K28 Dihydrocodeine-Related Deaths: A Ten-Year Review

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The goal of this presentation is to present a retrospective analysis of dihydrocodeine (DHC) related deaths in the Yorkshire and Humberside regions of the U.K. over the ten-year period 1991-2000, to determine the fatal concentration of the drug in such deaths and to compare the results with experience in the published literature.

DHC is a semi-synthetic opioid drug similar in structure and biotransformation pathway to codeine. It is licensed for use in the U.K. as an analgesic and antitussive drug but over recent years it has found increasing popularity as replacement therapy for heroin and morphine addicted patients, and amongst illicit drug users. Its increasing use in the treatment of opioid drug addiction is thought to relate to its short halflife (4 hrs), less severe withdrawal symptoms and relative lack of potency in comparison with methadone. In common with codeine, some of the DHC metabolites are pharmacologically active, and may contribute to the development of tolerance. Relatively few studies have been published with respect to the pharmacology and toxicology of DHC, although recent literature from the UK and continental Europe points to a general increase in drug deaths in which DHC has been a significant contributory factor. There has been a wide range in the reported DHC levels in these cases, thought mostly to be due to the synergistic effect of other drugs, varying degrees of tolerance and the genetic control of some metabolic steps.

The postmortem records of all cases in which DHC was detected on toxicological analysis were reviewed for the period 1991-2000. A total of 250 such deaths were identified and the vast majority of these cases were suspected overdoses where a full screen was routinely performed. DHC was detected in the blood in trace amounts in 12%, within quoted therapeutic levels in 47%, higher than therapeutic levels in 12% and potentially fatal levels in 29% (n = 72). In those fatalities where DHC was considered the sole or major contributor to the cause of death, the mean age was 42 years (range 1673 years) and there was a male predominance. The range of DHC concentrations in these fatalities was 0.468.7 mg/L (mean 9.7), and in over half of the cases the concentration was less than 10 mg/L. DHC was detected in combination with alcohol and/or other drugs in all such cases and of the 70 cases where analysis of blood alcohol was performed, the level ranged from 6481 mg/100ml. Of the other drugs detected, the most commonly encountered were, not surprisingly opioids (63 cases). The effect of other drugs with central nervous system-depressant qualities, and the development or loss of tolerance has made a quantitative assessment of a 'fatal' DHC level problematic, and similar problems beset any analysis of opioid related deaths, nevertheless, the striking feature of this review was the marked increase in cases where DHC was detected over the study period, and, concomitantly, in the number of cases were death was attributable, at least in part, to DHC toxicity. A significant influence on these figures has no doubt been the increasing prevalence of the drug amongst illicit drug users and its increased prescription by individual physicians. The numbers of cases appear to have reached a plateau by the end of the decade, but nevertheless remain high. In fact, due to the 'targeted' nature of toxicological screening in the jurisdictions covered by this study, the true incidence of DHC-related deaths is most probably significantly under-reported, particularly with respect to road trauma, where blood alcohol is the only analysis performed in many cases.

In conclusion, this study shows that DHC has assumed increasing prominence in drug overdose deaths over the past decade. Possible over-prescription, poor supervision and increasing prevalence amongst illicit drug users are all causes for concern.

Dihydrocodeine, Opioids, Autopsy

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