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Detection of benzodiazepine abuse in opiate addicts

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Abstract

There is an increasing problem with benzodiazepine co-abuse in the opiate dependent population of Dublin. The importance of early detection of the co-abuse is essential as there is an increased risk of dangerous injecting practices such as sharing of needles and criminality in those who co-abuse benzodiazepines and opiates. This study was carried out in the National Drug Treatment Centre, Dublin. It aims to describe the current difficulties in identifying the co-abuse of short acting benzodiazepines including flunitrazepam in a cohort of opiate dependent patients. Using a sample of those attending the clinic it was discovered that standard methods of urinalysis failed to identify 10% of co-abuse, for those patients whose abuse of flunitrazepam is undetected on screening, clinical interventions which aim to minimize the consequence of the co-abuse and reverse the chaotic drug using patterns fail to be put in place at the earliest possible time.

Introduction

The co-abuse of benzodiazepines and opiates is associated with poor treatment outcome and greater risk of HIV infection.[1] It is essential to be aware of benzodiazepine abuse occurring in an opiate dependant patient in order to allow early intervention addressing polydrug abuse. Flunitrazepam (Rohypnol) is a short acting benzodiazepine prescribed as a hypnotic. Its use has decreased over the years with the development of other compounds and its high potential to lead to dependence. The pattern of drug use in any country varies according to market availability.[2] While 5 years ago the benzodiazepine most commonly abused by opiate dependent patients was temazepam with recent changes in its categorisation and more stringent prescribing regulations the most frequently abused benzodiazepine in our population is now flunitrazepam. Its poor reactivity with the standard method of testing, short half life and rapid clearance from the body makes its detection difficult. We have noted increasing abuse of flunitrazepam within the opiate addicted population as they have become aware of difficulties in its detection in urine samples. When co-abused with opiates it leads to disinhibition. The amount of flunitrazepam taken by those abusing it in association with opiates can be up to twenty times the normal dose with patients usually taking between 10 and 15 lmg tablets. At these doses the amount of disinhibition leads to significant consequences for both harmful drug taking behaviours and criminality. Patients described feeling they have no worries, feeling invincible and note that their

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concerns about using clean needles and safe injecting practices become secondary to their need for further opiates, thus patients will commonly revert to sharing of needles and syringes whilst intoxicated with flunitrazepam. Darke has previously described increasing frequency of needle sharing with benzodiazepine co-abuse in intravenous drug abusers.[3] At the large doses used during co-abuse with opiates patients also become markedly less concerned about the consequences of their actions and describe shoplifting and violent robberies as being relatively "easy" to carry out whilst intoxicated with little fear and indeed often little recollection of the event. This phenomena has previously been described by Rubens *et al*[4] with temazepam abuse where patients reported taking benzodiazepines to give confidence to engage in criminal activity. Currently the identification of flunitrazepam is by either Enzyme Multiplied Immunoassay Test (EMIT)[5] or by High pressure Liquid Chromatography (HPLC),[6] with HPLC being the most sensitive for detection but rarely available in the normal clinical setting. With a view to examining the amount of concomitant benzodiazepine abuse in our treatment population which escapes detection by the current standard methods of testing (EMIT) we undertook to survey the urine samples in our clinic using two EMIT methods of differing sensitivity.

Materials and Methods

The Dublin Drug Treatment Centre Board is an urban based out-patient facility with an annual attendance of 47,160. (An attendance is defined as each visit by a patient to the clinic.) There are an average of 1500 patients treated by the clinic during the year. The centre is staffed by a Consultant Psychiatrist and 6 NCHDs. There is a nursing team and social workers are available to the patients. The centre provides both methadone detoxification and substitution treatment. All patients attending are routinely monitored using supervised urinalysis. This occurs as part of their treatment programme and is carried out at least twice weekly in a random fashion. The current test used for detecting the abuse of benzodiazepines is the Syva EMIT d.a.u. assay. This test has a sensitivity threshold of 200ngl/ml.[7] To establish the level of undetected abuse, each sample was re-tested on the survey day with a more sensitive test, the Roche Abuscreen ONLINE Benz test kit. This test has a sensitivity extending to 40ng/ml[8] This test is used in the centre only when clinical evidence of intoxication is not reflected by positive urine results. On the day of this study all urines that were found to be negative on testing for benzodiazepines using the standard test were re-analysed using the more sensitive technique.

Results

On the day of the survey 107 patients provided urine samples for testing. The samples were collected with a witness observing the patient while they provide the specimen as is the normal practice in the clinic. All patients were providing samples as part of their normal treatment programme. The patients sampled included those on methadone detoxification programmes, as well as those on methadone substitution programmes. Additionally, the sample included patients preparing to commence a detoxification programme who had not yet been prescribed medication. 35% (n=37) of the total sample of urine's tested positive for benzodiazepines using the standard assay. Samples which tested negative for benzodiazepines with the standard test (n=70) were re-evaluated with the more sensitive technique as described above with an additional 10% (n=11) of the total sample found to be positive for benzodiazepines. Interestingly when a subgroup of patients who were on a methadone substitution programme were found to be also abusing heroin (n=25), standard testing revealed that 52% of the group were abusing benzodiazepines (n=13) while with the more sensitive test 16% of those recorded initially as negative were found to be positive (n=4).

Figure 1. Testing Methods for Benzodiazepine.

	Standard Testing Method		Sensitive Testing Method		
	Sample	BD	BD	BD	BD
	No	Positive (%)	Negative (%)	Positive (%)	Negative (%)
Total Sample Methadone	107	37 (34.6)	70 (65.4)	11 (10.3)	59 (55.1)
Stabilization*	25	13 (52)	12 (48)	4 (16)	8 (32)

BD Benzodiazepine.
*with continuing opiate abuse.

Discussion

At initial assessment on entry to the clinic flunitrazepam abuse is specifically elicited as is diazepam and nitrazepam, all of which are currently popular benzodiazepines of abuse in this group. Where benzodiazepine co-abuse exists the choice of drug includes all three of the above benzodiazepines in varying quantities depending on the current availability on the black market. Williams *et al* showed that 8% of intravenous opiate abusers in 1992 were using flunitrazepam. While at that time 84% of this group reported using temazepam,[9] it would appear that in recent years flunitrazeparn abuse has replaced temazepam abuse as strict controls regarding the prescription of the latter were introduced in Ireland during 1995. Once patients are enrolled in the clinic a policy of early intervention regarding co-abuse is practiced. We have noticed that the pattern of abuse may alter towards flunitrazepam abuse alone. When questioned regarding this practice, patients refer to their perception that flunitrazepam abuse will not be detected on urine testing. Although this is not universally true this perception is supported to a degree by the findings of undetected abuse in this survey. The findings of Darke[1] in Australia regarding increases in risk taking, and injecting behaviour in those co-abusing benzodiazepines are understandable in light of the disinhibiting effect of benzodiazepines and thus less concern about the long term effects of sharing needles.

The level of HIV infection in IV drug abusers in this clinic population is 2%. However, it is important to note that there is a seroprevalence rate for Hepatitis C virus of 80% and while sharing of needles and syringes may lead to HIV infection, it will almost certainly lead to Hepatitis C infection because of the large pool of infected cases. The finding in this study of a higher level of flunitrazepam abuse in those patients who have the most chaotic habit, taking both prescribed methadone and illegal opiates, suggests that this group who are already at high risk of infection because of their addiction are at additional risk because of their benzodiazepine co-abuse. It can also be argued that their use of flunitrazepam may encourage the loss of stability provided by a methadone programme and may therefore be contributing to their chaotic habit in its own right. Rubens[4] finding of co-abuse to instill confidence prior to criminal activities is born out by interview with patients in this centre who describe a sensation of being invulnerable and even invisible when taking flunitrazepam in conjunction with an opiate. Anecdotally patients will describe outrage at been arrested for shoplifting while under the influence of flunitrazepam which is taken in excessive doses in this group of patients. When clinicians are aware of co-abuse of benzodiazepines a strict date to clear their urine is given, supported by a behavioural programme based on reduction of methadone dose if continuing co-abuse occurs. This intervention is accompanied by an explanation of the problems of the increased risk of Hepatitis C infection and HIV infection found in those co-abusing benzodiazepines as a result of increased dangerous injecting practices. When addressed the patient either manages to clear their urine or if this is not possible in-patient benzodiazepines detoxification may be offered. However the level of undetected abuse means that patients may be exposed to increased risks with no intervention from staff and it is thus essential that every effort is made to establish co-abuse also using the most sensitive

testing available. Awareness of the possibility of missed co-abuse also ensures a high index of suspicion. This issue should be addressed at the earliest opportunity in those with no objective evidence of co-abuse but subjectively appear intoxicated and are not maintaining previous levels of progress.

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