CIRCULATORY RESPONSE TO TILT WITH SOME ANTI-EMETIC AND SEDATIVE DRUGS*

ALLEN B. DOBKIN, M.D.,† AND V. GUY CRISWICK‡

THE CIRCULATORY RESPONSE to tilt by normal healthy male subjects has been studied and compared in the large group of commonly used phenothiazine derivatives and with several narcotic analgesic drugs. With each of these drugs the dose selected for the study was within the therapeutic range of its most desirable action.[1,2] Several anti-emetics and sedative drugs are now being used or tested widely, although no specific comparative studies have been made of their effect on the human circulation. It was felt that such comparative data would be useful when selecting among the wide variety of premedicant drugs, and would also alert the anaesthetist when his patient was already receiving such medication for other reasons. The following report describes the comparative effect of the intravenous administration of trimethobenzamide, trimeprazine, diphenhydramine, dimenhydrinate, cyclizine, methaminodiazepoxide, and haloperidol on the pulse rate and blood pressure before and after 60° head-up tilt.

METHOD

Serial tests were done at intervals on eight healthy male subjects who were all between 20 and 30 years of age and weighed between 145 and 190 lb. The dose selected for each drug was within the optimum therapeutic range and was administered intravenously. The technique employed in studying these drugs was the same as reported previously.[1,2] Side-effects observed were annotated during and immediately after each experiment and every subject was requested to report on any discomfort or unusual symptoms during the 24–36 hours after each test.

RESULTS

The mean and standard deviation of the blood pressure and pulse rate at each time interval during each drug test was computed for the eight subjects and is shown in the Figures 1–7. Figure 8 shows the mean blood pressure and pulse rate during the periods in which the subjects were in the supine position and during 60° head-up tilt before and after each drug test.

All of the drugs caused a very slight decrease in the blood pressure shortly after administration without a consistent alternation in the pulse rate. The normal circulatory response to tilt was not impaired in the subjects after any

*From the Department of Anaesthesia, University of Saskatchewan College of Medicine and University Hospital, Saskatoon, Sask.

†Present address: Department of Anesthesiology, University Hospital, Upstate Medical Center, Syracuse, New York.

‡Medical Student Research Assistant.

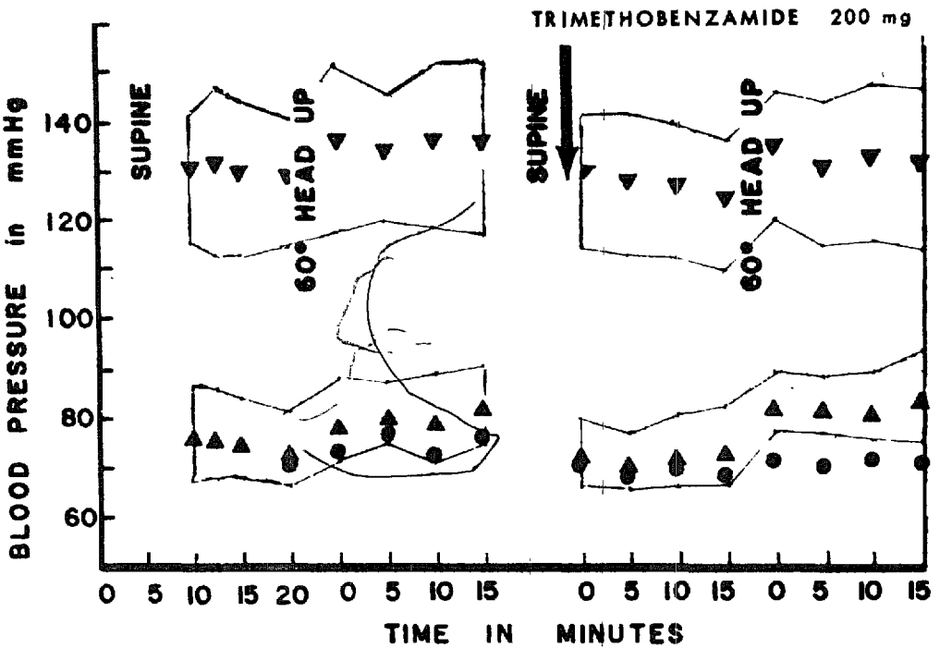

FIGURE 1. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with trimethobenzamide 200 mg. (Tigan®). One standard deviation for systolic and diastolic blood pressure is represented by solid lines.

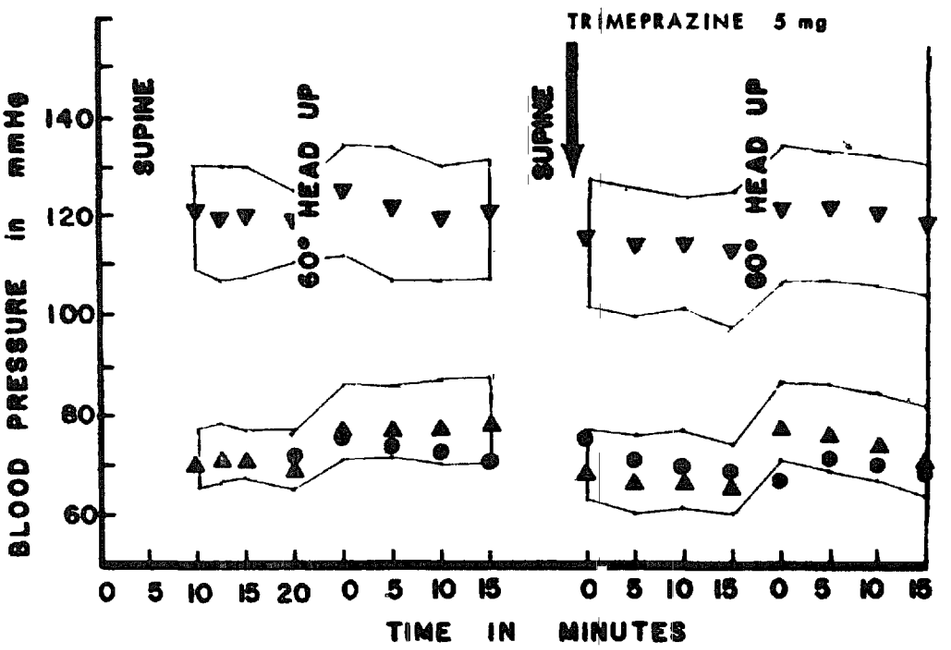

FIGURE 2. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with trimeprazine 5 mg. (Panectyl®). One standard deviation for systolic and diastolic blood pressures is represented by solid lines.

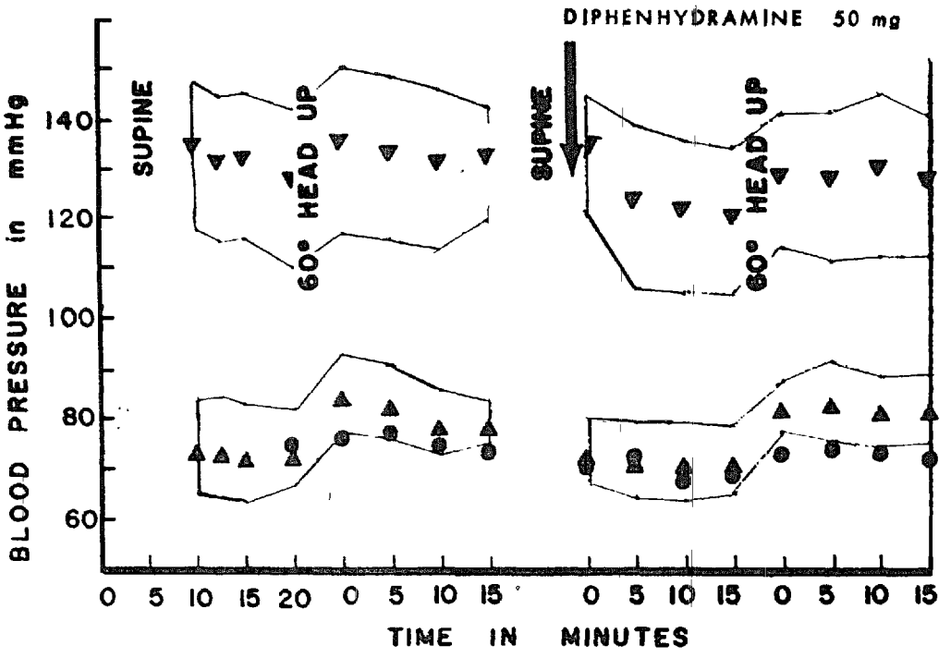

FIGURE 3. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with diphenhydramine 50 mg. (Benadryl®). One standard deviation for systolic and diastolic blood pressure is represented by solid lines.

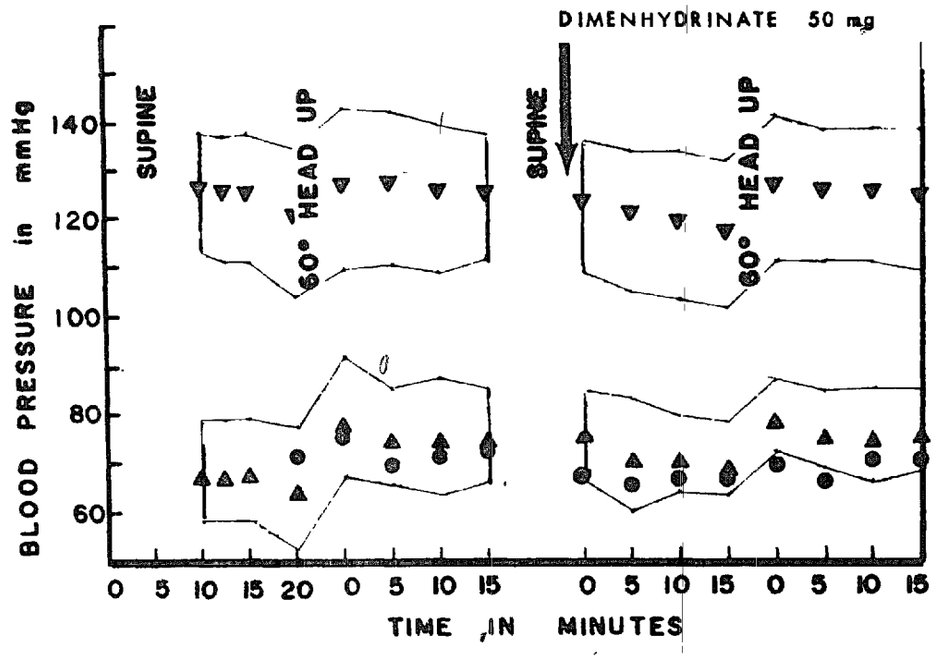

FIGURE 4. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with dimenhydrinate 50 mg. (Gravol®, Dramamine®). One standard deviation for systolic and diastolic blood pressure is represented by solid lines.

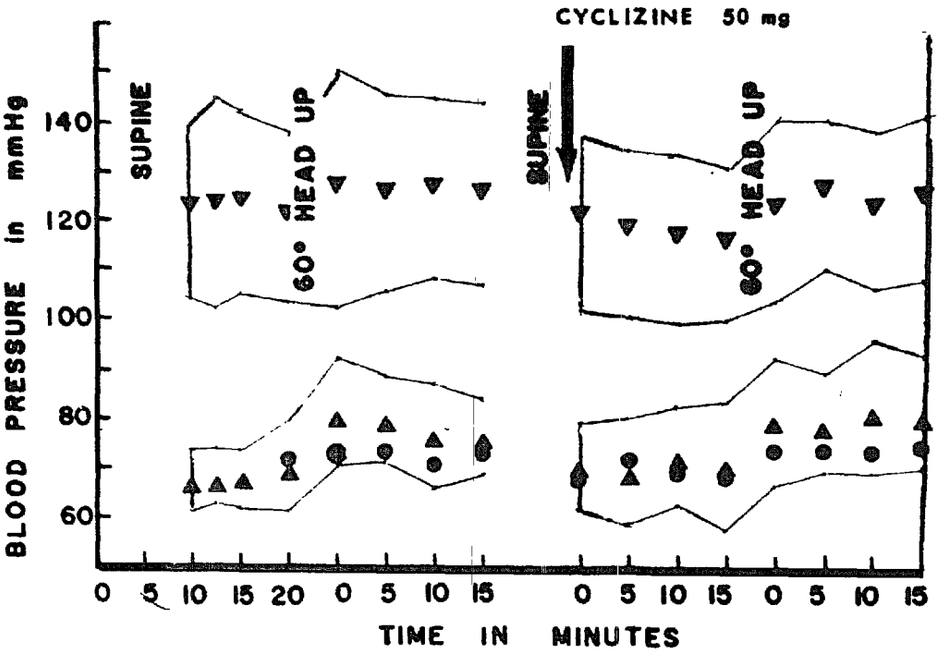

FIGURE 5. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with cyclizine 50 mg. (Marzine®, Marezine®). One standard deviation for systolic and diastolic blood pressure is represented by solid lines.

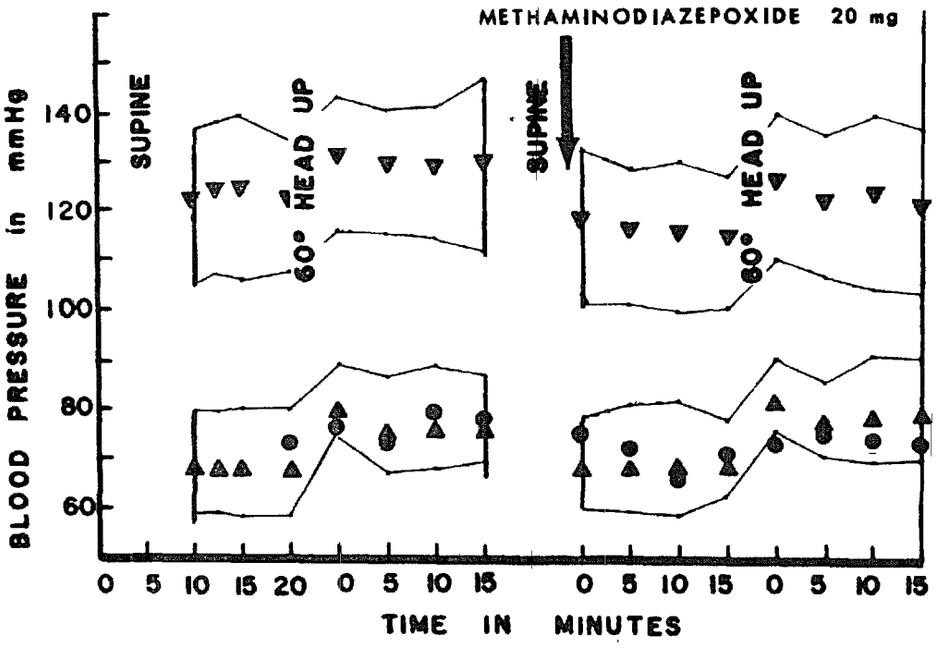

FIGURE 6. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with methaminodiazepoxide 20 mg. (Librium®). One standard deviation for systolic and diastolic blood pressure is represented by solid lines.

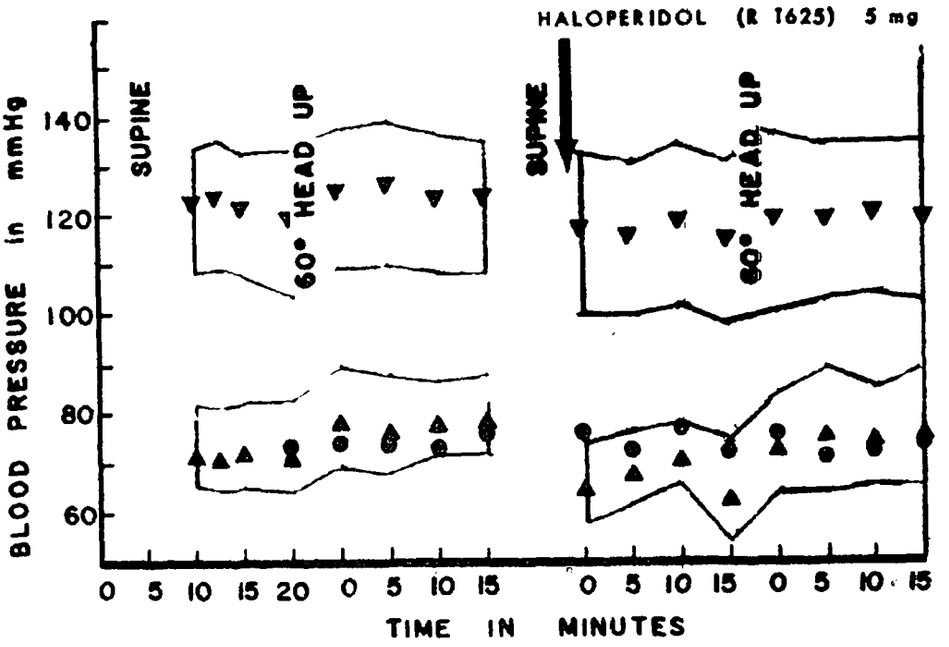

FIGURE 7. Blood pressure (systolic ▼, diastolic ▲) and pulse rate ● during test with haloperidol 5 mg. (R 1625). One standard deviation for systolic and diastolic blood pressure is represented by solid lines.

of the drugs. Aside from varying degrees of drowsiness, which became apparent after each of the drugs except trimethobenzamide, no undesirable side-effects were observed, except with haloperidol which caused a variety of neuromuscular disturbances affecting the face and neck. This undesirable response to haloperidol usually did not appear for several hours and was delayed for almost 24 hours in three subjects.

DISCUSSION

There was less tendency to hypotension with a full therapeutic dose of each of the drugs tested in this report than was seen with the phenothiazine derivatives.[1] The circulatory response was similar to that seen during similar tests with narcotic analgesics.[2] In some of the subjects it appeared as if the drugs that produced more drowsiness also caused the greater tendency to a lowering of the systolic blood pressure, but when the data was examined closely, this was not in fact the case. Trimethobenzamide did not cause any subjective or objective effect, yet caused a similar change in the blood pressure and pulse rate to dimenhydrinate, which caused moderate drowsiness and a tired feeling. Similarly, trimeprazine, diphenhydramine, and cyclizine caused marked drowsiness and tiredness, and had virtually the same circulatory effect as methaminodiazepoxide and haloperidol, both of which only caused a pleasant relaxed feeling, without subjective drowsiness or tiredness. The antisialogogue effect of several of the above drugs were previously studied and the varying degrees of drowsy response were also observed for corresponding dosages, so that this effect is quite consistent.[3]

MEAN BLOOD PRESSURE & PULSE RATE IN SUPINE & 60° HEAD UP TILT BEFORE & AFTER ANTIEMETICS & SEDATIVES

DRUGS & DOSE	mgm.		BEFORE DRUG SUPINE (A)	BEFORE DRUG TILT (A)	AFTER DRUG SUPINE (B)	AFTER DRUG TILT (B)	CHANGE SUPINE (A TO B)	CHANGE TILT (A to B)
Trimethobenzamide	200	BP	128/74 ± 15/9	134/78 ± 16/8	125/72 ± 14/7	130/82 ± 14/7	-3/-2	-4/+4
TIGAN		P	70 ± 8	73 ± 7	68 ± 7	70 ± 8	-2	-3
Trimeprazine	5	BP	118/71 ± 10/6	120/78 ± 8/7	113/68 ± 13/8	119/76 ± 13/9	-5/-3	-1/-2
PANECTYL		P	71 ± 7	73 ± 7	70 ± 10	70 ± 7	-1	-3
Diphenhydramine	50	BP	130/74 ± 14/9	132/82 ± 16/8	124/72 ± 15/7	127/82 ± 14/7	-6/-2	-5/0
BENADRYL		P	74 ± 6	75 ± 8	71 ± 7	72 ± 9	-3	-3
Dimenhydrinate	50	BP	122/66 ± 13/11	124/75 ± 15/11	118/71 ± 15/9	123/75 ± 14/8	-4/+5	-1/0
GRAVOL;DRAMAMINE		P	70 ± 7	71 ± 8	65 ± 7	68 ± 7	-5	-3
Cyclizine	50	BP	122/68 ± 19/7	126/78 ± 20/9	117/70 ± 17/11	123/80 ± 16/8	-5/+2	-3/+2
MARZINE; MAREZINE		P	71 ± 8	72 ± 8	69 ± 7	73 ± 7	-2	+1
Methaminodiazepoxide	20	BP	122/69 ± 15/11	129/78 ± 14/9	115/69 ± 14/10	124/80 ± 16/9	-7/0	-5/+2
LIBRIUM		P	73 ± 7	76 ± 9	74 ± 9	74 ± 8	+1	-2
Haloperidol	5	BP	120/73 ± 13/8	123/79 ± 14/9	114/69 ± 16/8	117/74 ± 17/11	-6/-4	-6/-5
R 1625		P	73 ± 9	74 ± 12	73 ± 10	72 ± 9	0	-2

FIGURE 8

Summary and Conclusions

The circulatory response in the supine position and in the 60° head-up tilt was compared in eight healthy male subjects with a therapeutic dose of trimethobenzamide, trimeprazine, diphenhydramine, dimenhydrinate, cyclizine, methaminodiazepoxide, and haloperidol. None of these drugs caused a significant alteration in the pulse rate or blood pressure, even in the head-up tilt position. Aside from drowsiness, none of the drugs except haloperidol caused undesirable side-effects.

Acknowledgment

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Résumé

Nous avons comparé chez huit sujets mâles en santé, la réponse circulatoire à une élévation de la tête de 60°, après une dose thérapeutique de triméthobenzamide, de triméprazine, de diphenhydramide, de cyclizine, de méthaminodiazepoxide et de halopéridol. Aucun de ces médicaments n'a causé de changement important de la vitesse du pouls ou de la tension artérielle. Si l'on excepte les étourdissements, aucun de ces médicaments, à part l'halopéridol, n'a causé d'effets secondaires indésirables.

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