STUDIES ON BILE SECRETION

Influence of vagal stimulation and acetylcholine on the secretion of bile in dogs.

By

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Though much is known about the constituents of the bile in health and disease, the fundamental knowledge governing the secretion and regulation of the flow of bile is still far from clear. While parasympathetic stimulation normally increases the glandular secretions in general, vagal stimulation on the flow of bile has yielded varying results (Tantury and Ivy, 1938). This problem has now been studied under different physiological conditions, both by stimulation of the vagus and administration of acetylcholine, the parasympathetic mediator.

In our earlier studies, besides quantitative alteration, qualitative changes in the composition of the bile have been shown to occur during administration of adrenalin and nor-adrenalin (Ramprasad and Sirsi, 1959). Hence an analysis of the constituents of the bile has also been carried out in the present investigations.

METHOD AND MATERIAL

Dogs generously supplied by the Bangalore Corporation were used in these experiments. The methods of cannulation, collection of bile, anaesthesia used, and procedures for the estimation of bile salts, bilirubin, cholesterol and fatty acids, as also the pharmacodynamic techniques have been described in earlier papers (Ramprasad and Sirsi, 1956; 1957). The vagus was stimulated by severing the right vagal nerve between two ligatures and placing the ends on a shielded electrode through which controlled stimulation was administered from an electronic stimulator. Acetylcholine was used as acetylcholine hydrochloride salt.

The stimulations and injections were given only after the bile secretion had attained equilibrium and three successive samples during ten minute intervals were quantitatively same. In some dogs, these manipulations were carried out successively while in others the order was changed. The results given in the tables and kymographic records are those of representative experiments.

RESULTS

The effect of vagal stimulation, both peripheral and central, on haemodynamic responses and bile volume is shown in Fig. 1 and Table I and analysis of the bile constituents in Table II. The results obtained after acetylcholine administration are seen in Fig. 2 and Tables III and IV.

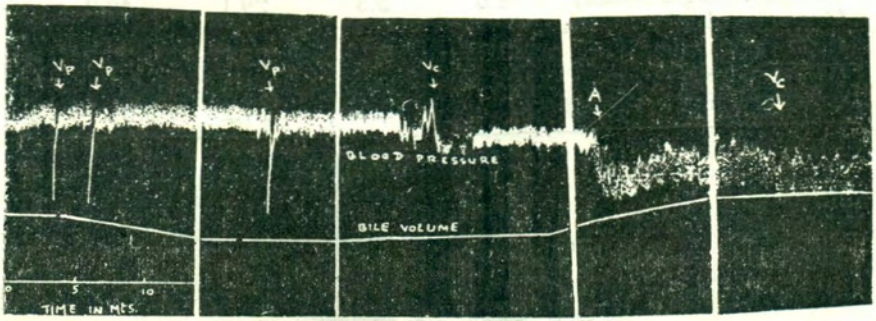


Fig. 1

Effect of vagal stimulation on blood pressure and bile secretion
Dog - male Wt. 3.75 kg. Anaesthesia: Seconal sodium. 30 mg/kg. i.p.

V_P Vagal stimulation. Peripheral end 5 secs.

V_C ,, central end 10 secs.

A Artificial respiration (after division of both vagi)

TABLE I.

Effect of vagal stimulation on bile secretion.

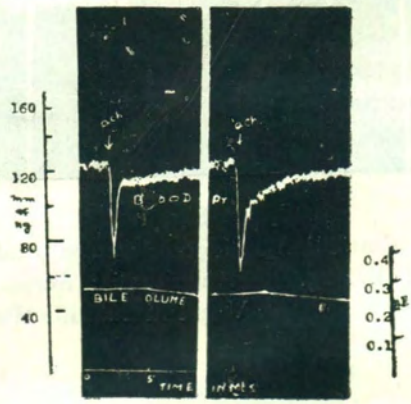
Operation	Normal	Volume of bile in ml after the stimulation of vagus nerve. Time in minutes.					
		0-10	10-20	20-30	30-40	40-50	50-60
Peripheral end stimulated (Right vagus)	0.24	0.20	0.20	0.22	0.21	0.22	0.22
Central end stimulated with other vagus intact	0.22	0.21	0.21	0.32	0.34	0.25	0.23
Artificial respiration after cuting both vagi	0.23	0.31	0.29	0.29			
Central end (Right vagus) stimulated	0.29	0.28	0.29	0.32	0.28		

TABLE II.

Analysis of bile constituents.

Weight of the dog : 4.8 kg. Seconal sodium : 30 mg/kg.

Operation	Solids g/100 ml	Bile salts g/100 ml	Bilirubin mg/100 ml	Cholesterol mg/100 ml	Fattyacids mg/100ml
Normal	8.8	5.0	34.5	39.3	540
Peripheral end stimulation (Left vagus intact)	4.6	3.3	29.1	40.2	288
Central end stimulation (Left vagus intact)	3.9	3.1	29.3	39.2	260
Artificial respiration (after severing both vagi)	2.7	2.15	31.2	39.1	160



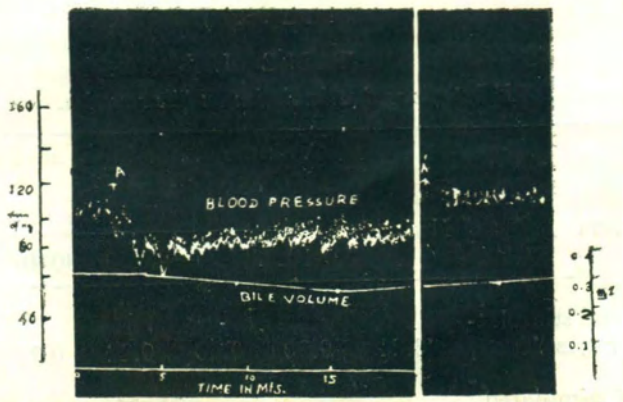


Fig. 2 Effect of acetylcholine on blood pressure and bile secretion

(a) dog—male 3.5 kg. →Seconal sodium
ach—acetylcholine 3γ/kg.
ach_1— ,, 5γ/kg.
Dog: male 4.1 kg. See. Sodium.

(b) A=acetylcholine, continuous infusion 1γ/ml at a rate of 4 ml/min.
A_1=acetylylcholine stopped after half an hour.

TABLE III.

Acetylcholine and bile volume.

Dosage	Normal ml	Volume of bile in ml after administration of Ach (in ten minutes intervals) 0-10	10-20	20-30	30-40	40-50	50-60
3γ / kg. Ach	0.24	0.18	0.16	0.20	0.22		
5γ / kg. Ach	0.22	0.18	0.20	0.22	0.22		
Continuous infusion of acetylcholine (1γ/ml) at a rate of 4 ml per minute							
Continuous infusion	0.30	0.24	0.27	0.29	0.29		

TABLE IV.

Analysis of bile constituents

Weight of the dog: 3.5 kg. Seconal sodium: 30 mg./kg.

Operation	Solids g/100ml	Bile salts g/100ml	Bilirubin mg/100 ml	Cholesterol mg/100 ml	Fatty acids mg/ 100 ml	Specific gravity
Normal	3.4	1.8	29.2	50.8	214.3	1.2
3γ / kg. Ach	2.01	1.3	26.0	53.2	160.4	1.2
5γ / kg. Ach	1.5	0.8	26.0	52.5	160	1.2
Normal (Specimen II)	1.7	0.9	22.4	54.4	186	1.2
Continuous influsion of acetylcholine (1γ/ml) at a rate of 4 ml per min.						
Weight of the dog: 4.1 kg.				Seconal sodium: 30 mg./kg.		
Normal	8.02	4.8	48.2	58.3	430	0.7
Continuous infusion	7.01	4.0	43.2	49.1	410	0.7
Normal (Specimen II)	7.2	4.3	46.6	54.2	423	0.7

Specimen II: Obtained after the bile flow had regained the normal volume.

Stimulation of the severed peripheral right vagus caused a decrease in bile secretion which persisted for more than an hour. Stimulation of the central part at this stage increased the flow of bile after an interval of twenty minutes. After the secretion had reached normal, severance of the left vagus and artificial respiration caused an immediate increase in the bile flow and even at this stage, the stimulation of the central right vagus tended to increase the volume of bile. Similar trends though to varying degreeswere noticed in other five experiments (Table I).

In spite of the volume variations, the composition of the bile tended to show an uniform decrease of the total solids, fatty acids, bile salts and pigments; cholesterol remained the same (Table II).

Acetylcholine, given in single doses or as continuous infusion, exhibited results similar to those seen after stimulation of the peripheral vagus both qualitatively and quantitatively (Tables III and IV).

DISCUSSION

Even in the absence of all nerve supply, the liver is capable of secreting bile (Brauer *et al.*, 1957). The autonomic nervous system seems to be only regulatory in nature. Our experiments on the stimulation of peripheral vagus and acetylcholine administration point to the fact that the parasympathetic nervous system is a depressor of bile secretion unlike its effect on other secretory glands of the digestive system.

Also, the view, that the vagus carries the sensory stimulatory nerves to the centre (Tanturi and Ivy, 1938) is confirmed by the increasd flow observed after central stimulation of the severed right vagus. That the general systemic blood presure changes do not exercise any specific effect can be inferred from the fact that while fall in blood pressure caused by acetylcholine or vagal stimulation diminished the flow, the fall in pressure after artifical respiration and bilateral vagotomy increased the flow of bile. The role of anoxaemia in these findings needs elucidation.

SUMMARY

The influence of parasympathetic nervous system, on the secretion of bile has been studied by vagal stimulation and acetylcholine administration, under varying physiological conditions. The quantitative and qualitative responses noticed are reported in this communication.

The stimulation of the peripheral end of the cut right vagus caused a decrease in bile secretion which persisted for about an hour. The stimulation of the central end, with the left vagus intact increased the flow of bile. After severance of both vagi, artificial respiration by itself caused an increased

flow. The qualitative changes noticed in all these cases were a decrease in the content of total solids, fatty acids, bile salts and pigments.

The nature of changes seen after the administration of acetylcholine, in single doses and during continuous infusion were similar to those observed after stimulation of the peripheral end of the severed vagal nerve.

The effects of some regulatory mechanisms on bile secretion are discussed.

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