CHARACTERISTICS OF COMPLEX REFLEX REGULATION OF BLOOD SUGAR LEVELS IN MAN

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It was shown in a previous communication [1] that sham feeding of animals with gastrostomy and esophagogastrostomy led to a prolonged rise of blood sugar and gas exchange. This suggested a complex reflex mechanism of carbohydrate metabolism regulation. However, this fact, established on animals, required similar observations on man for its more precise definition.

The present communication deals with the study of the effect of sham feeding and of other means of introducing food on regulation of blood sugar levels in man.

Investigations were carried out at the otolaryngologic clinic of the Leningrad Medical Stomatologic Institute, directed by Professor N. A. Karpov* on patients who had been subjected to therapeutically indicated extirpation of the pharynx and sometimes of the larynx. Postoperatively the patients had an esophagostomy which disconnected the oral cavity from the stomach. These patients are fed for some time postoperatively through a stomach tube introduced into the lower aperture of the esophagus or through a fine tube introduced into the stomach by way of the lower nasal passage. This makes possible separate investigation in these patients of the effect of sham intake of carbohydrate on the blood sugar level and the effect of the same substances on the blood sugar on being introduced directly into the patient's stomach.

METHOD

Investigations were performed on 16 patients. All the patients had completely recovered from the operation by the time of the experiments, were in satisfactory condition, had an adequate appetite and moved freely about the clinic.

Observations were made in the morning, in the fasting state. The sterile dressing was removed from the esophagotomy aperture and the patient was given 500 ml warm tea sweetened with 50 g glucose. While the patient was drinking, a vessel was placed so as to collect all the liquid drunk as it escaped from the esophageal aperture. The tube and cotton-wool tampon present in the lower part of the esophagus disconnected the latter from the upper part of the esophagus and precluded any possibility of the ingested liquid gaining acess to the stomach. The total period of sham drinking usually lasted 5-6 minutes. Fasting blood sugar level was determined prior to the sham ingestion of glucose and the blood sugar examinations were repeated 5-10-20-30-45-60-90-120-180 minutes after the sham intake of glucose. Blood sugar estimations were made by the Hagedorn-Jensen method.

All the patients participating in these observations drank the sweet tea with pleasure and at the end of this sham intake spoke of the pleasant gustatory sensation experienced. The patients mentioned that the postoperative absence of feeding by mouth was trying and were very happy to experience again the partially forgotten pleasure associated with normal eating.

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RESULTS

The results of the observations are presented as mean data in Fig. 1, a, and show that sham ingestion by the patients of 10% solution of glucose is followed within 5 minutes by a rise in blood sugar level. The blood sugar content continues to rise, reaching a maximum usually 20 minutes after the sham feeding. This raised level is maintained for 10-30 minutes, after which a gradual decline begins. The blood sugar content remains above the initial level for the next 2 hours, although in isolated cases there are deviations from the mean value.

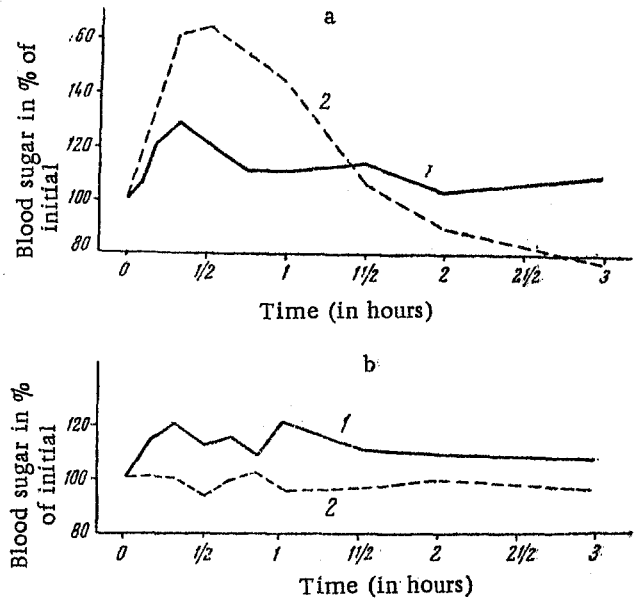

Fig. 1. Effect of sham feeding (—) and introduction through the esophagostomy (— — —) of solutions on blood sugar content in patients. a) 500 ml 10% glucose solution; b) 500 ml 0.01% solution of saccharin.

Sham glucose ingestion thus gives rise to hyperglycemia, despite the fact that the patient can see that all the ingested fluid is completely removed; this hyperglycemia persists throughout the 3 hours of observation. This suggests that the ingestion of glucose exerts a complex reflex action on blood sugar content in man. The observed rise in blood sugar under these circumstances is, of course, connected with specific stimulation of oral receptors which leads to increase in blood sugar content [2].

When the procedure is repeated (such investigations were carried out on 3 patients) the hyperglycemic effect is diminished (Fig. 2, a), i.e., extinction of the natural conditioned food reflex takes place.

The effect of glucose solution, introduced directly into the stomach, on blood sugar content was studied in 11 patients under observation. The patients were unaware of the nature of the fluid being introduced into the stomach and were under the impression that it was water. The results of these investigations, presented in Fig. 1, a, show that introduction of glucose solution through the esophagostomy into the stomach also causes a rise of blood sugar which begins in most of the patients in question 10 minutes after introduction and reaches a maximum within 30 minutes. The blood sugar level returns to the initial within 1 hour and drops below that by the end of the period of observation. The period of hyperglycemia following introduction of glucose through the esophagostomy into the stomach thus lasts $1^1/_2$ hours, dropping to an average of 21.4% below the initial blood sugar level within the next $1^1/_2$ hours. The blood sugar content curve is diphasic following introduction of glucose solution directly into the stomach: the first phase is hyperglycemic and is associated with absorption and passage of glucose into the blood, the second is hypoglycemic and is, evidently, associated with increased absorption of sugar by tissues and its combustion, or perhaps with increased secretion of insulin. Thus in summary, the blood sugar curve is monophasic in sham feeding with glucose and diphasic when glucose solution is introduced through the esophagostomy.

The work of I. S. Kanfor and R. P. Olnianskaia [2] on the role of oral receptors in the regulation of carbohydrate metabolism demonstrated the effect of ingestion of saccharin on blood sugar content and on gas exchange. These observations were made on healthy subjects. It was important to re-examine this question on patients, making a study of the effect of saccharin intake both in sham feeding and in direct introduction through the esophagostomy.

These experiments were performed on 5 patients. Saccharin was given in 1:10,000 solution in amounts of 500 ml. Sham ingestion was accompanied by a sensation of sweet taste, whereas when saccharin was introduced directly into the stomach through the tube, the patient was unaware of the composition of the fluid.

The results of these observations show that sham drinking of saccharin solution produces increased blood sugar content throughout the whole 3-hour period of observation. Introduction of saccharin solution through

the esophagostomy directly into the stomach produced no rise in blood sugar content. Comparison of blood sugar curves in sham ingestion of saccharin solution and in its introduction through the esophagostomy is clearly illustrated in Fig. 2, b.

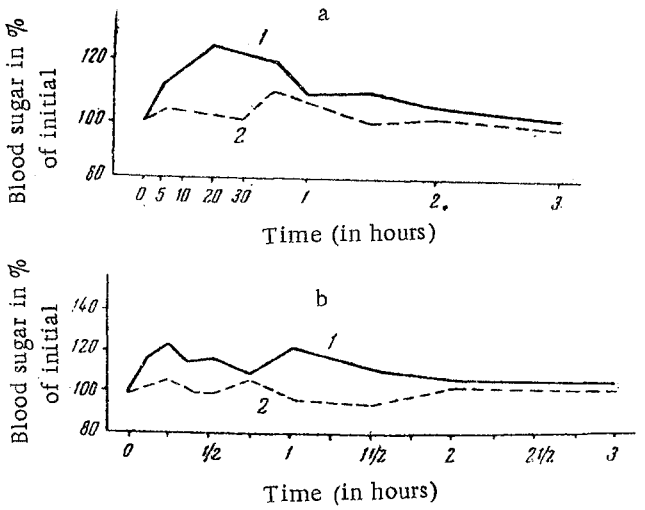

Fig. 2. Effect of first (—) and repeat (— — —) sham ingestion of solutions on blood sugar content in patients. a) 500 ml 10% glucose solution; b) 500 ml 0.01 % saccharin solution (mean data of all observations).

These data indicate that the hyperglycemic action of saccharin is only manifested when it enters the organism by way of the oral cavity. It follows from this that this action of saccharin is associated with stimulation of taste receptors in the mouth; in the absence of this condition, when saccharin is introduced directly into the stomach, its ability to elicit a rise in blood sugar content is abolished.

The material presented provides a basis for assuming that the rise in blood sugar seen after drinking saccharin solution is conditioned reflex in nature and is connected with excitation of peripheral receptors of taste nerves in the mouth.

Repeat sham drinking of solutions of saccharin and of glucose produces a smaller hyperglycemic effect (Fig. 1, a and b). It follows from this that conditioned reflex increase in blood sugar content which develops after sham ingestion of glucose and saccharin solutions is unstable and quickly extinguished. Comparison of the results of sham ingestion of saccharin and of glucose solution shows no essential difference in the dynamics of blood sugar content.

The opinion expressed in the literature that a hyperglycemic effect can only be obtained following administration of saccharin if it acts on gastric receptors [3, 4] is, in our view, insufficiently well founded. The hyperglycemic effect of saccharin ingestion, as shown by our observations, develops predominantly when the oral taste receptors are stimulated in the act of ingestion.

In summary, the data presented permit the conclusion that regulation of blood sugar content is mediated by a complex reflex route. The most important role in this process is the act of eating the carbohydrates itself, which achieves excitation of oral receptors and this in turn elicits, through the afferent system, complex reflex stimulation of carbohydrate metabolism. This complex reflex rise in blood sugar level exerts an influence on the dynamics of carbohydrate metabolism generally.

The presence of food in the mouth thus plays an extremely important part both in the process of digestion and in metabolism. Despite the short time during which food is present in the mouth, important biologic processes take place during the act of eating; these processes consist of reflex excitation of the whole glandular digestive apparatus, stimulation of carbohydrate metabolism and enhancement of oxidative processes in tissues, which in its turn leads to enhancement of the whole energy turnover.

SUMMARY

Sham feeding of glucose solution and saccharin to patients after esophagotomy causes prolonged (3 hours) rise of blood sugar of almost equal degree. Administration of glucose solution through the esophagostomy directly into the stomach causes an increase in blood sugar for 1½ hours with subsequent fall below (by 21.4%) the initial level. Administration of saccharin solution into the stomach and through the esophagostomy causes no rise in blood sugar level whatsoever. The results which were obtained emphasize the significance of the act of eating as the leading link in the control of blood sugar in man. Thus, it was shown that the control of blood sugar is effected in a complex reflex way, including both unconditioned and conditioned natural food reflexes.

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