Notes and miscellanea

Interaction between drugs and solvents as a cause of fatty change in the liver?

Occupational exposure to chlorinated and non-chlorinated solvents has been associated with liver dysfunction.^{1,2} The levels of exposure have usually been high, but experimental evidence indicates that interaction may occur between different solvents at relatively low levels of exposure.^{3,4} The following three case histories suggest that drugs and solvents may also interact.

Case 1

A 52-year-old man with no history of gastrointestinal disease suffers from lumbago, for which he took acetylsalicylic acid (Paraflex comp). He drank less than 30 cl of alcohol a month. As an orthopaedic shoemaker (1946-76) he was exposed mainly to acetone, but also to thinner, chloroform, trichloroethylene, and tetrahydrofuran. In 1967 he had raised γ -GT (2.16-2.32 μ kat/l, normal < 0.70), and three years later also increased ALAT (0.81 μ kat/l, normal < 0.70). A liver biopsy specimen showed "liver with moderate centriacinar fatty change and pronounced siderosis."

Case 2

Another 52-year-old man with previous hospital treatment for cholecystectomy, operation for a slipped disc, and myocardial infarction received digoxin (Lanacrist), verapamil (Isoptin), and paracetamol (Lunedon), but took no alcohol. As a painter (1950-73) he was exposed to thinner. In 1974 he had persistent increase in ALAT (0.72-1.34 μ kat/l, normal 0.08-0.58) and ASAT (1.94-2.20 μ kat/l, normal 0.08-0.84). A liver biopsy specimen in 1974 showed "pronounced fatty change in the liver."

Case 3

A 42-year-old man with high blood pressure and cardiac enlargement but no previous history of

gastrointestinal disease took digoxin (Lanacrist), hydralazine (Apresolin), and propranolol (Inderal). He drank under 30 cl of alcohol a month. He was a painter (1964-76) exposed mainly to xylene. In 1976 he had raised ASAT (1.03-1.31 μ kat/l, normal < 0.70), and ALAT (2.22-2.86 μ kat/l, normal < 0.70) but normal γ -GT. A liver biopsy specimen showed "fatty change in the liver."

When considering increases in aminotransferases, alcohol consumption always has to be considered. It is, however, well known that people with alcohol problems often understate their consumption; on the other hand, they appear to consume less alcohol than those who admit their drinking.⁵

In all three cases drugs had been taken. Paraflex comp contains dextropropoxyphene (45 mg) which, in animal tests, has produced hepatic enlargement and fatty change in the liver.⁶ There are case reports where a daily intake of 130 mg of dextropropoxyphene has caused an increase in liver enzymes, but liver biopsy specimens showed no fatty changes.⁷ Lunedon contains paracetamol, which may cause liver damage.⁸ Neither Apresolin, Lanacrist, nor Inderal are reported hepatotoxins.⁹ There are reports, however, of hypertension giving rise to liver dysfunction, but this seems to be related to alcohol consumption rather than to the hypertension itself.^{10,11}

As to the solvents in use, chloroform is a known hepatotoxin and could perhaps explain the picture in one of the cases. In solvent sniffers exposure to thinner has resulted in fatty changes in the liver,¹² and exposure to xylene is known to produce mild hepatic steatosis.¹³

In conclusion, it seems difficult to explain the fatty changes in the liver in these patients only from the use of alcohol. Solvents could be a cause, or the combination of toxic substances. Potentiation between alcohol and solvents has been shown in animal experiments,^{3,4} but the combination of medical preparations and solvents has not been properly studied. It seems reasonable, therefore, in the investigation of liver dysfunction of unknown aetiology to consider the possibility of exposure to solvents in combinations not only with alcohol but also with the use of drugs.

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