THYROID VASCULARITY – DOCUMENTATION OF THE IODIDE EFFECT IN THYROTOXICOSIS

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ABSTRACT

Thyroid vascularity was measured in 101 thyrotoxic patients by analysis of 99mTc pertechnetate thyroid flow studies obtained with a gamma camera – minicomputer system. The diffusely hyperplastic goitres tended to have higher vascularity than the toxic multinodular goitres, and many of the solitary toxic nodules had vascularity results within normal limits. Potassium iodide therapy, 60 mg b. d. for 10–14 days results in a dramatic reduction in thyroid vascularity in diffuse thyroid hyperplasia and toxic multinodular goitre but the effect on toxic nodules was marginal.

99mTc pertechnetate thyroidal uptake is now an accepted thyroid function test and is considered to be a valid index of the thyroid trapping mechanism (Marion et al. 1974; Shimmins et al. 1968). Studies in this laboratory utilizing a minicomputer interfaced with a gamma camera have shown that very early 99mTc pertechnetate flow curves over the thyroid show two separate components; an initial rapid rise to a shoulder in the curve usually before 30 seconds, followed by a more gradual slope. It has been shown that the height of the knee of the curve is an index of thyroid vascularity (measured as a percentage of the dose injected), whereas the slope of the second component is an index of the thyroid trapping mechanism (Armstrong et al. 1976). This estimate of thyroid vascularity is thought to be the first in vivo non-invasive measure to have been obtained in man. Hitherto, such measures of thyroid blood flow have been obtained from animal experiments (Monkus & Reinke 1958) or indirectly from thyroid iodine clearance estimations in man (Myant et al. 1949).
In this paper thyroid vascularity measurements in thyrotoxicosis are reported, and the effect of potassium iodide on thyroid vascularity is documented.

PATIENTS AND METHODS

Thyroid vascularity was measured by utilizing analysis of isotope flow curves obtained from a gamma camera (Nuclear Enterprises Scinticamera III) interfaced with a PDP/8I minicomputer. The pinhole collimator was positioned 7 cm from the skin surface and 4 mCi of $^{99m}$Tc pertechnetate was administered by rapid intravenous injection into an antecubital vein. Net thyroid vascularity (expressed as a % of dose above neck background) was estimated from the height of the shoulder of the observed thyroid isotope flow curve, after appropriate corrections had been made (Armstrong et al. 1976).

To establish a normal range for thyroid vascularity, thyroid blood flow studies were performed in patients receiving 2.5 mCi of $^{99m}$Tc sulphur colloid for liver spleen scans. The mean thyroid vascularity measured in the 20 liver scan patients assessed in this way was 0.4% of the dose above neck background, with an upper limit of "normal" thyroid vascularity of 0.8%.

Thyroid vascularity was measured in 101 thyrotoxic subjects (whose thyroid status had been confirmed by free thyroxine index and serum triiodothyronine determinations), 64 patients with diffuse thyroid hyperplasia, 24 patients with toxic multinodular goitre and 13 patients with toxic uniniocular goitre (toxic nodule).

The effect of potassium iodide on thyroid vascularity was studied in 17 patients with diffuse thyroid hyperplasia, 3 patients with toxic multinodular goitre and in 6 patients with toxic uniniocular goitre. The potassium iodide studies were performed either:

(a) – Pre-operatively in patients already rendered euthyroid by thionamide therapy where potassium iodide was added to thionamide therapy prior to surgery. The thyroid vascularity measurements were made 30 min after the administration of 400 mg of potassium perchlorate by mouth. Potassium iodide 60 mg b. d. was then commenced and the vascularity studies repeated 10 days later on the day prior to surgery, again after perchlorate blockade.

Or:

(b) – In previously untreated thyrotoxic patients where potassium iodide was administered as an adjunct to thionamide therapy to obtain rapid control (Turner et al. 1976). Pre-treatment vascularity and technetium uptake measurements were made and the patients were then commenced on thionamide (carbamazole 40 mg daily or propylthiouracil 400 mg daily) together with potassium iodide 60 mg b. d. The technetium uptake and vascularity studies were then repeated 14 days later.

RESULTS

Thyroid vascularity measurements in thyrotoxic subjects are shown in Table 1. The diffusely hyperplastic glands tended to have higher vascularities than the toxic multinodular goitres and many of the toxic nodules had vascularity measurements within normal limits. Twenty-one of the 64 patients with diffuse thyroid hyperplasia had vascularity values greater than 2 %, which is more than twice the upper limit of normal.
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<th>Vascularity measurements in thyrotoxicosis.</th>
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<td>Diffuse thyroid hyperplasia (N = 64)</td>
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<td>Toxic multinodular goitre (N = 24)</td>
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<td>Toxic uninodular (N = 13)</td>
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The effect of potassium iodide on thyroid vascularity in patients with diffuse thyroid hyperplasia or toxic multinodular goitre is shown graphically in Fig. 1. The 10-day responses represent the pre-operative studies and the 14-day responses the studies in previously untreated thyrotoxic patients.

The fall in vascularity for the 22 patients was highly significant ($P < 0.005$ by the Wilcoxon signed-rank test), the mean value falling from 1.96% to 0.87%. The drop in vascularity was still statistically significant when the 10-day responses and the 14-day responses were analysed separately ($P < 0.005$ and $P < 0.01$, respectively). The mean pre-treatment thyroid vascularity value was higher in the previously untreated thyrotoxic patients. This is probably due largely to the selection of only severely thyrotoxic patients for carbimazole-potassium iodide therapy in the initial treatment of thyrotoxicosis, whereas
the selection of patients for subtotal thyroidectomy was based on clinical and social factors. The initial vascularities obtained in these patients were not, however, significantly related to thyroid gland mass (which was estimated by palpation and/or from the thyroid scan).
The thyroid vascularity studies in patients with toxic uninodular goitre before and after potassium iodide administration are shown in Fig. 2. Again the 10-day responses represent pre-operative studies and the 14-day responses acute control studies in previously untreated thyrotoxic patients. The drop in vascularity was less marked in this group, the mean pre-treatment value being 0.85 %, and the post-iodide mean value 0.61 % (P < 0.03).

Fig. 3 shows the thyroid blood pool scan (perchlorate blocked 99mTc pertechnetate scan (Armstrong et al. 1976)) obtained from a patient with Graves' disease with a loud thyroid bruit, thyroid vascularity 3 %. There was a dramatic loss of visualization in the thyroid blood pool scan after 10 days potassium iodide 60 mg tabs 1 b.d., thyroid vascularity 0.4 %. The scans were taken with similar gamma camera settings 3–4 min after injection.

**DISCUSSIONS**

The computer-gamma camera system used in these studies has enabled the simultaneous measurement of thyroid vascularity and 99mTc uptake per min corrected for intrathyroidal vascularity. Almost one-third of patients with diffuse thyroid hyperplasia had very vascular goitres as assessed by this technique and the majority but not all of these patients had loud thyroid bruits. The technique for measuring thyroid vascularity has errors of the same kind and same order of magnitude as occur in orthodox early thyroid 99mTc uptake measurements (Armstrong et al. 1975); there is an additional possible error in picking the shoulder of the uptake curve, but in practice this is rarely a problem. We therefore have confidence (based on extensive experimental trials) that the vascularity measurement is reproducible and accurate to within ± 20 %.

99mTc pertechnetate is now widely used to enable simultaneous assessment of thyroid anatomy and thyroid function. It is our view that early isotope (99mTc or 131I) thyroid uptake measurements should always be corrected for intrathyroidal vascularity. This would seem to be particularly important when early isotope uptake measurements are used in serial T3 suppression studies to indicate remission in thyrotoxicosis. The current disappointment in the predictive value of T3 suppression studies may to some extent be due to a lack of recognition of the possible separate effects of longterm drugs on thyroid vascularity and on trapping function.

Iodide, first introduced more than 40 years ago (Plummer 1923) for the pre-operative management of thyrotoxicosis is still used in most centres in an attempt to diminish bleeding at the time of operation, and to reduce the risk of post-operative wound haematoma, but the lack of the previous in vivo technique to measure thyroid vascularity has led to some scepticism as to its effectiveness. The present 99mTc vascularity studies in diffuse thyroid hyperplasia and
toxic multinodular goitre have confirmed the validity of the surgical impression that iodide reduces blood flow although other factors such as tissue friability may be just as important at surgery. The mechanism by which iodide reduces vascularity remains uncertain but the histological changes during the process of “involution” are well documented.

Toxic uninodular goitre is relatively common in this part of New Zealand (12% of thyrotoxic patients) and surgery is considered by many to be the treatment of choice. In this study the iodine effect on nodule vascularity was not considered to be very significant, and the observed vascularity levels were often within the normal range. Thyroid vascularity is not a frequent technical problem at operation in such patients and the present vascularity measurements would suggest that iodide therapy has little or no place in the pre-operative management.

The factors regulating thyroid blood flow in man remain unclear but recent studies in laboratory animals suggest that the complex innervation of thyroid blood vessels (Tice & Creveling 1975), may be important, and it has been recently postulated that local amines released by thyroid mast cells may play an important role (Melander et al. 1975). The gamma camera computer system promises to be a useful tool to evaluate the possible relevance of the animal studies to human pathophysiology.

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REFERENCES


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