A multicentre study of coproxamol poisoning suicides based on coroners' records in England

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Keywords

coproxamol, suicide, poisoning,
coroners

Received

23 June 2004

Accepted

24 August 2004

Aims

To examine in detail a series of coproxamol overdose deaths in order to provide information that will assist in the development of strategies to prevent such fatalities.

Method

Inquest records in 24 coroners' jurisdictions in England on deaths between January 2000 and December 2001 which received a verdict of either suicide or undetermined cause (with a high or moderate probability of suicide) were examined.

Results

One hundred and twenty-three coproxamol poisoning suicides were identified. Alcohol was involved in 58.5% of the overdoses and these individuals generally had lower blood drug levels and consumed fewer tablets. Younger people were more likely to have consumed alcohol and to have lower levels of suicide intent. Nearly half the individuals had a history of self harm, and a third were under psychiatric care. The coproxamol had been prescribed for the individual in 81.5% of cases, although only in 55.0% of those aged 10–34 years. In other cases the source of the coproxamol was nearly always a family member or partner. Some deaths resulted from relatively small overdoses.

Conclusions

Strategies to reduce self poisoning deaths due to coproxamol should take account of the high toxicity of coproxamol in overdose, especially when combined with alcohol, and the fact that risk of death extends beyond the person for whom the drug is prescribed.

Introduction

Self poisoning with coproxamol (a combination of dextropropoxyphene hydrochloride 32.5 mg and paracetamol 325 mg) has been highlighted as an important method of suicide in the United Kingdom [1–3]. This issue was first raised in the UK in 1977 [4, 5]. Dextropropoxyphene poisoning has also caused concern in

other countries [6–8]. Between 1997–9 there were on average 255 deaths per year from coproxamol poisoning in England and Wales [3]. These deaths accounted for 5% of all suicides; coproxamol was the second most commonly used drug in overdose suicides. Death from coproxamol overdose results from respiratory depression and/or cardiac effects, including prolonging

atrio-ventricular conduction and slowing of the heart rate [9, 10].

Restriction of availability of specific methods of suicide is an important component of national suicide prevention strategies [11, 12], and analgesics have been highlighted in this regard [11]. Coproxamol is a prescription-only drug. Therefore prevention initiatives should largely focus on prescribing practices. In deciding which approach to prevention would be likely to be most effective, and in what groups of people who die by suicide, detailed information on cases is required. We have conducted a multicentre study of a recent series of coproxamol poisoning suicides in England, based on examination of coroners' records.

Methods

Coproxamol suicides

The study was conducted from research centres in Oxford, Bristol and Manchester. We initially approached the coroners in each of these cities and then used a random number method to select a further seven jurisdictions for each centre that were within 50 miles or 1.5 h-travelling time.

The coroners' lists of deaths between 1st January 2000 and 31st December 2001 were searched for poisoning deaths in which a suicide or open verdict was recorded. For the open verdicts, details of the cases were discussed and rated within each research team and those where the probability of suicide was rated as high or moderate were included in the study. The ratings were based on all the available evidence about the circumstances of the act, plus the individual's prior history and any statements by the person of suicidal intention [13, 14]. A prior comparison of ratings of a series of 47 cases by researchers in the three centres had demonstrated good reliability, with agreement in 90% of cases. The record for each poisoning death was examined to identify those in which coproxamol was involved. We included in the study those in which coproxamol was either the only drug involved in the overdose, or where it was judged that coproxamol contributed to the death based on factors such as recorded cause of death, toxicology reports and the relative toxicity of other drugs taken.

Details of demographic characteristics, nature of the overdose, postmortem toxicology, source of the coproxamol, and drug and alcohol misuse were collected. We also recorded whether alcohol had been consumed around the time of the overdose, based on postmortem alcohol levels and evidence in the inquest records. Psychiatric diagnoses were based on all the information available in the reports. For recording whether or not

there was a history of previous deliberate self harm we included cases where either information was recorded for this item, or the notes of evidence were very detailed and a previous episode was not mentioned. For all other cases this item was recorded as not known.

We included in the study the circumstances section of the Beck Suicide Intent Scale [15]. Suicide intent is a measure of the extent to which a person appears to have wanted to die at the time of an act of self harm. The Beck Suicide Intent Scale is widely used in clinical practice with suicide attempters. It includes two sections, one based on self-report by patients and the other on the objective circumstances of the act. Only the latter section is suitable for use in cases of suicide.

Statistical analyses

The data from the three centres were combined. We used the chi square test, Spearman's rank correlation, *t*-tests and linear regression to analyse the data. The Statistical Package for the Social Services v11.5 [16], EpiInfo 6 [17] and STATA [18] were used to conduct the analyses.

Results

Cases and characteristics

There were 123 coproxamol poisoning suicides during the study period. The coroner's verdict was suicide in two-thirds (66.7%) of cases. Twenty-two of the 43 open verdicts were rated as having a high probability of suicide and 19 as of moderate probability. In a further two cases with open verdicts the probability of suicide was rated uncertain and these were excluded from the study (none were rated as low probability). Sixty-four (52.0%) cases involved females. The age distribution was: 10–34 years, 34 (27.6%); 35–54 years, 38 (30.9%); 55 years and over, 51 (41.5%). There were only five individuals in the 10–18 years age group, the youngest of whom was aged 14. Fifteen individuals were aged over 75 years, the oldest being 91 years old.

Information on contact with psychiatric services was available for 96 cases. Forty-six (47.9%) people had had such contact at some point in their lives, of whom 30 (31.3%) were in contact with a service at the time of death, and a further three (3.1%) had been during the previous year. Information on psychiatric disorder at the time of death was available in 102 cases. The main diagnoses were affective disorder (64; 62.7%) and alcohol dependence (13; 12.7%). Drug dependence was only recorded in two (2.0%) cases. However, evidence of alcohol abuse was present in the notes of a further nine cases and drug misuse in a further three cases. Fifty

(45.5%) out of 110 cases had a recorded previous episode of deliberate self harm.

Nature of the overdoses

In 119 cases in which toxicology results were available, coproxamol appeared to have been taken alone in 71. In 20 further cases other drugs had also been taken which may have contributed to the deaths. These drugs included other analgesics ($n = 10$ cases), antidepressants ($n = 6$), minor tranquillisers ($n = 3$) and 'other prescribed drugs' ($n = 2$). The remaining 28 cases involved other drugs, but these were unlikely to have contributed to death (in some cases the blood levels of these drugs were within the therapeutic range). The drugs involved included minor tranquillisers ($n = 19$), antidepressants ($n = 14$), 'other prescribed drugs' ($n = 8$), other analgesics ($n = 7$) and drugs of abuse ($n = 3$). Some individuals had taken drugs in more than one category. Most of the deaths occurred before the individuals could reach hospital (103, 83.7%).

Evidence of possible alcohol consumption shortly before death was available for 111 cases; alcohol had

been consumed in 65 (58.5%). This was more often the case for individuals in the two younger age groups ($\chi^2 = 14.91$, 2 d.f., $P = 0.0006$; Table 1). In 49 (45.4%) cases where alcohol levels were available from toxicology ($n = 108$) the level was above the legal driving limit of $80 \text{ mg } 100 \text{ ml}^{-1}$, and in 31 (28.7%) was known to exceed $150 \text{ mg } 100 \text{ ml}^{-1}$.

Information on the number of coproxamol tablets used in the overdoses was available in a minority of cases. In some cases an approximate number was deduced from indirect information, such as the number of empty blister packs found beside the body. An estimate of the amount consumed was possible for 46 cases. The numbers of tablets and cases were: <20, 4 cases; 20–39, 11; 40–59, 10; 60–79, 4; 80–99, 9; ≥ 100 , 8. Thus a third (32.6%) of overdoses involved an estimated ingestion of less than 40 tablets. The smallest number of tablets was ten. In cases where we had information on both the number of tablets taken in the overdoses and whether or not alcohol was consumed ($n = 40$), in a linear regression model controlling for age and sex we found that subjects who drank alcohol at the time of the act consumed on average 25 fewer tablets (95% CI 0–49) than those where alcohol was not involved ($P = 0.048$).

Table 1

Alcohol consumption at the time of overdose, and source of the coproxamol

<i>Alcohol consumed at the time of the overdose</i>				
Age group (years)	<i>n</i>	(%)		
10–34 (<i>n</i> = 31)	22	(71.0)		
35–54 (<i>n</i> = 36)	27	(75.0)		
55 and over (<i>n</i> = 44)	16	(36.4)		
All ages (<i>n</i> = 111)	65	(58.6)		
<i>Source of the coproxamol</i>				
Age group (years)	<i>n</i>	Coproxamol prescribed for deceased (%)	Someone else <i>n</i>	(%)
10–34 (<i>n</i> = 20)	11	(55.0)	9	(45.0)
35–54 (<i>n</i> = 28)	22*	(78.6)	6	(21.4)
55 and over (<i>n</i> = 44)	42*	(95.5)	2	(4.5)
All ages (<i>n</i> = 92)	75	(81.5)	17	(18.5)

*Includes one case in which coproxamol was prescribed both for the deceased and someone else

Postmortem toxicology

Dextropropoxyphene blood levels were recorded for 95 (77.2%) cases. The mean was 4.8 mg l^{-1} (range 0.028–42.7). In 36 (37.9%) of these cases the level was $= 2 \text{ mg l}^{-1}$, in 26 (27.4%) between ≥ 2 and 4 mg l^{-1} and in 33 (34.7%) $> 4 \text{ mg l}^{-1}$. Paracetamol blood levels were recorded for 106 (86.2%) cases. The mean was 246.1 mg l^{-1} (range 20–1041). In 46 (43.4%) of these the level was between 0 and 200 mg l^{-1} , in 34 (32.1%) between > 200 and 300 mg l^{-1} , and in 26 (24.5%) $> 300 \text{ mg l}^{-1}$. There was a positive correlation between blood levels of dextropropoxyphene and paracetamol, although this was not particularly strong (Spearman's $\rho = 0.37$, $P < 0.0001$). Information on the number of tablets taken in the overdoses was available in 36 cases in which both postmortem blood dextropropoxyphene levels and paracetamol levels were recorded. There was no association between the number of tablets and dextropropoxyphene levels (Spearman's $\rho = 0.06$, $P = 0.74$). Paracetamol levels showed a weak association with the number of tablets (Spearman's $\rho = 0.30$, $P = 0.083$).

In the 89 cases in which both postmortem blood dextropropoxyphene levels and alcohol levels were available there was a weak inverse association between the two (Spearman's $\rho = -0.28$, $P = 0.008$). There was a

similar association between alcohol and paracetamol levels (Spearman's $\rho = -0.34$, $P = 0.001$).

Suicidal intent

Scores on the circumstances section of the Suicide Intent Scale are shown in Table 2. Two-thirds of overdoses occurred with no-one nearby. In nearly all cases intervention by other people was unlikely. Over one-third of individuals had taken active precautions to avoid discovery. Very few people had contacted someone after taking the overdose. On the other hand, in few cases was there evidence of planning for the act or making arrangements (e.g. wills, gifts, insurance) in anticipation of death. In nearly half the cases a suicide note was left. Nearly two-thirds of individuals had not communicated

their intention of taking an overdose to others, although in one in five cases there had been clear communication of intent.

The Suicide Intent Scale scores were compared across age groups for the 107 cases which had complete information on all items. Total SIS scores increased with age (Spearman's $\rho = 0.45$, $P < 0.0001$). Analysis of individual items revealed that for the older suicides the act was more often timed so that intervention was unlikely ($\rho = 0.25$, $P = 0.006$), and that they were less likely to seek help after the act ($\rho = 0.33$, $P < 0.0001$), more likely to have made definite plans in anticipation of death ($\rho = 0.21$, $P = 0.021$), and to have planned the act extensively ($\rho = 0.26$, $P = 0.006$). Thus there were several aspects of the act by older people which indicated more serious suicidal intention. In contrast, the overdoses in younger persons often appeared to be impulsive and not necessarily associated with a clear intention to die.

In age and sex adjusted models based on subjects with complete data on all items of the SIS we found no evidence of an association between suicide intent and alcohol consumption: difference in SIS score between those who consumed and those who did not consume alcohol 0.41 (95% CI -0.5 – 1.4 ; $P = 0.40$). In the cases with information on estimated number of tablets consumed, suicide intent was not associated with the size of the overdose in age- and sex-adjusted models ($P = 0.31$).

Source of the coproxamol

The coproxamol had been prescribed for the deceased person in 81.5% of the 92 cases for which this information was available (Table 1). However, this differed by age group ($\chi^2 = 15.17$, 2 d.f., $P < 0.001$); in nearly half the cases in the youngest age group the person had taken coproxamol prescribed for someone else. The source of the coproxamol where not prescribed for the deceased was a relative or partner in all but two cases. In all 46 cases in which the prescriber could be ascertained, this was the general practitioner.

Discussion

In this study we have investigated a representative series of recent suicide deaths involving coproxamol overdose. The method of selecting cases, based on including both those with a coroner's verdict of suicide or undetermined cause (open verdict) is accepted research practice [19]. However, we have restricted the open verdict cases to those where there was a relatively high probability of suicide. The coroners' reports varied in the extent of detail recorded on individual cases, which resulted in

Table 2

Scores on the circumstances section of the Suicide Intent Scale

Item (number of cases with a score)	Number of cases	(%)
Isolation ($n = 122$)		
Someone present	2	(1.6)
Someone nearby	41	(33.6)
No one nearby	79	(64.8)
Timing ($n = 120$)		
Intervention probable	8	(6.7)
Intervention unlikely	42	(35.0)
Intervention highly unlikely	70	(58.3)
Precautions to avoid discovery ($n = 121$)		
No precautions	11	(9.1)
Passive precautions	62	(51.2)
Active precautions	48	(39.7)
Help-seeking after the act ($n = 122$)		
Notified helper	11	(9.0)
Contacted but did not notify helper	8	(6.6)
Did not contact helper	103	(84.4)
Arrangements in anticipation of death ($n = 123$)		
None/not mentioned	105	(85.4)
Some arrangements	8	(6.5)
Definite plans	10	(8.1)
Planning for the act ($n = 114$)		
None/not mentioned	71	(62.3)
Minimal to moderate	39	(34.2)
Extensive	4	(3.5)
Suicide note left ($n = 122$)		
No note	62	(50.8)
Note torn up	0	
Note present	60	(49.2)
Communication of intent ($n = 120$)		
None/not mentioned	77	(64.2)
Equivocal communication	17	(14.2)
Unequivocal communication	26	(21.7)

there being missing information for some of the items we have studied. This study has focused on people who died following coproxamol overdose including those who reached hospital alive and then died. While coproxamol is extremely dangerous in overdose [3, 20], it should be noted that a minority of those who reach hospital following coproxamol overdose actually die [20]. Since various factors can determine whether a person reaches hospital alive after an overdose, including the chances of discovery, prompt action by those finding the individual, treatment on the way to hospital, and distance travelled, and in-hospital treatment can determine subsequent survival, caution must be exercised in extrapolating from our findings to coproxamol overdoses in general (i.e. fatal and nonfatal).

The largest proportion of deaths occurred in people aged 55 years and over, in keeping with trends found in our study of an earlier series based on data for England and Wales supplied by the Office for National Statistics [3]. This reflects prescribing patterns. However, suicidal intent generally tends to be higher in older than younger people who take overdoses [21], as was the case in this study. Also, older people are generally more vulnerable to the toxic effects of coproxamol due to concomitant physical disorders [22]. As in other series of suicides, depression [23] and alcohol abuse [24] were common features.

Alcohol had frequently been consumed at the time of the overdoses. This finding was based on postmortem alcohol levels and evidence taken from informants. The toxicity of coproxamol, especially respiratory depression, can be considerably enhanced by alcohol [2]. This is in keeping with our findings that those who consumed alcohol had generally taken fewer tablets in their overdoses. Also, consistent with earlier research [22, 25], we found that dextropropoxyphene (and paracetamol) levels were negatively correlated with blood alcohol levels.

A limitation of the findings regarding postmortem drug and alcohol levels is, however, that the precise time of death was often unknown and therefore the time interval between death and blood being taken for analysis could not be ascertained. Furthermore, it is recognized that postmortem propoxyphene levels are difficult to interpret [26] and that there is the potential for postmortem production of alcohol [27].

While the size of the overdoses was only known for a subgroup of cases, the findings indicate that the range of the number of tablets taken was very wide. In some cases the blood levels of dextropropoxyphene were relatively low, in keeping with the findings of a large Swedish study of fatal poisonings [28]. However, the potential difficulty of interpreting postmortem dextro-

propoxyphene levels again needs to be highlighted. The relatively quick action of coproxamol in causing death [2] was confirmed by the fact that in most cases the person did not survive long enough to reach hospital, although, as noted above, other factors can influence survival.

It was difficult to determine in how many cases the act had been impulsive. In few cases was there evidence of planning, yet there was usually little opportunity for intervention once the overdose had been taken. Also, the fact that a suicide note was left in nearly half the cases suggests many had serious suicidal intent [29]. Suicide intent was higher in older individuals, whereas younger individuals showed less evidence of planning the act and anticipation of a fatal overdose.

Coproxamol is mostly prescribed by general practitioners. Considerable care should be exercised in prescribing coproxamol for patients with depression, especially if they have a history of previous self-harm and/or alcohol abuse. While in more than four out of five cases the prescription had been for the person who took the fatal overdose, younger individuals differed from this pattern. This is in keeping with previous findings regarding fatal coproxamol overdoses [30] and the fact that overdoses by young people often involve medication available in their households [31]. The source of the coproxamol when not prescribed for the individual was nearly always a relative or partner. We found little evidence of access to coproxamol being related to drug misuse.

In deciding what might be the most effective strategy for preventing fatal coproxamol overdoses one needs to consider the variability in characteristics of those at risk. One also needs to consider the evidence that coproxamol may be no more effective for pain control than, for example, paracetamol alone [32], at least in short-term use. Options include educating doctors (especially general practitioners) about the dangers of coproxamol, reducing the frequency of prescribing and the size of prescriptions, restricting prescribing to specialists, advising patients about safe keeping of medication and disposing of unwanted tablets, and withdrawal of the drug from the market. There is early evidence to suggest that restricting prescribing may reduce the number of coproxamol poisoning suicides [33]. In view of the high toxicity of coproxamol [3], especially when combined with alcohol, and the fact that the risk of overdose extends beyond the person the drug is prescribed for (particularly in young people), withdrawal from the market might be considered the most appropriate option, especially if less dangerous alternatives are available.

The study was supported by a grant from the Department of Health for England. Views expressed in this paper are those of the authors and not necessarily those of the Department of Health. Keith Hawton is supported by Oxfordshire Mental Healthcare NHS Trust and Sue Simkin by Oxfordshire Research and Development Consortium Strategic Research Fund. We thank the coroners who gave us access to their records and their staff who also gave us assistance.

Ethical approval: None required

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