Contemporary Themes

Dextropropoxyphene (Distalgesic) overdose in the West Midlands

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I wish to draw attention to the acute danger of overdose with the analgesic drug dextropropoxyphene, which is most commonly prescribed in Britain as Distalgesic (paracetamol 325 mg and dextropropoxyphene hydrochloride 32.5 mg). The fatal results from taking this drug are becoming apparent to forensic toxicologists, but medical practitioners may not be so aware of the dangerous consequences of overdose.¹ I present the picture as I see it in Birmingham and the West Midlands.

Case details

During the past three years, 26 deaths due to Distalgesic have been investigated by the Home Office Forensic Science Laboratory, Birmingham. Some were suicidal, but many were more in the nature of "cris du coeur." All died at home except one, when the overdose was taken in hospital. In 12 cases an appreciable amount of alcohol was an additional factor. It is interesting that the average age at death was 36.1, whereas the average for all types of overdose was 57.4, thus emphasising the danger for younger people. Distalgesic is currently the commonest cause of death in those cases of drug overdose referred to the forensic science laboratory. For instance, during this period, they have only done analyses on three fatal cases of paracetamol overdose alone, compared with the 26 due to Distalgesic.

A different picture, however, emerges from hospital practice. Last year, the West Midlands Regional Toxicology Laboratory analysed 222 paracetamol overdoses of which two patients subsequently died of hepatorenal failure. In contrast, there were 60 cases of Distalgesic overdose, none of which were associated with alcohol, and none of whom died. The number of tablets taken were known to vary from two to 40. All these came from various hospitals in the West Midlands region.

A striking feature in the 26 overdose cases at the forensic science laboratory is that in these cases, when the time interval between ingestion of the Distalgesic and death was known, death occurred very rapidly. The amount of overdose seems to vary, but is commonly estimated to be in the range of 20 to 30 tablets.

DANGERS OF ALCOHOL

In the Birmingham Coroner's Court we have recently held six inquests on cases of Distalgesic overdose, again mostly in young people (see table). In addition, a healthy girl of 14 was recently found dead in her bed with a characteristic cyanotic discolouration after it was known that she had been out with an older man and had drunk

three whiskies. A specific inquiry was made into the availability of Distalgesic because of the sudden respiratory failure associated with the recent consumption of alcohol. This revealed that she was menstruating and suffered from dysmenorrhoea, and that tablets were missing from her elder sister's bottle of Distalgesics, prescribed for a similar condition. An excess of paracetamol and dextropropoxyphene was found in the stomach contents. Results of detailed analyses and the inquest are awaited. These seven cases show the rapidity of the fatal outcome, and this would probably be due to the known respiratory depressive effect of the dextropropoxyphene element in Distalgesic tablets. Alcohol (and other sedative drugs) would have an additive effect. Distalgesic is a drug that is acceptable to patients and, certainly, it is effective in pain relief.

The *Extra Pharmacopoeia* (Martindale)² refers to it as having an analgesic effect of a little less than that of codeine. In overdose, however, shallow slow respiration and respiratory depression are described. It is interesting that with those patients who were admitted to hospital after an overdose, the main problem seems to be the onset of acute hepatic failure due to the paracetamol constituent. The stage of serious respiratory depression due to dextropropoxyphene has usually passed and so is not observed if the subject survives to obtain treatment in hospital.

There have been other reports of the rapid death in overdose with Distalgesic—for instance, there was a series from the American Army in Germany in which 13 young servicemen died from overdose.³ In all these fatalities the drug was taken by mouth, and death occurred within 30 to 45 minutes, sometimes with associated convulsions. In eight of these cases alcohol was taken as well. Nearer home Carson and Carson⁴ have reported that in three years they have investigated 30 rapid deaths in Belfast, which they were convinced were due to dextropropoxyphene, and they again emphasised the danger of taking Distalgesic with alcohol. It would seem that the dextropropoxyphene portion of Distalgesic and not the paracetamol is responsible for the sudden deaths.

Lack of usual side effects

Distalgesic is a drug that is growing in use because it is free of many of the unwanted side effects of other common analgesics. This increase is apparent in the Midlands, and in one Birmingham general hospital the dispensing of Distalgesic increased by 35% last year. A local warehouse supplying retail chemists and prescribing doctors despatched 27% more Distalgesic tablets than the year before and a central Birmingham retail pharmacist told me that their dispensing rate for the product had increased by half in the past year.

A recent advertisement for Distalgesic recommends it "for everyday aches and pains"⁵ and, in a review of mild analgesic drugs, Sampson Lipton⁶ describes Distalgesic as an effective combination and one that is liked by patients and is a useful alternative to paracetamol with its danger of liver failure in overdose. Likewise, in *World Medicine*,⁷ in a discussion of the drug control of common symptoms, Distalgesic was recommended for mild pain and is described as an equivalent alternative to soluble aspirin or paracetamol.

Thus a popular belief is developing that Distalgesic is a safe analgesic that may be prescribed with increasing frequency, often at doses above those recommended by the manufacturers—that is, two tablets three or four times a day. The third case in my table shows this, as

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TABLE—Details of cases of Distalgesic overdose from the Birmingham District Coroner's Court

Age and sex	Blood alcohol or other drugs	Estimated overdosage (tablets)	Source of tablets	Time to fatal onset (hours)	Verdict
26 (F)	280 mg/100 ml. No other drugs	15	50 tablets prescribed 16 days before death	1	Killed herself
33 (M)	Nil	40	Prescribed for mother	Considerably less than 10	Killed himself
29 (M)	Nil	30	100 tablets (three four-hourly) prescribed by GP for sinusitis	<2	Killed himself
20 (M)	145 mg/100 ml. No other drugs	20–30	Prescribed for friend	5	Open verdict. Intention uncertain
25 (M)	Nil	40–45	Not known	Uncertain	Killed himself
47 (F)	Alcohol nil. Quinalbarbitone 400 mg	10–20	60 prescribed for self 3 days before	<6	Killed herself

the dosage prescribed was up to 18 tablets to be taken a day—more than twice the manufacturers' recommended maximum dose. Both doctors and patients, therefore, may be lulled into a false sense of relative complacency over the taking of this drug. For instance, to take 20 aspirins may not be disastrous, but an equal number of Distalgesics may kill in a very short time. The manufacturers themselves state in their latest data sheet* that the product in serious overdosage is narcotic and provokes respiratory depression, and this may be additive with alcohol. Dependence with dextropropoxyphene has been reported and overdosage symptoms are indeed similar to morphine with the addition of convulsions.

The very real dangers from overdosage with products containing dextropropoxyphene, particularly when taken with alcohol, are becoming clear to forensic toxicologists but may not be appreciated by clinicians, as the unfortunate people, often young and healthy, who take these drugs, whether intentionally to kill themselves or not, often die rapidly at home before they are found and so never reach hospital for treatment. Prescribing physicians, therefore, should remember the potential

toxicity when considering to whom to prescribe dextropropoxyphene, the dosage advised, and the quantity to be dispensed.

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Letter from . . . Denmark

Planning of scientific-ethical committees

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During the past few years the Western European societies have been increasingly interested in citizens' rights in relation to professions, and medicine has certainly not been excluded. The medical profession itself has also shown an increasing interest in the ethical and judicial aspects of medicine. Examples are the recommendations on genetic manipulation and on human experimentation. Recommendations on human experimentation were contained in the revised Helsinki Declaration of the World Medical Association, as adopted by the WMA's General Assembly in Tokyo 1975. The revised declaration, called the Helsinki Declaration II, aimed at increasing

the protection of the research subject while not inhibiting medical research unnecessarily.

Helsinki Declaration II

Among the important paragraphs of Helsinki Declaration II are those stating that the declaration covers not only treatment, but also diagnoses and prophylaxis and those that make a written research protocol obligatory; emphasise that ethical aspects of biomedical research should always be included in a report; emphasise the patients' and other research subjects' right to decide (via informed consent) whether to join the project or not; accept the use of control groups as a necessary tool of the controlled trial; realise that clinical research can never guarantee a result beneficial to the patients participating—but only a *potential* gain; and, probably most important, demand that the research protocol, if man is the scientific object, be referred (paragraph 1 2) to an independent committee "for consideration, comment, and guidance."

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