

EFFECTS OF DRUGS ON RADIOACTIVE IODINE UPTAKE BY THYROID IN RATS

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Effect of phenyl butazone, sulphadimethoxine, reserpine and nialamide on thyroïdal iodine uptake at four hrs. in rats has been studied. Phenyl butazone in a single dose of 50 mg/kg I.P. or 20 mg/kg for seven days intramuscularly caused a marked depression in I^{131} uptake. Reserpine 5 mg/kg given twenty four hrs. previously caused a significant inhibition of radio iodine uptake. These findings are discussed.

Thyroid function is known to be affected by many commonly used drugs of varied chemical structures. It is known that substances like sulphonamides, perchlorates, nitrates affect thyroid activity. With the introduction of radio active iodine in experimental and clinical medicine, it has been possible to study critically the effect of drugs on thyroid activity, on the basis of iodine uptake by thyroid gland, this being useful and convenient method for assessing thyroid function.

Recently long acting newer sulphonamides, certain analgesics, combination with steroids, and tranquilizers have been introduced in therapeutics. Some of them are known to affect the thyroid function. In this study the effect of reserpine, phenyl butazone and long acting sulphonamides on thyroid iodine uptake was investigated.

METHODS

All experiments were performed on male Wistar albino rats, bred in our laboratory, weighing between 100 to 250, maintained on standard diet. The animals were divided into eight groups ; one remained as control and others received different drugs. Drugs were given either intramuscularly or intraperitoneally. Control animals received requisite amount of solvent.

Radio iodine I^{131} carrier free obtained from Atomic Energy Commission, Tromby was administered interaperitoneally in dose of 3 microcuries per rat and standards were prepared from the same stock. Both control and treated animals were sacrificed simultaneously after 4 hrs by exposing them to a high

concentration of chloroform in a bell jar. Thyroid gland in each rat was dissected out carefully and its wet weight was recorded. The entire gland was then dissolved in 10 mls of 10 per cent sodium hydroxide and was kept overnight. The solution was then diluted to 15 mls by distilled water prior to estimation of radio activity. Radio activity was measured by G.M. liquid counter using EKCO automatic scaler along with the standard. The mean uptake at the end of 4 hrs has been expressed as percentage of the dose administered. In some experiments thyroid was studied histologically.

RESULTS

Table I shows the mean percentage uptake of I^{131} in control and each of the treated groups. Radio active iodine uptake varied with the weight of the thyroid gland. This can be seen from Fig. 1 which shows the weight of thyroid plotted against percentage I^{131} uptake in the control group. The regression equation for this line is $y=0.822X+5.94$ and the value of F is 7.933 significant at 5 per cent level. Therefore it is evident that the uptake of I^{131} is related to weight of thyroid. In order to make a correction for the difference in weight of thyroid, a mean uptake per 10 mgs of thyroid weight in each animal has been calculated for comparison in the Table.

In a group of 15 control animals a mean uptake of I^{131} per 10mg of thyroid at 4 hrs was 11.24 per cent and a variation as seen by standard error is relatively small. In a group of 9 animals, 20mg/kg of phenyl butazone was given I.M. one hour prior to administration of Radioiodine. The uptake was 14.2 per cent per 10 mg of thyroid. This difference in uptake though statistically significant was relatively small. When the same dose of phenyl butazone was administered...I.M. for a period of 7 days, there was a marked inhibition of thyroid I^{131} uptake. Thus in this group the uptake was 3.4 per cent, the difference being highly significant ($P < 0.001$) when compared with previous group receiving a single injection of phenyl butazone. Thyroids from half the number of animals in this group were studied histologically. Fig. 2 shows histological appearance of thyroid after seven days of treatment in comparison with that of the control. A dose of 50 mg/kg of phenyl butazone I.P. given 1 hr prior to administration of I^{131} also caused a similar reduction of uptake by thyroid as phenyl butazone given for seven days. It was therefore decided to study whether addition of prednisolone in a dose of 1.25 mg/kg could affect this action. It can be seen that the average uptake of this group is 3.1 per cent showing there by that prednisolone in a given dose does not effect this action of phenyl butazone.

TABLE I

Drugs.	Dose & Route	No. of Animals	Mean I^{131} uptake at 4 hrs.	Mean I^{131} uptake per 10 mg	Fiducial Limits at 95%	Fiducial Limits at 99%	t
Control	—	15	21.1 %	11.24 % s.e. 0.74	± 1.48	± 2.14	—
Phenyl butazone	20 mg/kg I.M	9	28.1 %	14.20 % s.e. 0.74	± 1.48	± 2.45	2.6
Phenyl butazone	20 mg/kg I.M. (For 7 days.)	6	3.15%	3.4 % s.e. 0.67	± 1.34	± 2.8	7.4
Phenyl butazone	50 mg/kg I.P.	6	3.25%	3.2 % s.e. 0.5	± 0.98	± 2.0	9.02
Delta butazone	50 mg/kg of P.B. and 1.25 mg/kg Prednisolone I.P.	6	6.76%	3.1 % s.e. 0.37	± 0.92	± 1.48	10
Sulpha dimethoxine	25 mg/kg I.P.	6	5.0 %	3.7 % s.e. 0.36	± 0.72	± 1.42	9.12
Nialamide	25 mg/kg I.P.	6	19.0 %	10.4 % s.e. 1.01	± 0.02	± 4.0	0.598
Reserpine	5 mg/kg I.P. (24 hrs. before)	8	10.4 %	8.5 % s.e. 0.26	± 0.52	± 1.05	3.47

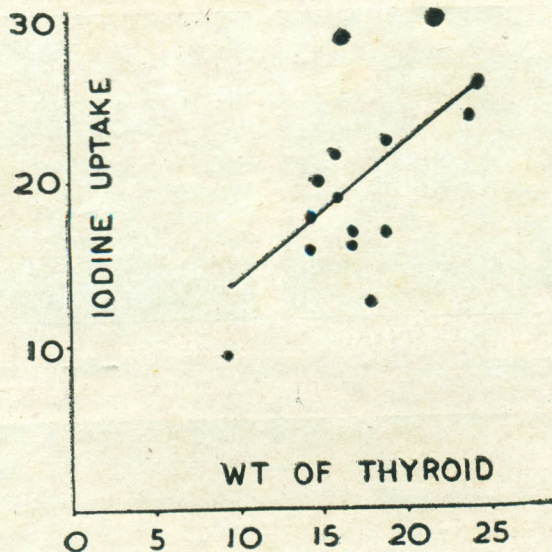


Fig. 1.

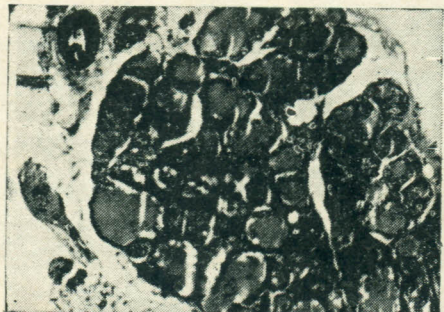
Showing the weight of thyroid plotted against percentage I^{131} uptake in the control group.

A group of six rats was treated with sulphadimethoxine in a dose of 25 mg/kg I.P. This drug produced a marked inhibition of I^{131} uptake.

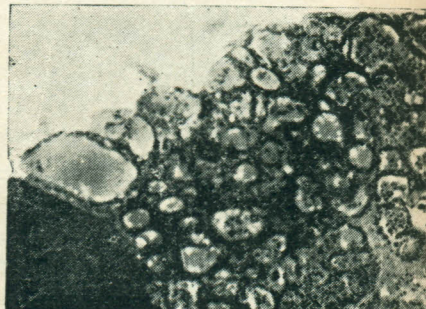
Since tranquilizers are often prescribed in thyroid disorders, effects of reserpine and monoamineoxidase inhibitor nialamide were studied. The dose of 5 mg/kg of reserpine was administered twenty four hrs prior to administration of radioactive iodine. The difference in average uptake was statistically significant. Nialamide was administered in a dose of 25 mg/kg one hour prior to administration of I^{131} . The mean uptake in this group was 10.4 per cent which was not significant with respect to control.

DISCUSSION

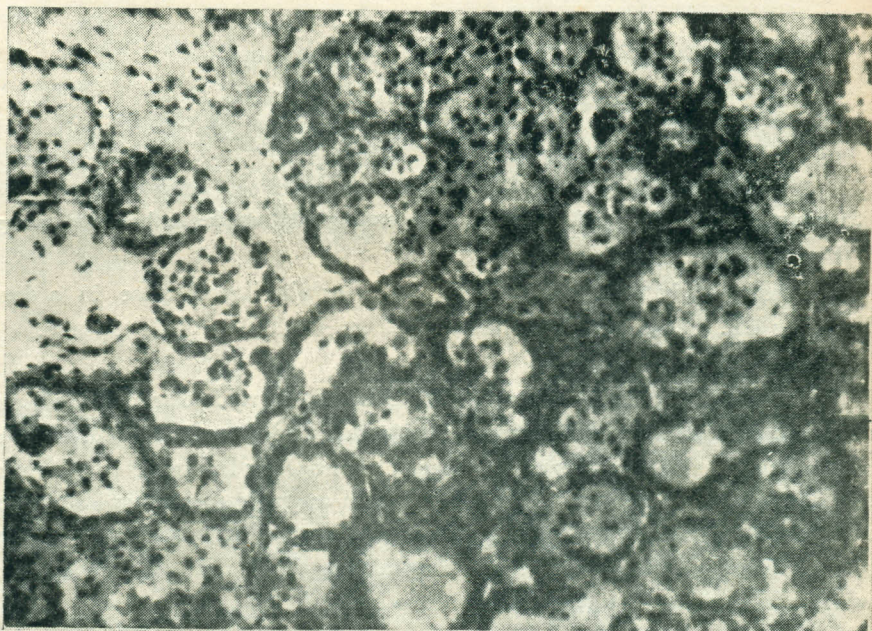
Thyroid function can be affected by large number of drugs which are used in clinical practice, and number of them are likely to interfere with thyroid function even in therapeutic doses, when used in, other than thyroid disorders. Grayson (1960) has recently reviewed various factors that are likely to influence the radio active thyroid uptake test. A drug may influence the tracer uptake by acting either on the thyroid or on the pituitary mechanism.



-A-



-B-



-C-

Fig. 2.

Showing histological appearance of thyroid after seven days of treatment in comparison with control.

A—Control showing colloid in the vesicles.

B—After Phenyl butazone, showing empty vesicles highly staining nucleus and infiltration.

C—Under high power, Fig. B.

In our study, phenyl butazone in a dose of 50 mg/kg caused a marked reduction in radio iodine uptake. This effect was comparable to 20 mg/kg given over a period of seven days. Linsk (1955) have reported a significant reduction of 24 hrs uptake following 4 days of therapy with phenyl butazone on 13 patients. The dose of phenyl butazone used here is comparatively larger than what is recommended for therapeutic use. However it is significant that phenyl butazone in a dose of 50 mg/kg did influence the thyroid activity within a short period of five hrs. Phenyl butazone in a dose of 10 mg/kg orally shows an antiinflammatory activity in formaldehyde induced arthritis in rats given over a period of ten days, and in this doses it is less likely to cause any marked inhibition of thyroid activity. Phenyl butazone is often given with prednisolone to enhance its antirheumatic activity. It was, therefore, significant to note that combination of the drug with prednisolone in a dose of 1.25 mg/kg did not cause any change in the action of butazone on the thyroid function. Berson and Yellow (1952) have shown a decrease in the 24 hrs I^{131} uptake in a group of 18 patients given 100-300 mg of cortisone daily for a period of six days. This effect was thought to be due to suppression of TSH formation. However, Epstein *et al* (1953) have reported on the direct action of corticoids on thyroid. There was no significant difference in the two groups receiving phenyl butazone and phenyl butazone along with prednisolone in our experiments.

Sulphonamides have been known to produce goitrogenic effect. Of recent, many long acting sulphonamides have been introduced in therapy. It is therefore of interest to note that single dose of 25 mg/kg of dimethoxine given parenterally caused a marked inhibition of thyroid activity in a period of 5 hrs. This drug is recommended to be used in a dose of 1 g per day. Since it is given orally one would not expect very high concentration of drug, as are attained by parenteral therapy. However, a prolonged treatment with long acting sulphonamides may cause deleterious action on thyroid.

Tranquilizers have often been used in hyperthyroid states. Besides, the thyroid activity is known to be influenced by the hyperexcitability of central nervous system. Yohalem (1957) found that in a dose of 400 mgs per day meprobamate has hardly any action on the radioactive iodine test while Friedell (1958) reported a reduction in I^{131} uptake after a therapy of three weeks. Newman and Fish (1958) reported the effects of reserpine, meprobamate and atarax in 31 euthyroid and 12 hyperthyroid patients. It is, therefore, necessary to ascertain that the tranquilizers used, does not significantly affect the radioactive iodine uptake test. In this study it has been found that reserpine in a dose of 5 mg/kg administered 24 hrs previously caused a significant de-

pression in thyroid uptake. In this dose rats were markedly sedated. Reserpine in this dose is known to cause a marked depletion of catecholamine and 5HT content of the brain. The lowering of iodine ¹³¹ uptake in this group could therefore be due to central action of reserpine. However, action of reserpine directly on the thyroid has not been excluded. Nialamide, a monoamineoxidase inhibitor has not caused any effect on thyroid function inspite of administration of large dose of 25 mgs/kg. parenterally.

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