Effect of diazepam and a soluble salt of diazepam (fosazepam) on sleep in man

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In previous work we have studied the effect of some benzodiazepines on visuo-motor co-ordination in man, and, though with many hypnotics impaired performance persists well into the next day, it would appear that with diazepam (10 mg) the duration of impaired performance may be limited (Borland & Nicholson, 1975a & b). Diazepam, or a closely related drug, could prove to be a useful hypnotic for persons involved in skilled activity. However, there has been little experimental interest in the effect of this drug on sleep, except for the brief report by Kales & Scharf (1973).

In this context we have studied the effect of diazepam and a soluble salt, fosazepam (7 - chloro - 1 - (dimethyl - phosphinylmethyl) - 5 - phenyl - 1,3 - dihydro - 2H - 1,4 - benzodiazepin - 2 - on), on sleep in man. Six healthy male volunteers, aged between 19 and 43 years, were used. They were not taking drugs, and abstained from unusual exercise and the use of caffeine and alcohol from noon of each day of a sleep recording. Subjects were familiar with the laboratory, and their sleep patterns after ingestion of placebo on three separate occasions did not reveal any significant trends. The experiments were double blind. Diazepam (5 or 10 mg), fosazepam (60 or 80 mg) or placebo were ingested as identical capsules at lights out, and recordings were made on the night of administration and the next (recovery) night. Experiments were separated by at least nine days.

It was not possible to establish dose-related effects for most of the sleep measures. Diazepam (5 and 10 mg) and fosazepam (60 and 80 mg) reduced the mean sleep onset latency from 30.7 to 21.6 and 20.1 min respectively ($P = 0.01$), and with fosazepam the mean latency to stage 3 was also shortened ($P = 0.05$). Stage 0 (wakefulness) was depressed by both drugs ($P = 0.001$), and with fosazepam stage 1 (drowsiness) and stage 4 were also reduced ($P = 0.01$). Dose related effects were observed with total sleep time. No change was observed after 5 mg diazepam, but with 10 mg mean total sleep time was increased from 413.1 to 457.7 min ($P = 0.05$). With fosazepam it was increased to 484.4 min after 60 mg ($P = 0.001$), and to 514.2 min after 80 mg ($P = 0.001$). On the recovery night the shortened sleep onset latency persisted with both drugs ($P = 0.01$), but there was little evidence of any other effect with diazepam, though with fosazepam there was a persistent depression of stage 1 ($P = 0.01$) and stage 4 ($P = 0.05$) sleep.

It is suggested that diazepam at 5 mg may offer some advantages as a hypnotic for occasional use by healthy persons. Sleep onset latency and awakenings are reduced without change in the overall sleep architecture or prolongation of the sleeping time. On the other hand the effects of fosazepam (60-80 mg) are more pronounced, though whether the changes in sleep patterns are dose-dependent or specific to the drug is not clear. The prolonged total sleep time suggests that a lower dose range may have comparable effects with 5-10 mg diazepam.

References

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