

PREVENTION OF AIRSICKNESS WITH MEPROBAMATE

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While the principal nervous pathways by which vestibular stimulation produces vomiting have been worked out (15, 16), the mechanisms and sites of action of drugs effective in motion sickness are unknown. These drugs, without notable exception, are either belladonna alkaloids or antihistamines with central parasympatholytic properties (2, 4, 5, 8). Despite the probable role of psychologic factors in motion sickness, ataractic drugs tested under controlled conditions have been of little value (9, 11-14). Since the tranquilizers tested thus far have all been of the autonomic type (1), we considered it of interest to examine meprobamate, a mild tranquilizer in wide use, which is inactive at the autonomic level.

METHODS

Four hundred and forty-one unselected airmen from 17 to 20 years old, with little or no flying experience, were tested in 16 flights in C-54 aircraft. Twelve to 32 volunteers, divided into 3 or 4 treatment groups, participated in each flight. Each group received either a placebo, meclizine (50 mg.), meprobamate (400 mg.), or a combination of meclizine (50 mg.) and meprobamate (400 mg.). Meclizine is a motion sickness preventive of proved effectiveness (3, 5, 6, 9, 12). The drugs were administered in identical opaque capsules 15 minutes before the noon meal (standard Air Force dining hall diet), about 2 hours before takeoff. Subjects in each treatment group were evenly distributed throughout the passenger compartment in varying order. After takeoff, there was a 60-minute period of straight and level flight. During this time all subjects appeared well. One hour after takeoff simulated turbulence was begun, con-

sisting of exaggerated pitching, yawing, rolling, turning, ascent, and descent of the aircraft. These maneuvers were continued from 10 to 25 minutes until approximately 50 percent of the placebo group had vomited. The experiment was then terminated, and landing was made within 15 to 45 minutes. Vomiting was the only accepted criterion of motion sickness.

RESULTS

Results are shown in table I. Only three treatment groups were studied in the first two series of flights; subsequently, all four groups were included. The average percent vomiting in each treatment group for all three series of flights was placebo, 46 percent; meprobamate, 26 percent; meclizine, 25 percent; and meclizine-meprobamate mixture, 24 percent. Using the sign test, each drug or drug combination was compared with the placebo and found to be significantly more effective ($P < .01$). By the same test, there was no difference in effectiveness among the three drug groups. Our results indicate that meprobamate affords significant protection against airsickness, equal to that of meclizine, and that a combination of the two drugs is no better than either drug alone.

UNTOWARD REACTIONS

No important drug side effects other than sedation were noted, and this was not critically evaluated. Acute aerotitis media occurred in 6 subjects, all vomiters, but they were easily relieved by use of the Politzer bag. Two placebo-treated subjects who vomited developed severe hyperventilation which led to tetany. Neither subject would tolerate breathing into a bag, but both responded to intravenous calcium gluconate.

TABLE I

Comparison of 4 treatments in the prophylaxis of airsickness

Flight	Number of subjects	Number in each treatment group	Number (and percent) vomiting in each treatment group			
			Placebo	Meprobamate (400 mg.)	Meclizine (50 mg.)	Meprobamate (400 mg.) and meclizine (50 mg.)
1	24	8	3	Not given	0	2
2	30	10	5	Not given	3	1
(Total)	54	18 (100%)	8 (44%)	—	3 (17%)	3 (17%)
3	12	4	3	1	0	Not given
4	30	10	6	3	5	Not given
5	30	10	4	4	2	Not given
6	27	9	4	1	2	Not given
(Total)	99	33 (100%)	17 (52%)	9 (27%)	10 (30%)	—
7	32	8	5	2	2	2
8	32	8	4	3	2	3
9	32	8	4	2	1	3
10	32	8	3	2	5	3
11	32	8	3	4	2	1
12	32	8	3	2	3	5
13	32	8	3	1	0	0
14	24	6	3	1	1	1
15	24	6	2	1	1	0
16	16	4	2	0	1	1
(Total)	288	72 (100%)	32 (44%)	18 (25%)	18 (25%)	19 (26%)
(Weighted mean percent vomiting in all flights)			46%	26%	25%	24%

DISCUSSION

Meprobamate is a relatively simple compound derived from a substituted propanediol. It differs distinctly from other recognized tranquilizers such as the phenothiazines, the *Rauwolfia* alkaloids, and the diphenylmethane derivatives (with which meclizine is closely related). Among these differences are depression of multineuronal reflexes with muscle relaxation, taming of monkeys and other animals without loss of conditional reflexes, a strong anticonvulsant effect, and a lack of autonomic and antihistaminic effects (1). Initial enthusiasm for meprobamate has waned, and some authors feel that it offers little more than phenobarbital in the treatment of anxiety states (7). It is surprising that meprobamate alone is so effective in the prophylaxis of motion sickness. Since it is not additive to meclizine, one might hazard a guess that it acts upon the same pathway as do meclizine and similar compounds, possibly through its depressant action on polysynaptic neurons. On the other hand, the exposure of

individuals who have had little previous flying experience to sudden, violent motion of short duration may provide a situation where tranquilization is uniquely effective. It would be of interest to evaluate mephenesin under similar conditions since this drug resembles meprobamate chemically and pharmacologically, but has only a slight tranquilizing action.

Whether meprobamate can be considered a useful drug in motion sickness prophylaxis is another question. Without evidence to the contrary, it is no less contraindicated in flying and combat personnel than are any of the standard drugs, and it may possibly be even more dangerous (10). It may be useful, however, in the prevention of airsickness in passengers since the drug is noted for its low level of toxicity (7). In this respect meprobamate is probably safer than either the phenothiazines or the piperazines for administration to large numbers of unselected passengers, although caution is required when alcohol is being used (17). Whether meprobamate is effective against prolonged exposure to motion and

whether it prevents motion sickness in individuals who are taking it regularly are questions that deserve inquiry before this drug is accepted as a motion sickness preventive.

SUMMARY

Meprobamate, a mild tranquilizer, was tested alone and with meclizine as an air-

sickness preventive in a study involving 441 volunteers. Meprobamate was found to be as effective as meclizine, but a combination of the two drugs was no better than either drug alone.

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