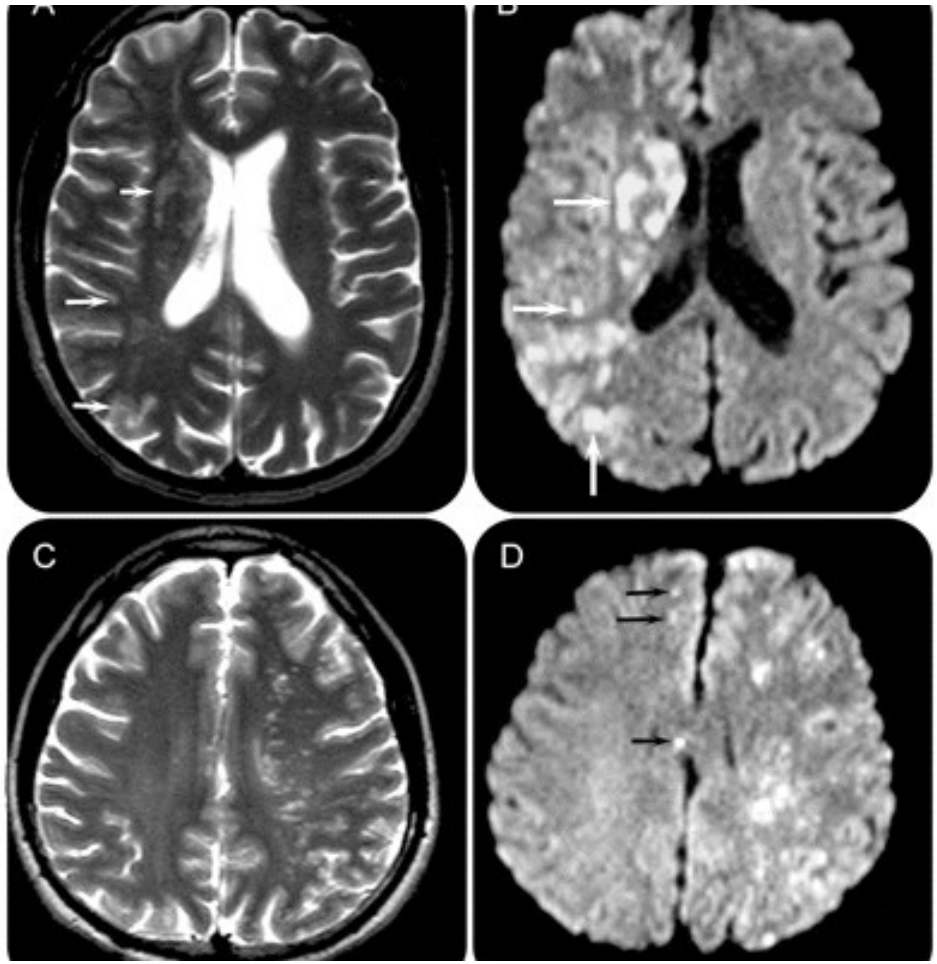

Buprenorphine tablets can be intentionally or inadvertently injected into the **carotid artery**, causing a characteristic appearance on diffusion-weighted imaging, consistent with embolic cerebral infarction.

C. C. Tchoyoson Lim, Sze Haur Lee, Yee-Choon Wong, Francis Hui
Neurology September 15, 2009
vol. 73 no. 11 876-879

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- Infezioni in cui i fattori facilitanti sono la promiscuità, lo scambio di siringhe, pratiche quali “ leccare l’ago”, “ sminuzzare “ le cpr tra i denti,” passare la saliva sulla pelle. Gli agenti patogeni in causa sono prevalentemente stafilococcus aureus epidermidis pseudomonas candida albicans il cui di

(S. Giancane,2014 - ed. Gruppo Abele)

- " agofilia" espressione del piacere che deriva dall'iniettare un farmaco sostitutivo con l'ago. La sostanza sembra assumere un significato più marginale rispetto all'enfasi ed al rituale del " buco". Questo spiega anche l'uso di sostanze più disparate quali calce, vino, detersivo…
- il desiderio di un piacere appagante ed immediato, la ricerca di quel " flash" che è sempre fervido e presente nella memoria del TD.

ASLNuoro

Ed ancora diversione è

- il fenomeno del " Doctor shopping" che si verifica quando una persona cerca assistenza da più medici con lo scopo di avere maggior numero di prescrizioni.
- Ed il misuso nelle prescrizioni è altissimo.
- Alcuni studi come quello di Goldsworthy 2008 e di SAMHSA nel 2014 riportano il primo che il 23% del campione aveva scambiato la propria ricetta e il 27% ammetteva di essersi fatto prestare farmaci da altri, il secondo 15.3 milioni di persone in USA hanno usato farmaci fuori prescrizione; 6.5 milioni nell'ultimo mese..

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La supervisione della terapia sostitutiva

“Bimba lasciata sola in casa tra rifiuti e metadone. Madre condannata”-2013

“RICOVERATA ALL'OSPEDALE DEI BAMBINI DI PALERMO
Bimba di 3 anni in rianimazione
Avrebbe bevuto metadone”-2015

“Empoli, bimba di tre anni in ospedale per aver bevuto metadone
Pubblicato il 3 maggio 2015”

ASLNuoro

Quello dell'affido è un tema importante e frequentemente non scevro da criticità nella metodologia di cura all'interno dei SERD

- Nel 2009 la World Health Organization (Guida per il trattamento psicologicamente assistito della dipendenza da oppiacei) mette in evidenza che la somministrazione non supervisionata della stessa aumenta l'uso improprio ed il mercato illecito
- Questo dato è confermato (Dale- Perera- Goulao- Stoever, 2012) dallo studio in cui le % di diversione in termini di cessione o scambio di farmaci variano dal 16% in Portogallo dove il 21% delle somministrazioni è supervisionato, al 16% in Grecia dove il 78% delle somministrazioni è supervisionato al 39% in Francia dove è supervisionato il 26% delle somministrazioni.

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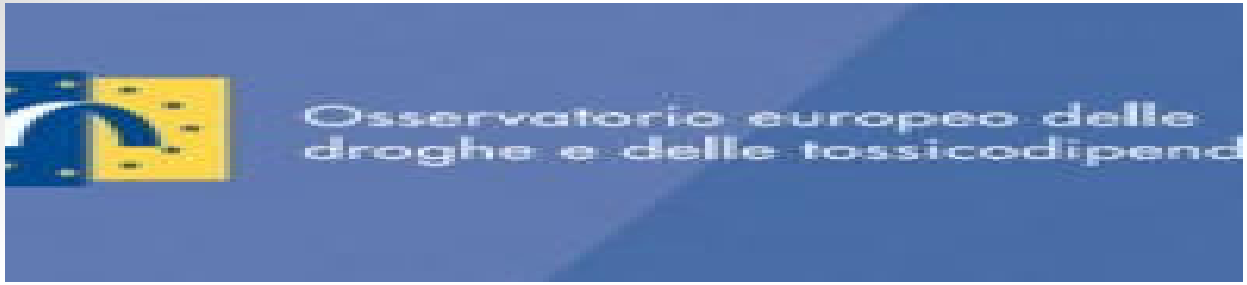

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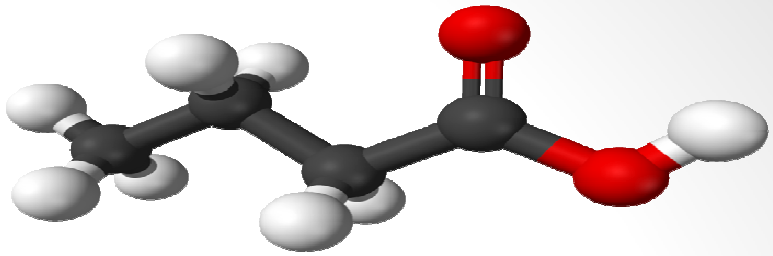
Relazione Annuale 2010

"Ogni anno sono riferiti diversi decessi che indicano la presenza di sostanze utilizzate nella terapia sostitutiva. Ciò riflette il gran numero di tossicodipendenti che si sottopone a questo tipo di trattamento e non implica che tali sostanze siano state la causa del decesso. I decessi da overdose tra i pazienti in terapia sostitutiva possono essere il risultato della combinazione di farmaci, poiché alcuni utenti continuano a consumare oppioidi acquistati per strada, bevono molto e utilizzano sostanze psicoattive… la maggior parte dei decessi dovuti a farmaci sostitutivi (spesso associati ad altre sostanze) si verifica tra le persone che non sono sottoposte a una terapia sostitutiva. I decessi attribuibili a intossicazione da buprenorfina sono un evento raro, nonstante l'aumento del ricorso a questa sostanza nella terapia sostitutiva in molti paesi europei"

HEINEMANN et al 2000



- Misuso relativo al farmaco GHB tra alcoldipendenti e non, con la motivazione della ricerca dello “sballo”
- L’impiego medico del GHB segnala l’insorgenza di fenomeni di dipendenza
- il GHB, si presta bene ad essere utilizzato a scopo criminogeno

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Riguardo alla terapia sostitutiva con farmaci oppiacei la letteratura è ricca di lavori

ELSEVIER

Buprenorphine-Induced Changes in Mu-Opioid Receptor Availability in Male Heroin-Dependent Volunteers: A Preliminary Study

Jon-Kar Zubieta, M.D., Ph.D., Mark K. Greenwald, Ph.D., Umberto Lombardi, M.D., James H. Woods, Ph.D., Michael R. Kilbourn, Ph.D., Douglas M. Jewett, Robert A. Koeppe, Ph.D., Charles R. Schuster, Ph.D., and Chris-Ellyn Johanson, Ph.D.

A principle of opioid pharmacotherapy is that high medication doses should occupy fractionally more opioid receptors that mediate heroin effects. In this preliminary study we examined in vivo *μ opioid receptor (μOR) binding in three healthy opioid-dependent volunteers during maintenance on 2 and 16 mg sublingual buprenorphine (BUP) liquid, and after detoxification (0 mg) under double-blind, placebo-controlled conditions, and once in matched controls. Binding measures were obtained with the μOR-selective radioligand [11C]carfentanil (CFN) and PET 4 hrs after BUP administration. BUP induced dose-dependent reductions in μOR availability, 36–50% at 2 mg and 79–95% at 16 mg relative to placebo. Heroin abusers also had greater μOR binding potential in the inferofrontal cortex and anterior cingulate regions during placebo, compared to matched controls. Further studies are warranted to examine the relationship of μOR availability with BUP therapeutic actions, and the clinical implications of increased μOR binding during withdrawal.*
[Neuropsychopharmacology 23:326–334, 2000]

KEY WORDS: *Buprenorphine; Positron emission tomography; Opiates; Opiate dependence; Mu opioid receptors; Carfentanil*

Medications for the treatment of substance abuse may be developed for a variety of purposes (e.g., ameliorate toxicity, treat overdoses) but a primary goal is to attenuate the subjective, behavioral, or physiological effects of the drug of abuse. Buprenorphine is a high affinity, mu opioid partial agonist, with kappa antagonist action (Cowan et al. 1977; Heel et al. 1979; Lewis et al. 1983). This compound is being evaluated as an alternative to methadone maintenance and detoxification in the treatment of opioid dependence (Bickel and Amass 1995). Buprenorphine's mu receptor (μOR) agonist actions could reduce opiate craving and prevent withdrawal, thus improving compliance with treatment compared to conventional opiate receptor antagonists (e.g., naltrexone). At the same time, its partial efficacy and high affinity at μOR's provide long lasting *functional* antagonism, making it an effective means of blocking the effects of abused opiates. This unique combination of

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Address correspondence to: Jon-Kar Zubieta, M.D., Ph.D., The University of Michigan, Neuroscience Building, 1103 E. Huron Street, Ann Arbor, MI 48104–1687.

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- La buprenorfina per la sua azione a lunga durata e l' elevata affinità recettoriale per recettori Mu e K si pone come valida alternativa al MTD
- Gli studi mostrano che la sua somministrazione per via sublinguale la rende efficace nel ridurre l'autosomministrazione di eroina durante il trattamento

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DRUG POLICY

www.elsevier.com/locate/drugpo

Research paper

Prevalence of diversion and injection of methadone and buprenorphine among clients receiving opioid treatment at community pharmacies in New South Wales, Australia

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Received 10 January 2007; received in revised form 28 March 2007; accepted 29 March 2007

Abstract

Background: This study aimed to investigate the prevalence of diversion and injection of methadone and buprenorphine among clients receiving opioid pharmacotherapy treatment at community pharmacies in New South Wales (NSW), Australia.

Methods: A multi-site cross-sectional survey design was utilised using a self-complete questionnaire. Participants were 508 clients receiving supervised methadone ($n = 442$) and buprenorphine ($n = 66$) at 50 community pharmacies. Participants were surveyed about whether they had diverted their currently prescribed pharmacotherapy, whether they had injected methadone or buprenorphine, the frequency, desirability and duration of action of injecting, and the ease of availability of street-purchased pharmacotherapies.

Results: The prevalence of recent diversion was more than 10 times higher among those receiving buprenorphine compared to methadone, with 23.8% of buprenorphine-maintained participants reporting diverting their dose in the preceding 12 months. Seventeen percent of methadone clients had injected methadone in the preceding 12 months compared with 9.1% of buprenorphine clients over the same time period.

Conclusion: The higher prevalence of buprenorphine diversion compared to methadone diversion is likely to be due to its sublingual tablet formulation and difficulty associated with supervising its consumption compared to that of an oral liquid. Methadone diversion is also less prevalent likely due to the high levels of methadone takeaway provision, which also helps to explain the higher levels of recent methadone injecting compared to buprenorphine injecting. A clearer understanding of the motivations for diversion and injection of opioid pharmacotherapies, and the relationship between them is required.

Keywords: Buprenorphine; Methadone; Diversion; Injection; Pharmacy

Introduction

The diversion and injection of methadone and buprenorphine is a problem for individuals, communities and treatment providers, and has been widely reported in Australia (Darke, Ross, & Hall, 1996; Humeniuk, Ali, McGregor, & Darke, 2003; Jenkinson, Clark, Fry, & Dobbin, 2005) and internationally (Best et al., 1998; Cicero, Inciardi, & Munoz, 2005; Fountain, Strang, Gossop, Farrel, & Griffiths, 2000; Guichard et al., 2003; Lauzon et al., 1994; Robinson, Kemp, Lee, & Cranston, 2000; Vidal-Trecan, Varescon, Nabet, & Boissonnas, 2003). Diversion is usually defined as diversion of medication to the illicit market, but importantly also includes diversion of supervised medication for personal use outside the supervised treatment site and may be for the purposes of injecting (Cole, 2001; Fountain et al., 2000; Ritter & Di Natale, 2005). The injection of buprenorphine and methadone is associated with adverse outcomes including high levels of local injecting site complications (Darke et al., 1996; Darke, Topp, & Ross, 2002; Jenkinson et al., 2005) and fatal overdose (Caplehorn & Drummer, 2002; Kintz, 2001, 2002; Perret, Deglon, Kreek, Ho, & La Harpe, 2000; Pirnay et al., 2004; Schifano et al., 2005; Shah, Lathrop, & Landen, 2005; Zador & Sunjic, 2000), particularly in the case of methadone.

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- Lo studio condotto su 508 pazienti in trattamento farmacologico sostitutivo mette in evidenza che l'utilizzo diversificato della terapia è maggiore di almeno 10 volte nei paz trattati con Bup rispetto a quelli trattati con MTD.

- La vendita illecita prevalente per la BUP viene dagli autori motivata dal fatto che essendo la BUP in cpr, è più difficile controllarne l'assunzione

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Buprenorphine Versus Methadone in the Treatment of Opioid Dependence: Self-Reports, Urinalysis, and Addiction Severity Index

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This article reports results for patients who completed the 16-week maintenance phase of a double-blind clinical trial comparing buprenorphine (N = 43; average dose = 9.0 mg/day sublingually) with methadone (N = 43; average dose = 54 mg/day orally) in the outpatient treatment of opioid dependence. In addition to pharmacotherapy, treatment during the clinical trial included individual counseling, weekly group therapy, and on-site medical services. Patients in both medication groups showed significant and substantial improvements over time in areas of psychosocial functioning, as assessed by the Addiction Severity Index, rates of urinalysis tests positive for opioids, and self-reports of opioid withdrawal symptoms, illicit opioid use, and cocaine use. Buprenorphine and methadone produced very similar outcomes on the wide array of outcome measures assessed, and improvements for both groups were large and occurred rapidly after treatment entry. A trend toward continued improvement in opioid-positive urines over time was noted for the buprenorphine but not the methadone group. These results provide further evidence of the efficacy of buprenorphine in the treatment of opioid dependence and provide a characterization of the time course of effects for buprenorphine and methadone. In addition, these results demonstrate the benefits of drug abuse treatment, both for drug and alcohol use and in other areas of psychosocial functioning. (J Clin Psychopharmacol 1996;16:58–67)

BUPRENORPHINE IS AN opioid partial agonist currently under development for the treatment of opioid dependence. Several features of buprenorphine suggest that it should be a useful substitution medication for this indication. Acute doses of buprenorphine are identified as being opioid-like.[1–5] Chronic dosing with buprenorphine blocks the effects of other opioids[6] and suppresses the self-administration of heroin by opioid abusers.[7] In addition, buprenorphine is well tolerated in outpatient clinical trials,[8–14] does not readily precipitate withdrawal in opioid-dependent volunteers,[15] and may be useful on a less-than-daily basis.[14,15] Preclinical evidence suggests that buprenorphine also can decrease cocaine self-administration,[16–18] although clinical evidence of this effect has been equivocal.[8,19,20]

Four double-blind studies have examined the efficacy of buprenorphine compared with methadone in the outpatient treatment of opioid dependence. The first compared buprenorphine, 2 mg/day, with methadone, 30 mg/day, and found that the two medications were equally effective on outcomes of treatment retention, rates of opioid-positive urines, and self-reports of opioid withdrawal symptoms.[8] The second compared buprenorphine, 8 mg/day, with methadone, 20 and 60 mg/day, and found that buprenorphine was equally effective as 60 mg of methadone daily and superior to 20 mg of methadone daily on outcomes of treatment retention and rates of opioid-positive urines.[9] The third compared buprenorphine, 2 and 6 mg/day, with methadone, 35 and 65 mg/ day, and found that methadone was superior to buprenorphine on outcomes of both treatment retention and rates of opioid-positive urines.[10] Finally, a recently reported study compared buprenorphine, 8 mg/day, with methadone, 30 and 80 mg/day, and found that methadone, 80 mg/day, was superior to buprenorphine and methadone, 30 mg/day, on outcomes of treatment retention and rates of opioid positive urines, whereas methadone, 30 mg/day, and buprenorphine, 8 mg/day, did not significantly differ on these measures.[21]

For these four studies, primary outcome measures were treatment retention and illicit opioid use as revealed by urine testing. Secondary outcome measures, such as self-reports of illicit drug use, patients' ratings of dose adequacy and withdrawal symptoms, and measures of other

Received January 17, 1995; and accepted July 6, 1995.
Address requests for reprints to: Eric C. Strain, MD, Department of Psychiatry, Johns Hopkins Bayview Medical Center, 5510 Nathan Shock Drive, Baltimore, MD 21224.

- Studio a “doppio-cieco” su pazienti in mantenimento per 16 settimane e che mette a confronto la Buprenorfina con il MTD nelle cure ambulatoriali.

- Nel gruppo Buprenorfina è evidenziata una migliore compliance dei pazienti segnata da una minore positività per oppiacei alle verifiche tossicologiche

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Drug and Alcohol Dependence 142 (2014) 98–104

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Factors contributing to the rise of buprenorphine misuse: 2008–2013

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Buprenorphine misuse, Heroin, Opioid misuse, Self-treatment of opioid dependence

ABSTRACT

Objective: The purpose of the present study was to examine the motivations underlying the use of buprenorphine outside of therapeutic channels and the factors that might account for the reported rapid increase in buprenorphine misuse in recent years.
Methods: This study used: (1) a mixed methods approach consisting of a structured, self-administered survey ($N = 10{,}568$) and reflexive, qualitative interviews ($N = 208$) among patients entering substance abuse treatment programs for opioid dependence across the country, centered on opioid misuse patterns and related behaviors; and (2) interviews with 30 law enforcement agencies nationwide about primary diverted drugs in their jurisdictions.
Results: Our results demonstrate that the misuse of buprenorphine has increased substantially in the last 5 years, particularly amongst past month heroin users. Our quantitative and qualitative data suggest that the recent increases in buprenorphine misuse are due primarily to the fact that it serves a variety of functions for the opioid-abusing population: to get high, manage withdrawal sickness, as a substitute for more preferred drugs, to treat pain, manage psychiatric issues and as a self-directed effort to wean themselves off opioids.
Conclusion: The non-therapeutic use of buprenorphinehas risen dramatically in the past five years, particularly in those who also use heroin. However, it appears that buprenorphine is rarely preferred for its inherent euphorigenic properties, but rather serves as a substitute for other drugs, particularly heroin, or as a drug used, preferable to methadone, to self-medicate withdrawal sickness or wean off opioids.

1. Introduction

Buprenorphine is a dose-dependent, mixed opioid agonist/antagonist with very high affinity for the mu-opioid receptor, but with limited intrinsic activity compared to other, more commonly used opioid analgesics (Walsh et al., 1994). Moreover, it has a very low dissociation constant from the opioid receptor, generating a very long half-life and limiting dosing frequency (Bickel et al., 1988; Donaher and Welsh, 2006; Greenwald et al., 2003). These properties have made this drug a particularly attractive agent for opioid substitution therapy programs across the world (Donaher and Welsh, 2006; Johnson et al., 1992; Ling et al., 1998; Fiellin and O'Connor, 2002; Degenhardt et al., 2009; Bell et al., 2009; Sullivan et al., 2008; Alford et al., 2011). While it is maintained that these programs have been successful in reducing use of illicit opioids, buprenorphine itself has become a leading drug of choice for non-therapeutic purposes (e.g., produce euphoria/get high) in many countries which have such programs (Bell, 2010; Auriacombe et al., 2004; Carrieri et al., 2006; Aalto et al., 2007; Yokell et al., 2011; Guichard et al., 2003; Vidal-Trecan et al., 2003; Lavonas et al., 2014).

Recognizing this fact, the manufacturer reformulated buprenorphine with low doses of naloxone prior to its release in the United States for opioid treatment (Reckitt Benckiser Pharmaceuticals Inc., 2014). It was assumed that naloxone would antagonize the euphoric properties of buprenorphine, or precipitate withdrawal in opioid tolerant individuals (Chiang et al., 2003; Mendelson and Jones, 2003; Walsh and Eissenberg, 2003; Stoller et al., 2001).Thus, its risk of misuse was considered to be quite low (Mammen and Bell, 2009; Alho et al., 2007; Comer et al., 2010; Schuster, 2006). Based on early assessments of the drug, the Food and Drug Administration not only approved buprenorphine and buprenorphine/naloxone as part of comprehensive opioid harm reduction program in 2002, but there was sufficient confidence with these drugs that they were approved to be prescribed for home use rather than made available only in stand-alone methadone clinics, which are inconvenient, carry a significant social stigma, and use an inherently less safe

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- L'articolo del 2014 fa riferimento al fenomeno dell'abuso di Buprenorfina in soggetti fuori da un percorso terapeutico. Si evidenzia che il farmaco è utilizzato come sostituto delle droghe, come cura per il dolore, come aiuto per gestire problemi psichiatrici, come auto-aiuto nella fase di disassuefazione da oppiacei.

- Si segnala l'utilizzo non terapeutico della buprenorfina che risulta drammaticamente aumentato negli ultimi 5 anni, soprattutto nei soggetti che fanno ancora uso di eroina.
- l'aumento dell'uso non terapeutico della Buprenorfina non è dovuto alle sue capacità euforizzanti, ma come sostituto dell'eroina

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Abuse liability of intravenous buprenorphine/naloxone and buprenorphine alone in buprenorphine-maintained intravenous heroin abusers

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ABSTRACT

Background Sublingual buprenorphine is an effective maintenance treatment for opioid dependence, yet intravenous buprenorphine misuse occurs. A buprenorphine/naloxone formulation was developed to mitigate this misuse risk. This randomized, double-blind, cross-over study was conducted to assess the intravenous abuse potential of buprenorphine/naloxone compared with buprenorphine in buprenorphine-maintained injection drug users (IDUs). **Methods** Intravenous heroin users ($n = 12$) lived in the hospital for 8–9 weeks and were maintained on each of three different sublingual buprenorphine doses (2 mg, 8 mg, 24 mg). Under each maintenance dose, participants completed laboratory sessions during which the reinforcing and subjective effects of intravenous placebo, naloxone, heroin and low and high doses of buprenorphine and buprenorphine/naloxone were examined. Every participant received each test dose under the three buprenorphine maintenance dose conditions. **Results** Intravenous buprenorphine/naloxone was self-administered less frequently than buprenorphine or heroin ($P < 0.0005$). Participants were most likely to self-administer drug intravenously when maintained on the lowest sublingual buprenorphine dose. Subjective ratings of 'drug liking' and 'desire to take the drug again' were lower for buprenorphine/naloxone than for buprenorphine or heroin ($P = 0.0001$). Participants reported that they would pay significantly less money for buprenorphine/naloxone than for buprenorphine or heroin ($P < 0.05$). Seven adverse events were reported; most were mild and transient. **Conclusions** These data suggest that although the buprenorphine/naloxone combination has intravenous abuse potential, that potential is lower than it is for buprenorphine alone, particularly when participants received higher maintenance doses and lower buprenorphine/naloxone challenge doses. Buprenorphine/naloxone may be a reasonable option for managing the risk for buprenorphine misuse during opioid dependence treatment.

Keywords Abuse liability, breakpoint, buprenorphine/naloxone, drug liking, heroin, intravenous, opioid dependence, progressive-ratio, self-administration.

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INTRODUCTION

Illicit use of heroin and other opioids is a serious international health problem affecting an estimated 16 million people world-wide [1–3]. Treatments for opioid dependence, such as methadone and buprenorphine, reduce substantially the morbidity and mortality associated with this disease and play a critical role in addressing the needs

associated with intravenous misuse that can compromise patient care and access to opioid treatment [1,8].

Buprenorphine (Subutex) is available in more than 40 countries world-wide. Despite its widespread success as a maintenance therapy for opioid dependence [1,9,10], buprenorphine misuse [11–14] and diversion to the black market have been reported. The use of a combination of buprenorphine plus the opioid antagonist naloxone in a fixed 4:1 ratio (Suboxone) would theoretically

Research

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A retrospective evaluation of patients switched from buprenorphine (subutex) to the buprenorphine/naloxone combination (suboxone)

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Abstract

Background: In Finland, buprenorphine (Subutex) is the most abused opioid. In order to curb this problem, many treatment centres transferred ("forced transfer") their buprenorphine patients to the buprenorphine plus naloxone (Suboxone) combination product in late 2003.

Methods: Data from a retrospective study involving five different treatment centers, examining the effects of switching patients to Suboxone, were gathered from 64 opioid-dependent patients who had undergone the medication transfer.

Results: Most patients (90.6%) switched to Suboxone at the same dose of buprenorphine that they had been receiving as Subutex (average 22 mg). The majority of these patients (71.9%) were maintained at the same dose of Suboxone throughout the 4-week study period. During the first 4 weeks, 50% of the patients reported adverse events and at the four month time point, 26.6% reported adverse events. However, due to adverse events one patient only discontinued treatment with Suboxone during the 4-week study period, and five during the four month follow-up period. Of the 26 patients in the follow-up period, Suboxone was misused intravenously once each by 4 patients and twice by 1 patient. These 5 patients all reported that injecting Suboxone was like injecting "nothing" with any euphoria, or that it was a bad experience.

Conclusion: We conclude that when patients are transferred from high doses (> 22 mg) of buprenorphine to the combination product, dose adjustments may be necessary especially in the later phase of the treatment. We recommend that a transfer from Subutex to Suboxone should be carefully discussed and planned in advance with the patients and after the transfer adverse events should be regularly monitored. With regard to buprenorphine IV abuse, the combination product seems to have a less abuse potential than buprenorphine alone.

Lo studio valuta il potenziale di abuso nell'utilizzo per via ev di Bup/Nal rispetto a quello di Bup da sola. I risultati mostrano che sebbene il Suboxone può determinare abuso se somministrato per via ev, questo risulta essere più basso rispetto alla sola Buprenorfina

Una valutazione retrospettiva su paz.ti passati da Bup a Suboxone

Studio finlandese evidenzia il misuso o piuttosto l'abbandono della terapia o ricadute nell'eroina con tale passaggio. Gli autori suggeriscono che tale passaggio debba essere accompagnato da una revisione del dosaggio farmacologico
E comunque confermano che il potenziale d'abuso è inferiore nel trattamento con suboxone rispetto alla sola buprenorfina

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Injection of buprenorphine and buprenorphine/naloxone tablets in Malaysia

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ABSTRACT

Background: Buprenorphine maintenance is efficacious for treating opioid dependence, but problems with diversion and misuse of buprenorphine (BUP) may limit its acceptability and dissemination. The buprenorphine/naloxone combination tablet (BNX) was developed to reduce potential problems with diversion and abuse. This paper provides data regarding the characteristics of BUP injection drug users in Malaysia and preliminary data regarding the impact of withdrawing BUP and introducing BNX. BUP was introduced in 2002 and subsequently withdrawn from the Malaysian market in 2006. BNX was introduced in 2007.

Methods: A two-wave survey of BUP IDUs was conducted shortly prior to BUP withdrawal from the Malaysian market ($n = 276$) and six months after BNX was introduced ($n = 204$). Six focus groups with BUP and/or BNX IDUs were also conducted shortly before the second wave.

Results: In addition to current BUP or BNX IDU, 96% of first wave participants and 97% second wave participants reported lifetime heroin IDU preceding the onset of their BUP/BNX IDU. Additionally, 58% of first and 64% of second wave survey participants reported current heroin IDU. Benzodiazepine abuse, often injected with BUP, was reported in both the surveys. Focus group participants reported that BNX was not as desirable as BUP; nonetheless, the results of the second wave survey suggest a continuing widespread BNX IDU, at least in Kuala Lumpur.

Conclusions: In Malaysia, BUP and BNX IDU occur among heroin IDUs. The introduction of BNX and withdrawal of BUP may have helped to reduce, but did not eliminate the problems with diversion and abuse.

1. Introduction

Heroin and injection drug use (IDU) are major public health problems in Malaysia. Between 1988 and 2006, more than 300,000 individuals, approximately 1% of the general population, were registered as substance abusers in Malaysia, with primary heroin abuse accounting for 62.6% of those registered (Narcotics Bulletin, 2007). In response to these problems, buprenorphine maintenance treatment, using buprenorphine mono-tablets (Subutex®; containing buprenorphine only (BUP), was introduced in Malaysia in 2002 (Schottenfeld et al., 2008). The initial uptake of BUP treatment in Malaysia was quite rapid: importation of BUP increased from 2 kg in 2002 to 12 kg in 2005 and 14 kg in 2006, and the number of general practitioners (GPs) prescribing BUP increased from less than 50 in 2002 to more than 500 in 2006 (Vicknasingam et al., 2007). Initially any practicing licensed general practitioner (GP) was allowed to prescribe Subutex for treatment of opiate dependence and to dispense the medication in their private offices. No training, guidelines, or oversight of prescription and/or dispensation procedures were offered or required, resulting in frequent prescribing and dispensing of weekly or monthly take-home supplies of Suboxone for patients from the beginning of treatment. BUP diversion and abuse, including injection abuse, began to be noted in 2006 (The Star, 25 November 2006). In 2008, Bruce and colleagues, based on qualitative interviews with 19 injectors, reported on BUP abuse in Malaysia and noted that co-administration of BUP and benzodiazepines (midazolam) was common in this sample (Bruce et al., 2008).

Problems with BUP misuse, including IDU, are not unique to Malaysia and have been reported in other countries (Cicero et al., 2007; Chua and Lee, 2006; Jenkinson et al., 2005; Hakansson et al., 2007; Lee, 2006; Nielsen et al., 2007; Obadia et al., 2001; Singh et al., 1992; Strang, 1985; Vidal-Trecan et al., 2003). While implementation of stringent regulations governing medication dispensing and unsupervised self-administration of the medication outside of clinic settings may reduce these problems, it may also limit the availability and accessibility of treatment which consequently

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- In Malesia, dopo l'introduzione del farmaco nel 2002, è emerso un rapido aumento dell'uso ev della Buprenorfina. Tale misuso si è diffuso ancora più rapidamente a causa della prescrizione da parte dei medici di assistenza primaria che non avevano ricevuto alcun training per la gestione dei trattamenti sostitutivi

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Factors Associated with Illicit Methadone Injecting in a Canadian Setting

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Background and Objectives: While methadone is well established as an evidence-based treatment for opioid use disorder, safety concerns persist regarding its diversion. The authors examine the prevalence of and risk factors associated with injection of methadone in an urban population.
Methods: Between December 2005 and November 2013, data were derived from two open prospective studies of persons who inject drugs (PWID) in Vancouver, Canada. Generalized estimating equations (GEE) logistic regression was used to determine factors independently associated with illicit methadone injecting.
Results: During the study, 1911 individuals (34% women) were recruited; 134 (7%) participants reported methadone injecting at least once. In multivariable analysis, Caucasian ethnicity [adjusted odds ratio (AOR) = 1.90, 95% confidence interval (CI) = 1.20–3.00]; homelessness (AOR = 1.46, 95% CI = 1.09–1.95); drug dealing (AOR = 2.10, 95% CI = 1.50–2.93); ≥daily heroin injection (AOR = 1.57, 95% CI = 1.08–2.26); ≥daily crack smoking (AOR = 2.06, 95% CI = 1.44–2.95); being a victim of violence (AOR = 1.48, 95% CI = 1.04–2.12); and non-fatal overdose (AOR = 1.67, 95% CI = 1.67 (1.00–2.79) were independently and positively associated with methadone injection; female gender (AOR = 0.47, 95% CI = 0.30–0.75) was negatively associated.
Discussion and Conclusions: The diversion of methadone for illicit injection in this urban setting was associated with several markers of addiction severity and other health and social vulnerabilities.
Scientific Significance: These findings underscore the need to ensure methadone accessibility while limiting diversion-related risk. (Am J Addict 2015;24:532–537)

INTRODUCTION

Opioid dependence is a global problem affecting upwards of 15 million people worldwide and is associated with significant morbidity and mortality.[1,2] In the United States in 2012, the Substance Abuse and Mental Health Services Administration estimated that 669,000 people used heroin in the previous year, marking five consecutive years of increases.[3]

Methadone is well established as an effective treatment for patients with opioid use disorder.[4] Methadone is also used for the treatment of cancer pain and chronic non-cancer pain in a variety of settings.[5–7] However, the risk of sedation and respiratory depression with improper methadone dosing remains. Specifically, despite precautions for methadone prescription such as the dispensing of methadone under daily witnessed supervision in unstable patients and regular urine drug screen testing to verify compliance, fatalities associated with methadone have increased markedly across numerous jurisdictions in recent years.[8–11]

The diversion and illicit use of methadone prescribed for opioid use disorders or for pain constitutes a major risk for fatal overdose involving methadone.[9,12] The prevalence of non-prescription methadone use has not been well described and the factors associated with injection of street obtained methadone have yet to be well defined, particularly in settings where methadone is widely available through programs that allow primary care physician prescription. Therefore, we undertook this study to evaluate the prevalence and factors associated with methadone injection in an urban Canadian setting with widespread access to methadone prescribed through primary care physicians and dispensed via a network of community pharmacies.

METHODS

Study Sample

This study made use of two open prospective cohorts of persons who use drugs in Vancouver, Canada: the Vancouver Injection Drug Users Study (VIDUS), and AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS). VIDUS and ACCESS follow identical recruitment and follow-up procedures, allowing for combined analysis; the cohorts differ

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- Secondo una ricerca canadese, l'utilizzo endovena del metadone è indice di una forte addiction e di una situazione sociale e di qualità di vita altamente compromessa.

Alcune riflessioni…

- Il misuso e la diversione sono certo un problema per i SERD soprattutto se facciamo riferimento a modelli psicopatologici largamente rappresentati nei nostri servizi: disturbi di personalità di cluster B (disturbi borderline ed antisociali). Sono pazienti con i quali è sempre molto complessa la possibilità di una relazione terapeutica basata sulla fiducia nell'ambiente di cura, nel rispetto dei trattamenti farmacologici e delle regole dei servizi stessi.

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Alcune riflessioni…

- Certo è che nella gestione del paziente TD il fenomeno del misuso e della diversione è un evento assolutamente prevedibile
- E' doveroso dunque per noi operatori mettere in atto tutte quelle strategie che possono concorrere ad una riduzione di tali pratiche.
- E' importante capire quanto il paziente si affida alla terapia stessa, quanto ci crede
- E' importante una adeguata informazione sui rischi dell'autosomministrazione e non da meno è fondamentale la gestione del craving promuovendo dosaggi farmacologici efficaci insieme ad altrettanti efficaci interventi di counselling

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