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**Injection into the jugular vein among people who inject drugs in the United Kingdom:
prevalence, associated factors and harms.**

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Running head: *Injection into the jugular vein in the UK.*

Abstract

Background: While people who inject drugs (PWID) typically use peripheral veins, some inject into their central veins, including the femoral and jugular veins. Injection into the jugular vein can have serious adverse health consequences, including jugular vein thrombosis, deep neck infections, pneumothorax, endocarditis and sepsis. This study examined the prevalence of, and factors associated with, jugular vein injection among a large sample of PWID in the United Kingdom.

Method: Unlinked anonymous surveys (2011-14) recruited PWID from agencies providing services to this population. Self-reported demographic and injection-related data were collected from consenting respondents using a brief questionnaire and dried blood spot samples were tested for exposure to HIV, hepatitis C virus (HCV) and hepatitis B virus (HBV). Univariate and multivariable logistic regression were used to examine factors associated with jugular vein injection.

Results: Among 5,261 PWID, one third had injected into a central vein in the previous 28 days, including 6% (n=339) who had injected into their jugular vein and 1% (n=52) who had used this site exclusively for recent injections. Factors independently associated with recent jugular vein injection in multivariable analysis included female gender, a lifetime history of imprisonment, sharing needles and syringes, poly-drug injection and injection into multiple body sites. Jugular vein injection was also associated with experiencing injection-related injuries, although no associations were identified with respect to exposure to blood borne viral infections.

Conclusion: A significant minority of PWID inject into the jugular vein in the United Kingdom. Public health responses should investigate ways to support and promote good injection site management in order to minimise vascular damage and reduce problems with peripheral venous access. Women who inject drugs, PWID with a history of imprisonment and those people who are experiencing early signs of injection-related skin and soft tissue injuries are priority sub-populations for interventions.

Introduction

People who inject drugs (PWID) typically inject into the peripheral veins in their arms (Harris & Rhodes, 2012). Problems with vascular access to peripheral veins may arise as a consequence of the vascular damage that can occur after regular injection into a body site over a long period of time. Damage to a peripheral vein, such as venous sclerosis (the hardening and thickening of the walls of a vein), can limit venous access at that site by making it difficult to locate the vein or inject into it. This limited venous access may result in people making several attempts to inject into a body site or using multiple sites on their body for injection (Darke, et al., 2001; Harris & Rhodes, 2012; Maliphant & Scott, 2005). It may also result in accidental subcutaneous and intramuscular injections, or 'missed hits', which can result in soft-tissue damage and infections (Hope, et al., 2016). Over time injection into accessible peripheral veins, such as the arms or legs, can become increasingly difficult (Darke, et al., 2001). An alternative is to inject into central veins, such as the femoral or jugular veins (Ciccarone & Harris, 2015). Injection into the central veins can be more difficult, and has high risk of complications and harm (Darke, et al., 2001). The use of such veins was often regarded as the "last resort" for people with vascular damage who had exhausted the option of using an alternate injection site (Darke, et al., 2001; Maliphant & Scott, 2005; Rhodes, 1995). However, studies indicate that the practice of injection into the central veins might have become more common in some countries, such as the UK, over time (Rhodes, et al., 2006; Hope, et al., 2015). Although a number of studies have examined injection into the femoral vein ('groin injection') and the factors associated with this practice (Maliphant & Scott, 2005; Rhodes, et al., 2006; Coffin, et al., 2012; Ti, et al., 2014; Hope, et al., 2015), there have been very few studies that have investigated injection into the jugular vein ('neck injection').

The few studies that have investigated injection into the jugular vein have reported substantial differences in the prevalence of this practice. In a recent study in Tijuana (Mexico) one third of PWID reported that the neck was the main site used for injection in 2011 (Rafful, et al., 2015). The high prevalence of jugular vein injection in Tijuana may reflect the predominance of black

tar heroin in this region, the use of this form of heroin has been associated with venous sclerosis that makes intravenous injection difficult (Ciccarone, 2009 ; Rafful, et al., 2015). In a cohort study in Vancouver (Canada), around one quarter of participants who were followed-up during 2004-2005 had used the jugular vein as an injection site during the preceding 6 months (Hoda, et al., 2008). In this Canadian study, injection into the jugular vein was associated with daily injection and the authors hypothesized that venous access difficulties were likely to occur among people engaging in high frequency injecting drug use (Hoda, et al., 2008). Frequent injection (that is injecting more than once daily) was also associated with jugular vein injection in Tijuana (Rafful, et al., 2015), and in both the Canadian and Mexican studies people who had injected into their jugular vein were more likely to require or seek assistance with injecting (Hoda, et al., 2008; Rafful, et al., 2015). In a national study undertaken in Iran in 2007, 12% of people who injected heroin daily or more frequently reported their neck as their usual injection site (Karimi, et al., 2014). However, an older study undertaken in Sydney (Australia) in 1999, found jugular vein injection to be much less common, with 10% of PWID reporting that they had ever injected into their neck and 4% reporting that they had done so in the previous six months (Darke, et al., 2001).

These studies support the notion that the practice of injection into the jugular vein may be relatively common. This is a concern as injection into the jugular vein has been associated with a number of significant, and potentially costly, health problems (Lewis, et al., 1980; Myers, et al., 1988; Hoda, et al., 2008; Rafful, et al., 2015), including jugular vein thrombosis, deep neck infections, pneumothorax, endocarditis and sepsis (Lewis, et al., 1980; Myers, et al., 1988). This study used data from a large national cross-sectional survey of PWID in the United Kingdom (UK), which purposively collected information on the injection sites used during the previous 28 days. Using this data we investigate a) the extent of jugular vein injection in the UK, b) factors associated with jugular vein injection, and c) health-related harms associated with this practice.

Methods

Recruitment and data

PWID at sentinel locations have been recruited into a voluntary unlinked-anonymous monitoring (UAM) system in the UK since 1990. Methodological details of this system, a series of annual cross-sectional surveys, have been published previously (Hope, et al., 2014). Briefly, agencies providing services to PWID (e.g. needle and syringe programmes and providers of addiction services such as opiate substitution therapy) invite clients who have ever injected psychoactive drugs to participate in the survey each year. The agencies are sentinel locations throughout the UK, except Scotland, and are selected to reflect both the geographic distribution and range of services offered to PWID. People who consent to participate provide a fingerstick capillary dried blood spot (DBS) and self-complete a short questionnaire focused on the injection of psychoactive drugs. The survey instrument includes a multi-response question on the use of specific injection sites, participants who had injected during the preceding 28 days were asked: *“In the last 28 days, into which parts of your body did you inject drugs?”* and indicate all of the listed body sites that they had used. In 2011, as part of questionnaire review and stakeholder feedback, the response categories were expanded to additionally include the ‘neck’. The UAM Survey has multi-site ethics approval.

DBS specimens were tested for antibodies to HIV (anti-HIV), hepatitis C virus (anti-HCV) and hepatitis B core antigen (anti-HBc). Anti-HIV was detected using an in-house GACELISA with similar performance to GACELISA HIV 1+2 (Abbott Murex Diagnostics Ltd, Dartford, UK). Reactive specimens underwent further testing according to a proven algorithm that included a second ELISA and Western Blot (Connell, et al., 1993). Anti-HCV was detected using a previously validated commercial enzyme-immunoassay (Ortho HCV 3.0 SAve, Ortho Diagnostics) (Judd, et al., 2003) and anti-HBc was detected using an in-house modification of the Biorad MONOLISA Anti-HBc PLUS Assay (code 72315/6) optimised and validated to detect anti-HBc in DBS.

Eligibility & analysis

We analysed data collected in UAM Survey over the period 2011 to 2014 inclusive. Where respondents participated in more than one survey wave, only their first participation record was retained. Respondents who had not injected during the preceding 28 days, and those who provided no response to the question on body sites used for injection were also excluded.

Bivariate associations ($p < 0.05$) between the outcome variable, that is reporting the use of the neck as an injection site during the preceding 28 days, and covariates (demographics, injecting practices (during the preceding 28 days), sexual behaviour (during the preceding year), and health services' use (during the preceding year)) were examined using Pearson's Chi-square test. Where possible associations were observed ($p < 0.10$) these were further examined via logistic regression to estimate crude and adjusted odds ratios (AOR) and 95% confidence intervals (CI) using a forward stepwise procedure to select variables for inclusion in the model based on the likelihood ratio test ($p < 0.05$). All analyses were undertaken using SPSS 23.

Associations between using the neck as an injection site and four health-related harms (testing anti-HIV, anti-HBc, anti-HCV positive, and self-reported recent symptoms of injection site infection during preceding year) were explored by examining the prevalence of injection into the neck among those with and without each of these four harms. Data were adjusted for age, gender and region as these factors are known to be associated with these health-related harms (Judd, et al., 2007; Hope, et al., 2005; Hickman, et al., 2007).

Results

Sample characteristics

During 2011-14, a total of 5,261 unique individuals were recruited. Just over half (51%, n=2,679) were aged 35-years or older (mean age 35 years, median 35 years), 23% (n=1,216) were women and 6% (n=316) were born outside of the UK. Almost two thirds (64%, n=3,391) of the sample reported that the main class of drugs injected was opiates, with a further 18% (n=970) of respondents reported that they injected both opiates and stimulants, predominantly heroin and crack. A minority of respondents reported injecting only stimulants (13%, n=672) or other drugs (4%, n=228). Just over one quarter (28%, n=1,469) of respondents reported that they had been homeless during the preceding year and almost three-quarters (71%, n=3,748) reported that they had a history of imprisonment.

Injection practice

The most commonly reported site on the body used for injection during the preceding 28 days was the arm (61%, n=3,219); with 36% (n=1,872) reporting injection into their groin (femoral vein), 27% (n=1,422) into their hand, 21% (n=1,127) into their leg, and 11% (n=593) into their foot. Injection into the neck was reported by 6% (n=339) of respondents, with 4% (n=183) reporting that they had used another unspecified site. Overall, 67% (n=3,547) of respondents had used a single injection site during the preceding 28 days; while 19% (n=991) had used two injection sites, 8% (n=407) had used three sites and 6% (n=316) had used four or more injection sites. For 52 respondents (1%), the neck was the only injection site they had used in the preceding 28 days.

[Insert Table 1 about here]

The factors associated with using the neck as an injection site in both bivariate and multivariable analysis are provided Table 1. In multivariable analysis, jugular vein injection was more common among women (AOR 1.89, 95% CI 1.42-2.52, p<0.001), those with a lifetime

history of imprisonment (AOR 1.51, 95% CI 1.12-2.03, $p=0.041$) and people who had shared (distributively &/or receptively) needles and syringes (AOR 1.67, 95% CI 1.25-2.24, $p<0.001$). Jugular vein injection was also associated with recent poly-drug use, with respondents increasingly more likely to have injected into their neck as the number of drugs injected in the previous 28 days increased. Similarly, the likelihood that respondents had injected into their neck increased as the number of injection sites increased.

Health Harms

Overall, 51% ($n=2,663$) of respondents had been exposed to hepatitis C (anti-HCV positive), 15% ($n=783$) had ever been infected with hepatitis B (anti-HBc positive) and 1% ($n=58$) had HIV infection. Just over one quarter (28%, $n=1,466$) of respondents reported they had experienced an abscess, open sore or wound at an injection site during the preceding year. In both bivariate and multivariable analyses there were no associations between jugular vein injection and HCV, HBV or HIV infection. However, experiencing an abscess, open sore or wound at an injection site during the preceding year was significantly more common among those who used the neck as an injection site, with 46% ($n=156$) of respondents who reported jugular vein injection experiencing these symptoms, compared with 27% ($n=1,310$) of those who did not report jugular vein injection (AOR 2.31, 95% CI 1.84 to 2.89, $p<0.001$).

Discussion

In our study, one third of respondents reported central venous injection and one in 15 had used their neck as an injection site during the preceding 28 days. Given that our study only investigated injection practice during the previous four weeks, it is likely that a higher proportion had injected into their neck in the previous year or had a lifetime history of jugular vein injection. Our findings on the prevalence of the practice of jugular vein injection are broadly similar to that reported in Australia (Darke, et al., 2001), but lower than that reported in studies undertaken in Tijuana and Vancouver (Hoda, et al., 2008; Rafful, et al., 2015). Among the few studies that have investigated this practice, variation in the prevalence of injection into the

jugular vein is likely to be related to differences in the physical properties of the drugs being injected (e.g. the use of viscous 'black tar' heroin), and the nature of populations recruited (e.g. how frequently they inject).

Consistent with the limited literature on jugular vein injection (Hoda, et al., 2008; Rafful, et al., 2015), we found that women were almost twice as likely to report neck injection compared to men. While peripheral venous access difficulties over the longer term are relatively common among PWID (Ciccarone & Harris, 2015), these difficulties may be exacerbated among women. Several studies have demonstrated that, compared to men, women are more likely to experience injection-related skin and soft tissue injuries which can lead to venous sclerosis and loss of venous functioning (Topp, et al., 2008; El-Bassel, et al., 2010). Previous studies also identified an association between injecting into the jugular vein and requiring assistance to inject, a practice which was not asked about in our survey (Hoda, et al., 2008; Rafful, et al., 2015).

We also found associations with recent poly-drug injection, use of multiple injection sites, and needle and syringe sharing. One in 100 respondents had exclusively injected into their neck during the previous 28 days, suggesting that this is their main or usual injection site. The association with needle and syringe sharing is of concern, and is contrary to findings from Tijuana, Mexico, where neck injection was associated with use of new or sterile needles (Rafful, et al., 2015). Our results indicate that people who inject into the jugular vein engage in range of high-risk injection practices. Providers of specialist services when delivering harm reduction interventions should be aware that the overall levels of risk behaviours are higher among those who inject into their neck.

The association between ever imprisonment and neck injection may also be related to those who inject into their jugular vein having a higher overall risk profile. Recent imprisonment was also weakly associated with jugular vein injection in Vancouver (Hoda, et al., 2008). Although

the association between jugular injection and imprisonment needs further investigation, there may be interplay between behaviours, such as injection in public spaces and poor injection practice, which might lead to greater likelihood of involvement with the criminal justice system, as well as to the use of the jugular vein for injection.

The association between neck injection and recent symptoms of an injection site infection might also reflect a higher level of overall injection risk in this group. In this study we did not ask about the body location of the injecting site infection(s), so this association may be due to people who, because of an infection are unable to use their usual injection site(s), using their neck as an alternative injection site. This finding needs further examination. However, considering we also identified association between jugular injections and the use of multiple body sites for injecting, the association with injection site infections could be related to vascular access issues at other body site(s) that have resulted in people moving on to alternative higher risk sites, such as the jugular vein, over time (Darke, et al., 2001).

Darke *et al* (2001) work in Australia indicated such a temporal progression in the body sites that PWID use for injection. They found that the initial progression was from the pit of the elbow (cubital fossa) to the forearm and then the upper arm. The use of the hand, legs and/or the neck often followed, then finally the use of the groin and/or digits. Such progressions are most probably related to the development of injection-related problems, such as vascular sclerosis and soft tissue infections and injuries, which are often experienced at frequently used injection sites and after injecting for long periods (Darke, et al., 2001; Harris & Rhodes, 2012; Hope, et al., 2016). The actual sites in such a progression and the order that they are used are probably affected by local injecting practices, such as what sites are already being used by other PWID, and so may vary between settings, countries and over time. This is an area requiring further investigation.

Considering this progression in the body sites used for injection, public health responses should first investigate ways to reduce the transition to, and practice of, central vein injection (including injection into the jugular vein) by supporting and promoting good injection site management and hygiene in order to minimise vascular damage, reduce problems associated with peripheral venous access, and promote vascular health. Further, the early treatment of injection site wounds and infections that do arise will help to preserve access to peripheral veins by reducing the likelihood of long term complications (Rhodes, et al., 2007). These should of course be in addition to the provision of high coverage of needle and syringe programmes and easy access to opiate substitution therapy (MacArthur, et al., 2014) in order to minimize injections using non-sterile injecting equipment that are detrimental venous health (Harris & Rhodes, 2012). Although these interventions, which both aim to reduce injection risk, are widely available in the UK, our findings show that substantial sharing and reuse of needles and syringes and other injecting equipment continues. Secondly, interventions should promote awareness among PWID of the risks that are associated with injecting into the neck. Advice and support should also be provided as appropriate to PWID on how to access peripheral veins even when they believe this is no longer possible (Zador, et al., 2008). As noted by Zador *et al* (2008), this strategy is particularly warranted in settings where injection practices are directly observed, such as supervised injection facilities. Finally, as smoking or snorting drugs, while not without risk, are safer than injecting, route transition interventions that support alternative routes of administration to injection should also be considered. Interventions, such as providing foil for heroin inhalation, have proven effective in some settings (Pizzey & Hunt, 2008; Advisory Council on the Misuse of Drugs, 2010).

Our study has potential limitations. Firstly, the illicit and marginalised nature of injection drug use makes the recruitment of representative samples difficult. To maximise representativeness, an accepted approach for surveillance surveys involving recruitment at multiple sites through targeted services for PWID as a sampling frame was used (European Centre for Disease Prevention and Control, 2009). In the UK, the provision of targeted services

is extensive, and the uptake and use of these has been found to be high in community-based studies (Hickman, et al., 2007). Secondly, behavioural data used are based on self-reports, the accuracy of which may be subject to recall bias; however, the reliability of self-reported risk behaviours among PWID has been shown in other studies (Latkin, et al., 1993). Considering these issues, the findings presented here should be generalised with caution.

Conclusions

A significant minority of PWID inject into the jugular vein in the UK and serious adverse health consequences are associated with this practice. Public health responses should investigate ways to support and promote good injection site management in order to minimise vascular damage, reduce problems with peripheral venous access, and promote vascular health among PWID. Women who inject drugs, PWID with a history of imprisonment and people who are experiencing early signs of injection-related skin and soft tissue injuries are priority sub-populations to receive interventions.

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Table 1 Factors associated with using the neck as an injection site among people who inject psychoactive drugs; United Kingdom, 2011-2014 (n=5,261).

		Injected into the neck?			Adjusted Odds Ratio, 95% CI.					
		Yes	N	p						
Gender of respondent	Male	5.6%	225	4,045	<0.0001	1.00	1.89	1.42	- 2.52	
	Female	9.4%	114	1,216						
Age, Years	Mean/Median	Yes 34/34; No 35/35		0.0981†	†					
Country / Region	Midlands & Eastern England	7.0%	97	1,382	0.0271	†				
	London & Southern England	7.2%	126	1,739						
	Northern England	4.9%	78	1,593						
	Wales & Northern Ireland	6.9%	38	547						
Ever imprisoned?	No	5.4%	81	1,513	0.0408	1.00				
	Yes	6.9%	258	3,748			1.51	1.12	-	2.03
Homeless during preceding year	No	6.1%	230	3,792	0.0726	†				
	Yes	7.4%	109	1,469						
Shared needle(s) or syringe(s) *	No	5.4%	239	4,413	<0.0001	1.00				
	Yes	12%	100	848			1.67	1.25	-	2.24
Shared a mixing container(s)*	No	5.3%	195	3,704	<0.0001	†				
	Yes	9.2%	144	1,557						
Shared a filter(s)*	No	5.3%	207	3,896	<0.0001	†				
	Yes	9.7%	132	1,365						
Injected with needle/ syringe after cleaning*	No	5.7%	212	3,725	0.0005	†				
	Yes	8.3%	127	1,536						
Number of injection sites used*	One	1.5%	52	3,547	<0.0001	1.00				
	Two	5.8%	57	991			3.92	2.67	-	5.77
	Three	21%	85	407			16.4	11.4	-	23.8
	Four or more	46%	145	316			48.6	33.9	-	69.6
Main drug type injected*	Opiates only	5.5%	188	3,391	<0.0001	†				
	Stimulants only	4.6%	31	672						
	An opiate & stimulant	11%	107	970						
	Other drugs or combinations	5.7%	13	228						
Number of drugs injected*	One	3.7%	96	2614	<0.0001	1.00				
	Two	7.7%	150	1954			2.11	1.57	-	2.84
	Three	11%	58	511			2.10	1.42	-	3.12
	Four or more	19%	35	182			3.02	1.81	-	5.05
Number of times injected*	<14	3.5%	55	1,550	<0.0001	†				
	14-27	3.8%	26	682						
	28-56	5.5%	61	1,113						
	57+	11%	147	1,357						
	Not reported	8.9%	50	559						

Ever exchanged sex for money, drugs or goods?	Never/not reported	6.0%	275	4,621	<0.0001 †
	Yes, not in preceding year	6.3%	20	320	
	Yes, in preceding year	14%	44	320	
Needle & syringe programme use and coverage (needles per injection*)	Not used	4.7%	15	321	0.0143 †
	Used: coverage 100% or less	7.0%	149	2,121	
	Used: coverage over 100%	5.3%	102	1,911	
	Use &/or coverage not known	8.0%	73	908	

There was no association in the bivariate analyses with: whether UK born; reporting anal &/or vaginal sex last year; being prescribed treatment for drug use; ever having voluntary confidential test for HIV; ever having voluntary confidential test for hepatitis C; or uptake of the hepatitis B vaccine.

Years since first injection was not considered in the analysis as age at first injection was sometimes missing, and where years since first injection could be calculated it was found to be correlated with age ($r=0.661$, $p<0.001$).

* During preceding 28 days.

‡ Mann Whitney U

† Not in final model

95% CI = 95% confidence interval