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The Emerging of Xylazine as a New Drug of Abuse and its Health Consequences among Drug Users in Puerto Rico

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ABSTRACT *During the last decade, the veterinary anesthetics have gained popularity as recreational drugs. The aim of this study was to document the use of "anestecia de caballo" (xylazine) and its consequences among drug users in Puerto Rico. The study combined a cross-sectional survey with 89 drug users and two focus groups conducted in Mayagüez with frontline drug treatment providers. Drug users were recruited from communities of the San Juan metropolitan area using a variety of ethnographic and outreach strategies. A short questionnaire developed for the study collected information on sociodemographics, xylazine use, and its consequences. The two focus groups were conducted to discuss the details related to xylazine use, its consequences, and utilization awareness. The sample comprised 63 males (70.8%) and 26 females with a mean age of 37.2 years. The mean number of years of drug use was 14.3, with a mean frequency of drug use of 5.9 times daily. More than 65% reported speedball as the principal drug of use. The prevalence of xylazine use was 80.7%. More than 42% of the sample used xylazine in a mixture with speedball. The main route of administration of xylazine was injection but 14% reported the use of xylazine by inhalation. More than 35% of the sample reported skin lesions and 21.1% reported at least one overdose episode. Multiple logistic regression analysis revealed that males (OR=3.47, CI=1.10–12.00) and those who reported speedball as their main drug of use (OR=9.34, CI=2.51–34.70) were significantly more likely to be xylazine users. Focus groups revealed that drug users claimed to recognize the presence of xylaxine in a mixture of speedball based on its effects, taste, the color of the drug (dark brown), and its odor. In conclusion, the use of xylazine among drug users in Puerto Rico seems to be an emerging trend with potentially serious health consequences.*

KEYWORDS *Xylazine, Puerto Rico, Injectors drug users, Health consequences*

INTRODUCTION

Sentinel drug forecasting systems often fail to adequately identify and assess emerging trends in the use of illegal drugs. As a result, public health systems are rarely able to

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adequately mobilize local, regional, and national prevention and treatment systems in a timely manner.[6] Drug adulterants are a prime example of this epidemiological problem because in many cases, such as heroin, adulterants change the well-known toxicity syndrome that accompanies an overdose causing unexpected effects.[16] Xylazine, an animal tranquilizer that is not approved by the FDA for human use, is an emerging heroin adulterant whose effects for recreational use and as a heroin adulterant have not yet been thoroughly studied in human populations. Some published reports, such as one from the Philadelphia County Medical Examiner's office, showed xylazine to be co-present with fentanyl in seven drug-related deaths, six of which also tested positive for heroin;[23] findings from the Poison Control Center at The Children's Hospital of Philadelphia also confirm xylazine as a heroin adulterant.[16] A study by Rodriguez and others[20] in Puerto Rico used gas chromatography/mass spectroscopy to analyze syringes for the presence of drugs and found that 90.6% of syringes containing xylazine also contained speedball, a mixture of heroin and cocaine; cocaine (without heroin) was present in 7.2%, and heroin (without cocaine) was present in 2.2%.

Xylazine is a partial alpha-2 adrenergic agonist with characteristics and toxic actions similar to the phenothiazines and clonidine.[3] In animals, this drug may be administered intravenously, intramuscularly, or subcutaneously by itself or in combination with other anesthetics such as ketamine, barbiturates, chloral hydrate, and halothane.[5] If used in humans, it is known to produce marked hypotension and bradychardia secondary to vagal stimulation.[13] Severe intentional intoxication from xylazine has been reported from ingestion,[12] inhalation,[3] and injection.[21] However, the subjective effects of mixing xylazine with heroin or cocaine remain largely unknown.

In Puerto Rico, use of animal tranquilizers as drug adulterants or recreational drugs has recently been reported in several studies, the mass media, and among health practitioners.[18,20,22] This trend became known to the general public by a series of reports in the popular media that associated the use of this drug to various deaths in a criminal justice hospital in Aguadilla, Puerto Rico[18]. The influence of xylazine as an emerging adulterant is of great concern not only because it is a drug whose effects are not known in humans, but because preparation practices in several studies in Puerto Rico show that even hardcore drug users might not be aware of what they are purchasing. A study by Colon and others[7] within the metropolitan area of San Juan, Puerto Rico found heroin over reporting when corroborating self-reports with drug urine tests. The authors suggest the over reporting might have something to do with the xylazine trend and that some study participants might be inadvertently consuming xylazine instead of heroin.[7] In the study previously mentioned by Rodriguez and others,[20] 22% of the syringes of participants who reported to be nonusers of xylazine actually contained the drug. Moreover, xylazine users were found to have a high prevalence of skin ulcers (38.5% vs. 6.8%, $p<0.01$).[20]

The aim of this study was to document the use of xylazine and its health-related problems among a sample of drug users in Puerto Rico. A combination of quantitative and qualitative techniques was employed to both gather and analyze data.

METHODS

The target population from which the sample was drawn included drug users out of drug abuse treatment residing in communities of San Juan, Mayaguez, and Aguadilla. The sample was recruited from May to August 2007. During this period, 89 drug users were contacted and recruited in 12 communities. Ethnographic mapping strategies were used to identify drug markets and other venues where drug

users were known to congregate. At predetermined sites and times, outreach workers approached drug users, determined eligibility, and invited them to participate. Individuals were considered eligible if they were at least 18 years of age, had used drugs in the last 30 days, and had not been enrolled in drug abuse treatment within the last 30 days. A short questionnaire developed for the study collected information on sociodemographic characteristics, xylazine use, and health-related problems. Drug use patterns and HIV risk behaviors were measured using a revised and culturally adapted version of the risk behavior assessment.[8,17,19]

Frequency distributions and descriptive statistics were used to describe the study sample. Bivariate analyses using chi-square tests of independence were used to examine the association between xylazine use and its covariates. A multivariate logistic regression model was fitted with xylazine use as the dependent variable and age, gender, years of injection, and speedball use as independent variables. The covariates included in the logistic regression model were chosen based on the bivariate analysis. All the statistical analyses were performed using SPSS for Windows version 15 (SPSS Inc., Chicago, IL, USA).

Observations and unstructured ethnographic interviews were conducted on the copping sites, shooting galleries, and other drug use venues in San Juan and Aguadilla. Two focus groups were conducted in Mayaguez with frontline drug treatment providers to explore details related to xylazine acquisition, use, health-related problems, and utilization awareness.

RESULTS

The sample was predominantly male (70.8%) with a mean age of 37.2±9.6 years (Table 1). The mean number of years of drug use was 14.3±9.7, with a mean frequency of drug use of 5.9±4.1 times daily. The prevalence of xylazine use was 80.7% (Table 2). The main route of administration of xylazine was injection (84.5%), but 14% reported the use of xylazine by inhalation (Table 2). More than 40% of the sample used xylazine in a mixture with speedball. Overall, the mean number of years of xylazine use was 3.4±2.9. In terms of health-related problems, 21.1% reported at least one overdose episode, and 35.2% reported skin lesions. On the other hand, 28.2% of the sample reported an increase in the frequency of injection since beginning to use xylazine. Table 3 shows a bivariate analysis of xylazine use. Xylazine users were significantly more likely to be males ($p=0.022$), to reside in a rural area ($p=0.003$), and to be speedball users ($p<0.001$). The results of the logistic regression revealed that males (OR=3.47, CI=1.10–12.00) and those who reported speedball use as their main drug of use (OR=9.34, CI=2.51–34.70) were significantly more likely to be xylazine users.

Ethnographic data from observations and interviews suggested that drug users, especially injectors, were well aware of a new *corte* (adulterant) that has been used with heroin known as *anestesia de caballo* (literally translated as horse anesthesia). Although most of the participants identified this new substance as some sort of veterinarian product, mostly an analgesic, none of them, including focus groups participants, related it to xylazine. In fact, none of them knew the term xylazine. Some drug users, however, reported that they began using *anestesia* without knowing it. Drug users from Aguadilla reported that xylazine (*anestesia*) could be purchased either as a heroin adulterant (known by the street name of *Piqui-piqui*) or a base drug adulterated with heroin (known by the street name of *anestesia*). In San Juan, drug users did not report such distinction. Participants in all sites reported that

TABLE 1 Sample characteristics and patterns of drug use

	n		(%)
Overall	89		–
Gender			
Females	26		29.2
Males	63		70.8
Age (in years)	Mean = 37.2	SD = 9.6	
24 to 34	39		45.9
35 to 44	28		32.9
45 or more	18		21.2
Years of drug use	Mean = 14.3	SD = 9.7	
≤5	11		12.8
6–9	16		18.6
10–15	35		40.7
≥16	24		27.9
Frequency of drug use	Mean = 5.9	SD = 4.1	
≤3 times	11		31.4
4–6 times	11		31.4
≥7	13		37.1

xylazine had turned into a dominant trend and finding heroin free of xylazine was becoming quite difficult. Several drug users from San Juan expressed concerns about being forced to purchase xylazine and consequently "getting hooked" to this substance.

TABLE 2 Patterns of xylazine use and health-related problems

Patterns of use	*n*		(%)
Xylazine use (ever)			
No	17		19.3
Yes	71		80.7
Route of administration			
Sniffing	10		14.3
Injecting	60		84.5
Smoking	1		1.4
Mixed with			
Alone	5		7.0
Cocaine	27		38.0
Heroin	9		12.7
Speedball	30		42.3
Years of xylazine use	Mean = 3.4	SD = 2.9	
Health-related problems			
Overdose episodes			
No	56		78.9
Yes	15		21.1
Skin lesions			
No	46		64.8
Yes	25		35.2
Increased frequency of injection			
No	51		71.8
Yes	20		28.2

TABLE 3 Xylazine prevalence and adjusted odds ratios for multiple logistic regression ($n=71$)

	Xylazine prevalence				
Variables	*n*	%	*p* value[a]	OR[b]	(95% CI)
Overall					
Gender					
Females	17	65.4		1.00	
Males	54	87.1	0.022	3.47	(1.10–12.00)
Age					
24 to 34 years old	33	86.8		1.00	
35 to 44 years old	24	85.7		1.24	(0.27–5.74)
45 years old or more	13	72.2	0.359	0.95	(0.20–4.61)
Geographical area[c]					
Rural	23	100.0			
Urban	48	73.8	0.003		
Years of drug use					
Less than 10 years	21	77.8		1.00	
10 years or more	48	81.4	0.699	1.79	(0.44–7.30)
Speedball user (last year)					
No	16	57.1		1.00	
Yes	55	91.7	≤0.001	9.34	(2.51–34.70)

[a]Fisher's exact test

[b]Multiple logistic regressions

[c]The geographical area variable was not included in the logistic regression because all participants of rural area reported xylazine use during the last year

Results from both focus groups and ethnographic interviews revealed that drug users claimed to recognize the presence of xylazine in the drug mixture based on its effects, taste, color of the drug (dark brown), and odor. Some of the participants also reported that occasionally, the drug solution crystallized during the drug preparation process. Drug users from all sites reported that since they began using xylazine, they noticed a strong odor coming from their breath, perspiration, urine, and feces. They also noticed they were spending more time sleeping since using it. Many of the drug users reported an increase in abscess, ulcerations, and other skin lesions. Figure 1 shows examples of the skin lesions observed in the study communities.

CONCLUSION

This study identified that xylazine is more likely to be used by males and it seems to be mixed mostly with speedball. These results are congruent with those reported by the Philadelphia County Medical Examiner's office.[23] The cases reported in Philadelphia were all male and in five of seven cases, xylazine's presence was detected along with fentanyl, heroin (or its metabolite), and cocaine (or its metabolite). Xylazine as an adulterant of speedball was also previously identified in Puerto Rico by Rodriguez and collaborators.[20]

Skin ulcerations could be considered the primary health concern identified in our study sample. This effect could be caused by the skin's oxygenation response to xylazine intoxication. Several cases of human xylazine intoxication have been documented, which include initial hypertension followed by hypotension, bradycardia,[2] orthostatic hypotension, and respiratory depression.[15] According to Abramovic and

FIGURE 1. Photos showing skin lesions among drug users in San Juan, Puerto Rico. *1* Cellulites in a female's leg. *2* Abscesses and cellulites in legs among male injection drug users.

collaborators,[1] most of these factors can influence the skin by lowering tissue oxygenation. Several clinical reports have suggested that lower skin oxygenation is associated with less wound healing and higher incidence of wound infection. The continued consumption of xylazine at unknown doses could progress skin oxygenation deficit contributing to chronic skin ulceration.

Our study identified overdose episodes reported by 21.1% of the study sample. This information should not go unnoticed since several authors have documented that some cases of severe human xylazine intoxication, either intentional or accidental, have resulted in fatalities.[2] In response to the documentation of an accidental fatal overdose of xylazine in the state of Kentucky, the Centers for Disease Control and Prevention (CDC)[4] recommended the following: (a) Farm personnel: owners, managers, and workers should be educated on the risk of adverse and fatal human effects associated with veterinary drugs; (b) manufacturers of veterinary drugs should include stronger label warnings against potential adverse human effects of the drugs, and (c) after mixing veterinary drugs on-site, vials or storage containers should be appropriately labeled with the correct contents and concentrations of the drugs. Considering the abuse pattern identified in Puerto Rico, the CDC recommendations could apply to every person that manages xylazine on the island.

Drug treatment programs should assess xylazine use at intake. Although many of the participants of our focus groups reported knowing how to recognize the presence of xylazine in a mixture of speedball, awareness should be raised among drug users of the possible presence of xylazine in drug mixtures. In case of an intoxication, Barroso and collaborators[2] and Liu et al.[15] have recommended the administration of IV fluids, atropine, and hospital observation. In some cases, endotracheal intubation may be needed.[15] While determining differential diagnostic, it is recommended to consider xylazine use in case of orthostatic hypotension and bradycardia without neurological symptoms.[15]

Some limitations should be considered when interpreting the results of this study. First, xylazine use was based on self-reports, and thus, its reports were subject to recall

bias and denial. However, self-reported data have been used in multiple epidemiologic studies of drug use and have proven to be reliable and valid.[9–11,14] Second, the cross-sectional design limits the inferences that can be made with respect to the establishment of a causal association between xylazine use and its health consequences. For example, xylazine by itself may not be the only contributor to skin lesions and overdose.

Despite these limitations, the findings of this study documenting the potential effects of xylazine among drug users in Puerto Rico are compelling. The findings of this study suggest the abuse of xylazine in Puerto Rico is an emerging public health problem. As reported by participants, xylazine is becoming a dominant adulterant in the drug market. In fact, drug users' reports suggest that xylazine could be shifting from a drug adulterant to a base drug. Further research is needed to identify the risk factors associated with xylazine use and its health consequences.

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