

THE INFLUENCE OF "CHOLELETIC" AND "HEPATO-TONICS" UPON THE DYE-EXCRETING FUNCTION OF THE LIVER IN THE ANURIC CONDITION

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It has been demonstrated by Matsuo and Mizuta (1935)¹⁾ and Matsuda (1936)²⁾ that the liver function (detoxication, and the excretion of foreign substances, especially of the synthetic dye-stuffs) are gradually accelerated with the advance in renal failure, because the liver compensates for the lost activity of kidneys.

Recently Mizuta (1952³⁾, 1953⁴⁾) has reported a favorable effect of duodenobiliary tubage and gall bladder fistula upon the anuria in genitourinary diseases.

The purpose of this paper is to present the data of the author's comparative experiments of "choleletic" and "hepato-tonics" upon the liver function thus accelerated by the renal disturbances, and evaluate these substances as applied to these cases.

METHODS AND MATERIALS

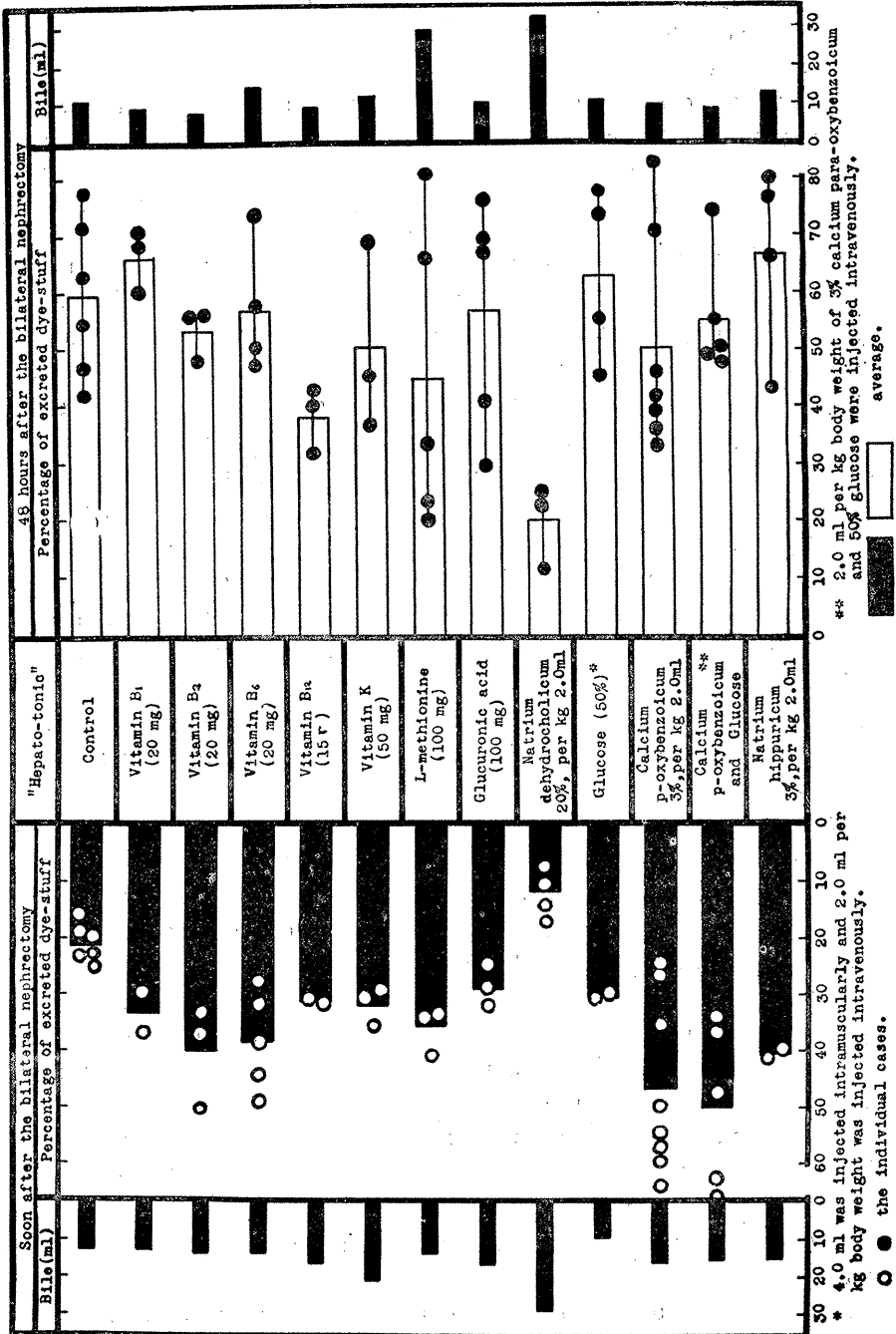
1) Biliary excretion of phenolsulfonphthalein soon after the bilateral nephrectomy: Adult rabbits weighing about 2 kg were nephrectomized bilaterally and glass canulae were inserted into their common bile ducts. Some amounts of choleletic and hepato-tonic were injected intravenously and 30 minutes thereafter 1.0 ml per kg body weight of 0.6 per cent aqueous solution of phenolsulfonphthalein, a dye-stuff which is excreted in urine under ordinary conditions, was administered through their ear-vein, and the bile was fractionatedly accumulated at 15 minute intervals for two hours. The amount of the dye-stuff excreted in the bile during the two hours after the administration was determined with Duboseq's colorimeter, and its percentage to the total amount injected was calculated.

2) Biliary excretion of phenolsulfonphthalein 48 hours after the bilateral nephrectomy (Anuric condition): The same procedures as described in 1) were utilized except that the dye was injected 48 hours after the bilateral nephrectomy when the liver displayed the most accelerated function, in case that the rabbits had been kept in fasting state²⁾.

3) The injection of "choleletic" and "hepato-tonics" to the nephrectomized rabbits: The "choleletic" and "hepato-tonics" which are listed below were injected to the rabbits which received the bilateral nephrectomy in the dose indicated in Fig. 1.

"Choleletic": Natrium dehydrocholicum.

Fig. 1. Percentage of Excreted Dye-stuff to the Total Amount Injected and Amount of Bile.



“Hepato-tonics”: Vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, l-methionine, glucuronic acid, glucose, calcium para-oxybenzoicum, natrium hippuricum.

4). The control group for the experiment consisted of nephrectomized rabbits which received the injection of 0.9 per cent saline solution (2.0 ml per kg body weight) instead of hepato-tonic.

RESULTS AND DISCUSSION

“Hepato-tonics”, which are referred to as such in the present experiment, have been highly appreciated by many authors, particularly by Inoue and Kitamura⁵⁾⁶⁾, who demonstrated the acceleration of detoxicating activity of the extirpated rabbit's liver by perfusing it with the artificial fluids containing vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, l-methionine and glucuronic acid. The hepatotonic effect of calcium para-oxybenzoicum and natrium hippuricum on the dye excretion and the detoxication has been observed by Inagaki (1937)⁷⁾ and Mizuta et al (1953)⁸⁾. Natrium dehydrocholicum has for a long time been well known for its choleletic activity.

The results which were obtained by the author are summarized in Fig. 1. From it is apparent that the liver function to excrete phenolsulfonphthalein is enhanced by all the hepato-tonics, whereas it is much suppressed by choleletic. The most marked increase in the excretion appears after the administration of calcium para-oxybenzoicum and natrium hippuricum, and somewhat less increase after the injection of vitamin B₂ and vitamin B₆. The diminution of dye excretion by choleletic (natrium dehydrocholicum) will be ascribed to the causation of a strong choleletic activity which drains the other hepatic activities.

The dye excretion rises 48 hours after the bilateral nephrectomy to a level two or three times as high as immediately thereafter, fluctuating in a considerably wide range. This phenomenon is presumably due to the appearance of “hepatotrop H”, a hepatotonic substance in the blood, which was extracted from blood in a crude state by Mizuta and Matsuura (1935)⁹⁾.

The effect of “hepato-tonics” upon a liver, the function of which is brought to an accelerated state by nephrectomy, undergoes a considerable variation. However, roughly speaking, vitamin B₁, vitamin B₂, vitamin B₆, vitamin K, glucose and natrium hippuricum exert little influence, and vitamin B₁₂, l-methionine, glucuronic acid and calcium para-oxybenzoicum cause an influence in the negative direction upon the hyperactive livers of the nephrectomized rabbits. The suppressive action of natrium dehydrocholicum on the excretion of dye-stuff is striking. Accordingly, all the hepato-tonics and choleletic mentioned above fail to stimulate further the hyperactive hepatic function which is induced by nephrectomy. For this reason it will be useless rather than helpful to prescribe “hepato-tonic” and “choleletic” to anuric patients in the hopes that the liver may compensate further for the lost function of kidneys (excretion of waste products).

That calcium para-oxybenzoicum combined with glucose elevates the lowest value for dye excretion over the level attained by calcium para-oxybenzoicum only, is suggestive of the necessity of liver glycogen to activate the calcium para-oxybenzoicum.

As for the choleletic effect upon the liver as observed 48 hours after the bilateral nephrectomy, natrium dehydrocholicum and l-methionine are among the most active, which natrium dehydrocholicum and vitamin K are most active as observed soon after the bilateral nephrectomy.

CONCLUSION

The effect of "choleletic" (natrium dehydrocholicum) and "hepato-tonics" (vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin K, l-methionine, glucuronic acid, glucose, calcium para-oxybenzoicum and natrium hippuricum) upon the liver to excrete phenolsulfonphthalein was studied in rabbits immediately and 48 hours after the bilateral nephrectomy. The results obtained are summarized as follows:

1) The excretion of the dye-stuff as observed soon after the bilateral nephrectomy is accelerated by the order given below; calcium para-oxybenzoicum, natrium hippuricum, vitamin B₂, vitamin B₆, l-methionine, vitamin B₁, vitamin K, vitamin B₁₂, glucose, glucuronic acid.

Natrium dehydrocholicum suppressed the excretory function distinctly.

2) The excretion of the dye-stuff as observed 48 hours after the bilateral nephrectomy is not accelerated further by any of the "hepato-tonics", but suppressed by natrium dehydrocholicum, vitamin B₁₂, l-methionine and calcium para-oxybenzoicum in the order given.

3) An appreciably favorable effect is obtained by using calcium para-oxybenzoicum combined with glucose rather than calcium para-oxybenzoicum only.

4) The choleletic activity of natrium dehydrocholicum appears more distinctly in the anuric state than in the ordinary urine outflow. A similar tendency is also noticed in l-methionine.

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