THE ANTISIALOGOGUE EFFECT OF HYDROXYZINE,
THIETHYLPERAZINE, AND N'-p-CHLORO-BENZYLHYDRYL-
N'-METHYL HOMOPIPERAZINE (SA 97)*

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MANY NEW DRUGS that have been introduced for use as premedication of surgical patients have a varying amount of antisialogogue activity.¹⁻⁴ Hydroxyzine (Atarax[®], Vistaril[®]) is now being tried widely as a neurosedative, thiethylperazine (Torecan[®]) is under trial as an antiemetic, and N'-p-chloro-benzyl-hydril-N'-methyl homopiperazine (SA 97) is being tested as an antihistaminic in the treatment of a variety of allergies. The following report describes tests of these three drugs to define their antisialogogue activity in man.

METHOD

Serial tests were done on 10 healthy male subjects who were between 20 and 30 years of age and weighed between 135 and 205 lb. (mean 168 lb.). The tests were done at one to three day intervals, with a carbaminoylcholine chloride - epinephrine mixture (control), hydroxyzine 50 mg., thiethylperazine 5 mg., and SA 97 25 mg. The intravenous dose used for each drug was based on previous experience and was selected so that there would be minimal side-effects and so that it would be within the therapeutic range for their primary use.

The technique for collecting and measuring salivary secretion was the same as reported previously.¹⁻⁵ In the control test saliva was collected for 10 minutes before any drug was administered, and then for 30 minutes after the intravenous injection of the carbaminoylcholine chloride - epinephrine mixture. In the remaining tests, each drug was injected intravenously at the beginning of the experiment, and saliva was collected for 10 minutes. Then the mixture of carbaminoylcholine chloride - epinephrine was injected and saliva was collected for a further 30 minutes.

The same parotid duct that was selected initially in each subject was used throughout the series, and the volumes collected were recorded at 10-minute intervals. The saliva was removed from the surface of the parotid duct by means of a cup that was applied over the area, and it was drawn into a calibrated glass tube by means of a Stedman pump.

RESULTS

A summary of the data is shown in Table I. The mean volume of saliva collected during the 10 minutes immediately following the injection of the mixture of

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TABLE I
ANTISIALOGOGUE EFFECT OF HYDROXYZINE, THIETHYLPERAZINE, AND SA 97

Drugs	Official name	Intravenous dose, mg.	Before		After		% reduction of salivary secretion
			10 min.	30 min.	20 min.	30 min.	
Carbachol	Carbaminoylcholine chloride	0.12	6	100*	16	19	
Adrenaline (control)	Epinephrine	0.06	±5	±56	±12	±22	
Atarax,	Hydroxyzine	50	8	216	39	12	0
Vistaril	Thiethylperazine	5	±8	±118	±20	±16	
Torecan			7	201	16	19	0
SA 97	N'-p-chloro-benzylhydrol-methyl homopiperazine	25	±8	±80	±12	±29	
			6	56	3	14	44
			±7	±51	±4	±23	

*All salivary volumes were computed on the basis of this volume = 100%.

carbaminoylcholine chloride - epinephrine was taken as 100 per cent. All other volumes of saliva that were collected were then computed on this percentage basis. Standard deviations were calculated for the mean volumes of saliva secretion expressed as a per cent as noted above, with each drug, at each time interval. These were noted under each mean value in the table.

None of the drugs caused suppression of salivation during the initial 10-minute period. SA 97 caused an appreciable decrease in salivary secretion, whereas hydroxyzine and thiethylperazine caused a rather marked increase. Aside from the mild discomfort occasioned by the injection of the mixture, slight drowsiness and burning from the intravenous injection of the hydroxyzine, there were no side-effects observed during these experiments.

DISCUSSION

A large number of sedatives, antihistaminic and antiemetic drugs have now been studied in order to evaluate their effectiveness as antisialogogues, as well as their efficacy as therapeutic agents in clinical anaesthesia.⁶ Table II summarizes

TABLE II
ANTISIALOGUE EFFECT OF SOME PREMEDICANT DRUGS

Drugs	Generic name	Dose	% reduction of salivary secretion
Atropine	<i>dl</i> -Hyoscyamine	0.6	96
Bellafoline	<i>l</i> -Hyoscyamine	0.3	99
Scopolamine	<i>l</i> -Hyoscyamine	0.2	97
Antrenyl	Oxyphenonium	0.5	99
Banthine	Methantheline	5	95
Tral	Hexocyclium	1.5	98
Atarax	Hydroxyzine	50	0
Vistaril			
Benadryl	Diphenhydramine	50	57
Dramamine	Dimenhydrinate	50	59
Gravol			
Marazine	Cyclizine	50	71
Marzine			
Tigan	Trimethobenzamide	200	0
Compazine	Prochlorperazine	3	46
Stemetil			
Dartal	Thiopropazate	2.5	65
Largactil	Chlorpromazine	20	33
Thorazine			
Mornidine	Pipamazine	2.5	60
Nozinan	Levomepromazine	5	45
Pacatal	Mepazine	10	33
Panectyl	Trimeprazine	5	53
Temaril			
Permatil	Fluphenazine	1	40
Prolixin			
Trancin	Promethazine	25	93
Phenergan			
Sparine	Promazine	10	27
Stelazine	Trifluoperazine	0.5	51
Tacaryl	Methdilazine	5	37
Timovan	Prothipendyl	5	48
Torecan	Thiethylperazine	5	0
Trilafon	Perphenazine	5	35
Vesprin	Triflupromazine	5	49

the data from several series of experiments done by the same method, and indicates the wide variation in antisialogogue activity that should be expected from their use. It is important, therefore, always to use one of the reliable and potent antisialogogues along with sedatives, regardless of whether they are phenothiazines, diphenylmethanes, or one from the wide variety of antihistaminic drugs, if adequate drying of secretions is essential to a smooth anaesthetic procedure.

SUMMARY AND CONCLUSIONS

The volume of salivary secretions from the parotid duct was measured in 10 healthy male subjects in response to intravenous injection of a stimulant mixture containing carbaminoylcholine chloride and epinephrine, and serial tests were carried out to determine whether hydroxyzine, thiethylperazine, and *N'*-*p*-chloro-benzylhydriyl-*N'*-methyl homopiperazine (SA 97) have any inhibitory activity in this respect. Only SA 97 had some antisialogogue activity, whereas the other two compounds appeared rather to stimulate salivary secretions. This study again shows that most sedative drugs are unreliable as antisialogogues, and should not be used without a belladonna derivative or some other potent anticholinergic drug, if adequate drying of secretions is desirable.

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RÉSUMÉ

Chez dix sujets mâles en santé, nous avons mesuré le volume de sécrétions sortant du canal de la parotide à la suite de l'injection intraveineuse d'un mélange stimulant contenant du chlorure de carbaminoylcholine et de l'éphédrine et nous avons fait une série de tests pour préciser si l'hydroxyzine, la thiéthylperazine et la *N'*-*p*-chloro-benzylhydriyl-*N'*-méthyl homopipérazine (SA 97) possédaient un pouvoir inhibiteur sur cette glande. Le SA 97 seul a montré un pouvoir antisialogogue; les deux autres produits, au contraire, ont semblé stimuler les sécrétions. Ces résultats démontrent que l'on ne peut pas se fier à la plupart des sédatifs comme antisialogogues et que les sédatifs ne devraient pas être employés sans l'addition de dérivés de la belladone ou d'autres puissants anticholinergiques, si l'on désire tarir convenablement les sécrétions.

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