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EFFECT OF MULTERGAN
ON VENTILATORY CAPACITIES IN PATIENTS
WITH GENERALIZED AIRWAYS
OBSTRUCTION

By

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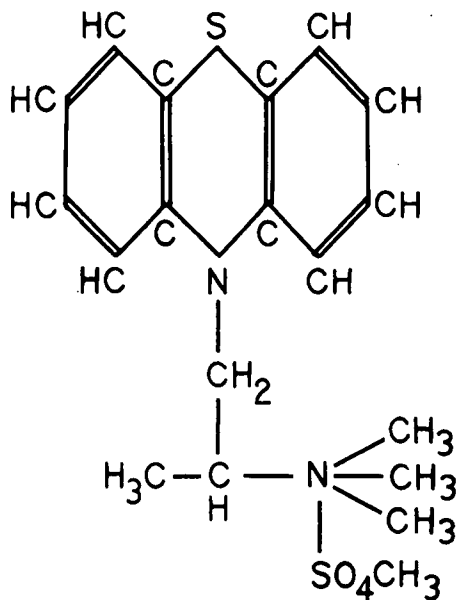
The therapeutic arsenal used against reversible airways obstruction has consisted of adrenergic substances, theophyllamine and cortico-steroids until recently. Antihistamines and anti-acetylcholinergic substances have long been considered as less useful in the treatment of airways obstruction. During the last decade, however, several new drugs with antihistaminic-anticholinergic properties have been found to be very valuable in this respect (Multergan, Banthine, Antallergan, Antrenyl) (3). One of the best of them seems to be Multergan¹ (β -[N-phenothiazinyl] isopropyl trimethylammonium methyl sulphate), which is used extensively in, for example, Holland (7). The drug is a strong antihistamine with a pronounced anticholinergic action, giving a good protection against histamin- and acetylcholine-induced airways constriction. Even the effect of antigen-antibody reactions is blocked. It is a ganglio-blocking agent with antiemetic and anti-secretoric actions, with a decrease in the capillary permeability (4).

At this laboratory Isoprenaline aerosol is usually given to reveal a reversible component of airways obstruction. In order

¹ Synthesized by Rhône-Poulenc, Paris, who kindly supplied the investigator with Multergan for this study.

MULTERGAN

β -(-N-phenothiazinyl)-isopropyl
trimethylammonium methyl sulphate



to evaluate the effect of Multergan, it was therefore compared to the effect of two inhalations of Isoprenaline Medihaler.

MATERIAL

Twelve patients with chronic generalized airways obstruction were studied. The group consisted of four females and eight males with an average age of 57 years (42-73).

METHOD AND PROCEDURE

The ventilatory effect was studied with dynamic spirometry. The spirometers used were built according to *Bernstein et al.* (1). After instructions and training

the patients performed 4-5 forced vital capacities 1-2 minutes apart. Four or five measurements with Wright's Peak Flow meter (12) were made between the spiograms. Later either 50 mg. Multergan were injected intramuscularly or two deep inhalations of Isoprenaline Sulfate-aerosol (0.12 mg.) were given about half a minute apart. Thirty minutes after injection of Multergan and immediately after inhalation of Isoprenaline, a new series of spiograms and peak flow measurements was made. The order of tests was varied in a random way such that 6 patients were studied on the first day with Multergan and on the second day with Isoprenaline; the rest were tested in the opposite order. Two days were allowed to elapse between the tests. No other drugs were given during this time and the tests were performed at the same time on the two days to prevent changes in basal volumes due to differences in bronchial reactivity (11).

CALCULATION AND STATISTICS

The forced expiratory volume in one second ($FEV_{1.0}$), the forced vital capacity (FVC) and the

$$\frac{FEV_{1.0} \times 100}{FVC}$$

(Called FEV%) were calculated from the spiograms (6). The mean values of the three largest volumes (ATPS) before and after the action of the drugs were calculated. The pre-drug values were related to normal values obtained in Göteborg (2).

The figures of the individual's per cent increase after Multergan were paired to corresponding values after Isoprenaline inhalation. The difference was tested by the "t-test" (10). If $P < 0.05$, the difference was considered to be significant. Even with only 12 patients tested, the significance level was reached.

RESULTS

In the table it is shown that the $FEV_{1.0}$ and the PEF were significantly larger 30 minutes after injection of 50 mg. Multergan than after two inhalations of Isoprenaline ($P < 0.025$). The average basic values in the two tests were the same regarding all parameters studied.

After Multergan four of the twelve patients felt some dry-

TABLE I
Effect of Isoprenaline and Multergan on Ventilatory Capacities in Twelve Patients with Airways Obstruction.

Subj.	Sex	Age	Isoprenaline					Multergan				
			Control values			After inhalation of 0.12 mg I		Control values			30 min. after im. inj of 50 mg M	
			FEV _{1.0}	FVC	PEF L/min.	FEV _{1.0}	FVC	PEF	FEV _{1.0}	FVC	PEF	PEF
			% pred.					Change in %	% pred.		Change in %	
E. B.	M	54	25	51	107	+12	+19	+37.	28	55	+11	+30
G. G.	M	49	59	93	420	+8	+2	+6	56	88	+23	+19
L. A.	F	58	66	86	218	+25	+18	+32	65	87	+33	+47
H. W.	F	55	30	53	97	+12	+21	—	35	70	+20	+16
H. L.	M	55	23	53	128	+15	+18	+17	30	51	— 7	+3
B. N.	F	42	28	45	140	+35	+23	+34	29	43	+58	+51
M. A.	M	65	40	64	173	+11	+1	+18	35	55	+33	+24
T. J.	M	63	51	85	192	+12	+9	+3	49	80	+21	+27
O. G.	M	48	73	81	416	+9	+4	+9	66	79	+18	+24
G. A.	M	69	53	74	193	+19	+8	+10	64	76	+22	+26
J. S.	M	73	33	49	112	+43	+31	+56	30	52	+62	+59
G. S.	F	54	32	53	97	+31	+16	+26	35	55	+63	+88
Mean values		57	43	66	191	+19*	+14	+21°	44	66	+30*	+34°

* ° Sign. difference $P < 0.025$.

ness of the mouth, one female was a little dizzy. In six subjects the average heart rate before injection of Multergan was 78/minute; 30 minutes after, it had risen to 110/minute.

DISCUSSION

Pharmacological tests of the acute effect of the drug were considered better than evaluation of long-term treatment when subjects with an often-unstable airways obstruction were studied. The study shows that the acute effect of 50 mg. Multergan on airways constriction is better than that from inhalation of Isoprenaline. As indicators of a change in obstruction, the FEV_{1.0} and FVC and the peak flow values were used. The FEV% was omitted as being of less value in intraindividual comparisons of drug effect.

In an earlier study it was shown that two inhalations of Isoprenaline gave the same effect on ventilatory parameters as multiple-breath inhalation of racemic adrenaline (9). This is in accordance with findings by Dautrebande, who stated that no further increase of airways dilation occurs after the first couple of breaths from a sympathicomimetic aerosol (5).

Booy-Noord *et al.* have compared 25 mg. Multergan and several other drugs with the effect on the vital capacity of 0.3 ml. Epinephrine given subcutaneously (3). Multergan was found to be superior to Epinephrine in this relatively small dose. Orie considers adrenergic drugs to be more efficient in young asthma patients, while the anticholinergic drugs are recommended in chronic airways obstruction (8). In the present small material most patients belong to the latter category.

SUMMARY

In twelve patients with generalized airways obstruction the ventilatory effect of 50 mg. Multergan given intramuscularly was compared within three days to the effect of two inhalations (0.12 mg.) of Isoprenaline-sulfate. The tests were made in a random way so that six of the patients started with Multergan. Series of forced expirograms and peak flow measure-

ments were performed before and 30 minutes after injection of Multergan, and before and immediately after inhalations of Isoprenaline. The pre-drug values were the same. After injection of Multergan the forced one-second volume and the peak expiratory flow increased significantly more than after Isoprenaline inhalation.

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