SOME UNRESOLVED ISSUES

In my mind, there are a number of unresolved issues relevant to the benefit/risk ratio of Darvon and its place as an analgesic which deserve further study.

1. Since a majority of fatal propoxyphene overdoses seem to result from mixed intoxication with propoxyphene and other central nervous system depressants [Finkle et al., 1976], some effort should be directed at determining whether propoxyphene is simply adding to the depressant effects of other drugs or is producing a supra-additive interaction which is particularly hazardous.
2. Although the descriptions of fatal poisoning with propoxyphene which I have studied suggest that this drug is producing death in the same way as any classical narcotic overdose (albeit, the overdose syndrome is usually complicated by the presence of convulsions), studies should be done to determine whether propoxyphene has a direct cardiovascular toxicity in excess of other narcotics, and further studies should be done to elucidate the role of norpropoxyphene in the toxicity produced by propoxyphene [Nickander et al., 1977].
3. Since codeine-containing combinations are the logical alternative to existing Darvon combinations and are prescribed to an ever greater extent than Darvon combinations, it would appear logical to make a concerted effort to determine whether the apparent lower incidence of codeine-related deaths is a real phenomenon and, if so, why?
4. Controlled analgesic studies involving repeated-dose administration of propoxyphene compared to other mild analgesics should be done to determine whether the predicted increase of efficacy of propoxyphene on repeated-dose administration really occurs.

ALTERNATIVES TO THE USE OF PROPOXYPHENE AND OTHER NARCOTICS

A number of oral analgesics which might be predicted to have advantages over propoxyphene and other currently available mild analgesics in terms of increased analgesic efficacy and/or decreased adverse effect liability are currently in various stages of clinical testing. These include the non-steroidal anti-inflammatory drugs such as indoprofen, suprofen, zomepirac, diflunisal and many others; narcotic antagonist analgesics such as butorphanol, nalbuphine, buprenorphine, propiram and others; and compounds of uncertain mechanism of action such as nefopam. There are controlled clinical studies indicating that all of these compounds are effective oral analgesics and other studies indicating they may have certain real advantages over existing drugs. The public interest would be served by seeing that these drugs get on the market without undue delay. I would point out that the average physician will very quickly start prescribing a drug which has real advantages for his patient if such a drug becomes available.

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