Unexplained illness and deaths among injecting drug users in England: a case control study using Regional Drug Misuse Databases

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In April to June 2000 an outbreak of unexplained illness in injecting drug users (IDUs) in parts of the UK led to hospitalisation and usually death among those affected.¹ For investigation purposes a new syndrome-based case definition was constructed as, extensive inflammation at a subcutaneous or intramuscular injection site and, either severe system toxicity or, postmortem evidence of a diffuse toxic or infectious process.² Between 1 April and 19 June investigation of 88 hospitalised or dead IDUs with injection site soft tissue inflammation found 35 met the case definition. Despite very high mortality (34, 97%) only limited epidemiological information is available.¹ However, empirical evidence identifying the characteristics of IDUs most at risk is fundamental to, better understanding the outbreak, preventing re-occurrence and developing appropriate advice should one occur in the UK or elsewhere.

By the end of June, 14 confirmed cases (12 fatal) were identified in the north west of England; the area with the majority of English cases¹ and historically a high prevalence of injecting drug users.³ Based on these cases, we present results from a case-control study that

provides the first empirical information on IDUs most at risk.

Methods and Results

As most cases had died, the Regional Drug Misuse Databases (RDMDs)^{4,5} were used to develop retrospective case (and control) histories on demographics and drug use. The North West RDMDs collect information on drug users combining data from diverse settings including; treatment services, police, prisons, and probation.^{4,5} Datasets do not store names but use anonymised identifiers (initials, birth date, sex, and a geographical marker). Using these, exact matches for 12 of the 14 cases were located on the databases and data from their most recent contact extracted (police surgeons n=2, community drug teams n=8, drug dependency unit=1, prison medical service n=1). Most (75%) cases had been seen within the past three years. For each case 10 controls were randomly selected from individuals attending the same agency within a period of $\pm$ six months. Identical data fields were extracted for controls and cases. All analyses were undertaken separately for each factor first without matching and then, using logistic regression

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Table 1 Cases control analyses of demographic and drug use characteristics

					Probability values	
Factor	Cases	n	Controls	n	Unmatched	Logistic regression
<i>At last database contact</i>						
Female	50.0%	12	14.2%	120	<0.005	<0.005
Number of previous database reports (mean)	2.7	12	2.2	120	0.426	0.545
Ever injected*	91.7%	12	85.1%	114	0.536	0.547
Ever shared†	77.8%	9	40.0%	60	<0.05	<0.05
Current injector	91.7%	12	62.8%	113	<0.05	0.069
Current sharer†	20.0%	10	8.2%	49	0.259	0.337
Reported heroin use	100.0%	12	86.7%	120	0.177	0.773
Reported injecting heroin	90.9%	11	79.8%	94	0.374	0.388
Age first used heroin (mean)	17.6	11	19.0	87	0.164	0.383
Reported cocaine use	39.2%	12	41.7%	120	0.866	0.860
Reported injecting cocaine	80.0%	5	52.9%	17	0.279	0.205
Age first used cocaine (mean)	20.5	4	22.0	13	0.732	0.638
Reported methadone use	58.3%	12	69.2%	120	0.442	0.433
Reported injecting methadone	16.7%	6	7.3%	41	0.443	0.423
Age first used methadone (mean)	22.8	6	22.6	36	0.745	0.933
Reported amphetamine use	25.0%	12	30.0%	120	0.717	0.676
Reported injecting amphetamine	100.0%	2	50.0%	6	0.206	0.923
Age first used amphetamine (mean)	19.5	2	16.5	4	N/A	N/A
Reported benzodiazepine use	66.7%	12	47.5%	120	0.205	0.161
Reported injecting benzodiazepines	42.9%	7	8.8%	34	<0.05	<0.05
Age first used benzodiazepines (mean)	19.7	7	20.6	32	0.726	0.314
<i>At 1st April 2000 (mid outbreak)</i>						
Age (years)	33.14	12	29.86	120	<0.05	<0.05
Years since first heroin use	14.64	11	10.42	87	<0.01	<0.05
Years since first cocaine use	10.89	4	7.98	13	0.07	0.168
Years since first methadone use	8.99	6	7.19	36	0.297	0.336
Years since first amphetamine use	12.29	2	14.82	4	N/A	N/A
Years since first benzodiazepines use	12.18	7	9.36	32	0.085	0.075

*One case was not reported to the drug misuse database as an injector. †Analysis of sharing is limited to injectors only. In all analyses matched controls are only included in analyses when case information is available. Comparisons of proportions injecting each substance are limited to users of those substances. Sample sizes (n) refer to number of cases and controls in each analysis.

and including a field linking each case to their controls.

Cases were significantly more likely to be female than controls (table 1) and were more than three years older (mean age 33 on 1 April 2000). Furthermore, duration of heroin use was 4.22 years greater for cases. At last presentation to services cases were more likely to be currently injecting (that is, injected in the previous four weeks) and of all injectors, cases were more likely to have shared needles. Furthermore, among benzodiazepine users, cases had higher levels of injecting benzodiazepines, indicative of more chaotic behaviour.

Comment

Using an established multi-agency drug database we have identified demographics and drug use risk factors for the recent unexplained illness affecting IDUs in the UK. Cases were more likely (than controls) to be female. Half of cases in this study and 49% of all cases identified across the UK were female¹ (compared with 30% women RDMDs⁴). Among injectors, cases also had higher levels of having shared needles and having injected benzodiazepines; indicative of more chaotic behaviour.

The most probable cause of this unexplained syndrome is *Clostridium novyi* infection; an anaerobic bacteria more likely to flourish in subcutaneous or intramuscular injection sites.¹ Prolonged injecting drug use, especially including benzodiazepine, can lead to venous damage while injecting cocaine constricts the blood vessels. Respectively, these factors promote a greater likelihood of accidental or intended non-venous injection and reduced oxygen to

blood vessels when venous injection occurs. Both factors are likely to aid growth of anaerobic bacteria. Furthermore, women have more difficulty accessing superficial veins.⁶

Critically, prevention and identification of further cases relies on better understanding of this condition. Extensive field studies being undertaken in Glasgow should elaborate more details of risk. In the meantime however, this study provides the first evidence of additional risk from this unexplained illness to women, older drug users and those with more chaotic injecting histories.

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