

Effect of Sodium Fluoride and/or Sodium Iodate on Blood Sugar Response to Thiopental in the Fasted Rabbit

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Abstract □ The intraperitoneal administration of sodium thiopental, 40 mg./kg., to young male New Zealand white rabbits pretreated for 2 days with either Philadelphia tap water, distilled water, or Springfield water *ad libitum* and fasted 24 hr. prior to glycemic determinations induced hyperglycemia. The most marked hyperglycemic response occurred in those animals pretreated with Philadelphia tap water, which contains sodium fluoride (0.92 mg./l.), to which sodium iodate had been added (0.2%). The addition of sodium fluoride to either distilled water or Springfield water, employed in the 2-day pretreatment period, resulted in greater hyperglycemia after thiopental than was noted when either type of water, devoid of fluoride, was utilized. Marked hypoglycemia occurred in response to thiopental in the group which received distilled water to which sodium iodate had been added. The presence of both halogens in the pretreatment liquid regimen, regardless of the kind of water used, resulted in hyperglycemia in response to thiopental.

Keyphrases □ Thiopental—hyperglycemic effect □ Sodium fluoride effect—thiopental hyperglycemia □ Sodium iodate effect—thiopental hyperglycemia

The profound influence exerted by thiourea and its derivatives on carbohydrate metabolism in the mature rat has been observed by numerous investigators. Perhaps the most dramatic response that results from the biochemical interaction of the goitrogen occurs at the enzymatic level and is reflected in hyperglycemia with the concurrent depletion of liver glycogen (1, 2). These effects are readily elicited by the intraperitoneal administration of thiourea and its alphanaphthyl derivative (ANTU) and prevented by a variety of measures, such as the injection of iodide every 4 days (3) and the oral administration of iodine, iodides, and iodates, either as Lugol's solution, or the sodium or potassium salt (4-7).

In rabbits, Blackberg and Hrubetz (8) successfully attained peak glucose levels within 20 min. after the intraperitoneal injection of sodium thiopental, a derivative of thiourea, at a dosage level of 40 mg./kg. of body weight.

Because of the chemical and pharmacological kinship which exists between thiourea and thiopental, it became the objectives of this study to ascertain whether or not the oral administration of sodium iodate could modify the hyperglycemia induced by the intraperitoneal injection of sodium thiopental in the rabbit, and further, to determine the effect of fluoridated *versus* nonfluoridated tap water and distilled water, with and without sodium iodate, on the nature of the glycemic response. Tap water with fluoride as an additive serves as a prophylactic measure to retard or prevent the onset of dental caries (9). However, in soft tissues the halogen may interfere with cellular metabolism through a variety of enzymatic interactions (10-19).

EXPERIMENTAL

Two hundred and thirty-eight male New Zealand albino rabbits, weighing between 1.6 and 2.5 kg., were employed in this investigation. Pretreatment consisted of maintenance on Purina rabbit pellets and Philadelphia tap water *ad libitum* for several days prior to the introduction of a particular liquid diet which consisted of either Philadelphia tap water (PTW), Springfield tap water (STW), or distilled water (DW), modified by the addition of either sodium iodate¹ (to make a 0.2% solution), or sodium fluoride,² (0.92 mg./l.), or a combination of the two salts. During the pretreatment phase, animals were allocated into four groups of 12, ten groups of 18, and one group of 10 for additional treatment as follows: all were fasted the last 24 hr. of the 48-hr. pretreatment period while receiving *ad libitum* a specifically designated regimen (Table I) for the entire 2-day period, with the exception of Group VI, which received a restricted quantity of distilled water with iodate to ascertain the relationship between iodate dosage and degree of hypoglycemia (Groups V and VI). Following the 2-day pretreatment period, blood was withdrawn from a marginal ear vein for glucose determination (20).

Immediately after withdrawal, the animals in the treated groups received either sodium thiopental³ intraperitoneally at a dosage of 40 mg./kg. of body weight or physiological saline⁴ in a volume equivalent to that of thiopental on a weight basis. Three groups, III, XIII, and XV, although subjected to a special diet for the 2-day pretreatment phase, received neither thiopental nor physiological saline, and were thus designated as untreated. The rabbits were allowed freedom of movement for 25 min. before being restrained for 5 min. prior to the procurement of the second and final blood sample. Fluid intake was measured daily from calibrated Girton drinking bottles.⁴

RESULTS AND DISCUSSION

The results of this investigation (Table I) indicate that the 2-day oral administration of either Philadelphia tap water, distilled water, or Springfield tap water, with and without sodium iodate and/or sodium fluoride, variably modified the 30-min. glycemic response that followed the intraperitoneal injection of thiopental in the 24-hr. fasted rabbit. It is noteworthy that the greatest deviation in the blood sugar level occurred in those animals which had been subjected to the sodium iodate in distilled water (Group V). In this group, marked hypoglycemia was observed, whereas, either hyperglycemia or slight hypoglycemia was noted in the other groups. These results are in direct contrast to those observed by McCreesh and Mann (7), who prevented the hyperglycemia that occurred in rats after thiourea administration preceded by the 2-day oral administration of sodium iodide or iodate. This study has revealed that fluoride ion antagonizes the hypoglycemic action of thiopental in the presence of distilled water containing sodium iodate. Furthermore, potentiation resulting in an increased blood sugar response was noted when the two halides were present in solution.

A probable explanation of these data may be attributed to the activity of fluoride ion in modifying various enzymatic reactions involved in carbohydrate metabolism. However, no valid conclusion

¹ Reagent grade product of Matheson Coleman and Bell, Inc., East Rutherford, N. J.

² Reagent grade product of Baker Chemical Co., Phillipsburg, N. J.

³ Commercially available product of Abbott Laboratories, North Chicago, Ill.

⁴ Girton Manufacturing Co., Millville, Pa.

Table I—Effect of Sodium Fluoride and/or Sodium Iodate on Blood Sugar Response to Thiopental in the Fasted Rabbit

Group	Pretreatment	Treatment	Av. Liq. Cons., ml.	Av. IO ₃ , mg.	Av. F, mg.	Blood Sugar Change, mg./100 ml.	SE	p ^a
I	P.T. ^b	thiopental	183.4	—	0.2	+ 9.6	±8.54	0.05
II	P.T.I.	thiopental	145.4	290.8	0.1	+12.4	4.56	0.001
III	P.T. ^c	—	219.6	—	0.2	+ 0.8	2.44	0.02
IV	D.W. ^d	thiopental	163.3	—	—	+ 3.3	6.27	0.05
V	D.W.I.	thiopental	75.1	150.2	—	-12.7	4.60	—
VI	D.W.I. ^e	thiopental	36.5	73.0	—	- 3.8	1.51	0.1
VII	D.W.F.	thiopental	264.2	—	0.2	+ 8.7	3.44	0.001
VIII	D.W.F.I.	thiopental	120.0	240.0	0.1	+ 7.6	6.46	0.02
IX	S.T. ^f	thiopental	309.2	—	—	+ 4.5	2.46	0.01
X	S.T.I.	thiopental	100.8	201.6	—	+ 5.3	3.46	0.01
XI	S.T.F.	thiopental	197.5	—	0.2	+ 7.5	2.18	0.001
XII	S.T.F.I.	thiopental	103.7	207.4	0.1	+ 9.6	1.39	0.001
XIII	S.T. ^g	—	108.8	—	—	0.0	1.73	0.02
XIV	P.T., D.W., S.T.	saline	165.0	—	—	- 0.9	4.37	0.1
XV	D.W.	—	196.7	—	—	- 0.02	2.20	0.02

^a p Value (calculated from Student's t test) <0.05 equals significant increase in glycemic response compared to the distilled water containing sodium iodate (DWI), Group V. ^b P.T., Philadelphia water. N = 18. ^c N = 12. ^d D.W., distilled water. ^e N = 10. ^f S.T., Springfield water.

can be made with regard to the mechanism of action of either iodate, in producing its hypoglycemia in the absence of fluoride ion, nor the negation of this action by fluoride ion, nor the resultant thio-barbiturate-induced hyperglycemia observed when both halides were present.

SUMMARY

1. Thiopental administration (40 mg./kg. of body weight, intraperitoneally) to male New Zealand white rabbits pretreated with either Philadelphia tap water, distilled water, or Springfield water caused hyperglycemia.
2. The greatest degree of hyperglycemia was noted in those animals which were pretreated with Philadelphia tap water, which contains sodium fluoride (0.92 mg./l.) to which iodate has been added (0.2%).
3. The addition of sodium fluoride to either distilled or Springfield water for the 2-day pretreatment period resulted in a greater hyperglycemia following the injection of thiopental than had been noted when either type water, in the absence of fluoride, was utilized.
4. When sodium iodate in distilled water was used as the liquid diet for the pretreatment period, marked hypoglycemia was observed following the injection of thiopental.
5. The simultaneous presence of both halogens in the pretreatment solution, regardless of the kind of water used, resulted in hyperglycemia after thiopental.
6. Insignificant glycemic changes occurred in the control groups which received neither thiopental nor saline.

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