DARVON® AND THE EEG

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Dextropropoxyphene hydrochloride (Darvon®) was synthesized in 1953 (Pohland and Sullivan 1953). Its analgesic effects have been compared to codeine (Gruber et al. 1956; Gruber 1957; Cass and Frederik 1963; Marrs et al. 1959; Sadove et al. 1961). Propoxyphene in overdosage is known to have central nervous system effects as manifested by stupor, coma, respiratory depression and convulsions (Cann and Verhulst 1960; Hyatt 1962; Frasier et al. 1963; Storts 1963; Swarts 1964; Cawood and Thirkettle 1966; Karliner 1967). The purpose of this study was to evaluate the effects of Darvon on the EEG of normal subjects.

MATERIAL AND METHODS

Eighty healthy male volunteers 24–34 years of age (average: 26.5, median: 25.5) were used. They were instructed to abstain from alcohol and medications for a period of 5 days prior to the study.

All records were obtained with a 16-channel Grass electroencephalograph and standard international electrode placement. Each tracing included 80 sec of each of 7 standard runs, 180 sec of hyperventilation with 100 sec post-hyperventilation, and photic stimulation at varying frequencies. Each subject served as his own control. After the control recording each subject was given Darvon 65 mg or a similar appearing placebo in amounts described below. The subjects were divided into two groups.

Group I (30 subjects). After the control record was obtained, each volunteer received 20 capsules to be taken every 6 h for 5 consecutive days, the last dose being scheduled 2 h before the second record. Twenty subjects were given active drug and ten were given placebo.

Group II (50 subjects, all fasting for at least 4 h). After the control record, two 65 mg capsules of Darvon (25 subjects) or placebo (25 subjects) were administered and the records were repeated 45 min later.

Control and test recordings were interpreted simultaneously and were compared without knowledge as to which record was the control or which subject had received active drug or placebo.

Chi-square analysis of group I shows $\chi^2 = 0.1$ and $P = 0.95$.

Group II (acute study)

A. Twenty-one record pairs (8 with placebo, 13 with active drug) were considered to be unchanged.

B. Twenty-one record pairs (13 with placebo, 8 with active drug) were considered to have developed changes. Two records (both placebo) showed increased amounts of low voltage fast activity.

C. Eight record pairs (4 with placebo, 4 with active drug) were “improved” in relation to the first one.

Chi-square analysis of group II reveals $\chi^2 = 0.24$ and $P = 0.90$.

CONCLUSIONS

Our impression that propoxyphene increases the amount of low voltage fast activity in the EEG of normal given pair. Minor changes (increased amounts of low voltage fast activity or, more frequently, a more prompt and prolonged response to hyperventilation) were occasionally noted. When these minor changes were greater in the second tracing than they were in the first, the second tracing was considered “worse”. When the minor changes were greater in the first tracing than they were in the second, the second tracing was considered “improved”.

RESULTS

Group I (chronic study)

A. There were 13 record pairs (4 with placebo, 9 with active drug) showing no change between first and second recordings. No significant difference was noted between those subjects taking drug and those taking placebo (expected ratio 8.7:4.3; observed 9:4).

B. There were 11 record pairs (3 with placebo, 8 with active drug) which showed changes in the second record when compared to the control. The most common changes would consist in a more prompt and longer response to hyperventilation. The expected ratio of placebo to drug subjects in a sample of 11 is 3.7:7.3. The observed ratio was 8:3. Only two record pairs (one on drug, the other on placebo) showed increased amounts of low voltage fast activity.

C. There were 6 record pairs (3 with placebo, 3 with drug) in which the second record could be considered as “improved” in relation to the first one.

Chi-square analysis of group I shows $\chi^2 = 0.1$ and $P = 0.95$.

D. There were 6 record pairs (3 with placebo, 3 with drug) in which the second record could be considered as “improved” in relation to the first one.

Chi-square analysis of group II reveals $\chi^2 = 0.24$ and $P = 0.90$.

subjects has not been confirmed in this study. Administration in both acute and chronic studies failed to reveal any significant EEG effect which might have been attributed to the presence of drug.

SUMMARY

Eighty normal male volunteers were employed in an acute and chronic double blind study of the effects on the EEG of dextropropoxyphene hydrochloride (Darvon®) and a similar appearing placebo. Each subject served as his own control.

Dextropropoxyphene produced no statistically significant change in the EEG of normal subjects.

RÉSUMÉ

EEG ET DARVON®

Quatre-vingts sujets volontaires normaux de sexe masculin ont servi à une double étude “à l’aveugle” des effets sur l’EEG de l’hydrochloride dextropropoxyphène (Darvon®) et d’un placebo de même apparence. Chaque sujet a constitué son propre contrôle.

Le dextropropoxphène ne provoque aucune modification statistiquement significative de l’EEG de sujets normaux.

REFERENCES


