JOURNAL OF NUCLEAR MEDICINE 6:598-604, 1965

Diagnosis of Hyperthyroidism by External Liver Counting: Correlation Between External Scintillation Counting of the Liver and Plasma Protein-Bound Iodine^{131}

S. M. Sharma, M.B.B.S., D.M.R.T., K. B. Desai, B.Sc., K. P. Mehan, B.Sc.,
R. D. Ganatra, M.B.B.S., F.C.P.S., M.Sc., M. N. Mehta, B.Sc.,
K. Sundaram, M.D., F. P. Antia, M.D., M.R.C.P.[1]

Bombay, India

Evidence from various sources indicates that a large portion of the circulating protein-bound iodine is located in the liver. A significant concentration of ^{131}I is observed in the liver of hyperthyroid patients on doing a "profile scan" 48 hours after an oral dose of ^{131}I (1). This liver concentration is predominantly due to the protein-bound iodine (PDI^{131}) as the circulating inorganic ^{131}I level at 48 hours is very low. Studies after an intravenous injection of ^{131}I labeled thyroxine also show a thyroxine concentration in the liver which is five to seven times larger than the plasma concentration (2). Recently, good liver scans have been obtained with doses as small as 60 μC of ^{131}I labeled thyroxine, again proving the existence of a large thyroxine concentration in the liver (3). It is therefore reasonable to suppose that external scintillation counting of the liver would be a good measure of PBI^{131} levels in the plasma in patients undergoing radioiodine thyroid uptake studies.

In the present paper, we describe the correlation between external count-

[1]Radiation Medicine Centre, Medical Division, Atomic Energy Establishment Trombay, Tata Memorial Hospital, Parel, Bombay-12, India.

ing of the liver and PBI^{131} in plasma at 48 hours and seek to relate this to thyroid functions.

MATERIAL AND METHODS

External counting of the liver and estimation of plasma PBI^{131} at 48 hours were done in 167 patients referred to the Thyroid Clinic for thyroid uptake studies with radioiodine. Seventy of these patients were euthyroid, 71 were hyperthyroid and 26 patients had a nontoxic goitre. Each diagnosis was based on the clinical findings, thyroid uptake measurements and the determination of plasma PBI^{131}. None of the patients included in this series were found having any apparent liver disease.

Thyroid uptake measurements with radioiodine were done in accordance with the I.A.E.A. recommendations (4).

Dose of Radioiodine

About 25 μC of ^{131}I as sodium iodide absorbed on anhydrous sodium phosphate in a gelatin capsule was administered orally.

Estimation of PBI^{131}

Plasma ^{131}I and PBI^{131} estimations were done 48 hours after the administration of the dose. Ten ml of the patient's blood was collected. Four ml of plasma was counted in a well type scintillation counter having a 3 inch thallium activated sodium iodide crystal. The plasma ^{131}I value was expressed as a percentage of the dose administered per litre of the plasma. In those cases where the plasma ^{131}I value was more than 0.2 percent, the plasma proteins were precipitated with trichloroacetic acid and PBI^{131} value was again expressed as a percentage of the dose given per litre of plasma. The protein precipitation was considered unnecessary in case where the plasma ^{131}I value was less than 0.2 percent per litre of plasma as it itself is well within the limits of normal PBI^{131} value (Mean normal PBI^{131} value is .099 $\pm$ .063% per litre of plasma). In case the plasma ^{131}I values were less than 0.2 percent, they have been plotted against the corresponding liver counts in Fig. 1 and Fig. 2.

^{131}I Thyroid Uptakes and Liver Counting

Thyroid uptake measurements were done with a scintillation probe having a 1¾ $\times$ 2 inch thallium activated sodium iodide crystal with a 20 degree flat field collimator. The counting was done with a pulse height analyzer on a 5 V window setting around the photopeak of ^{131}I. Immediately after the 48 hours thyroid uptake measurement the same equipment was used for external counting of the liver. For liver counting the probe was placed flush on the body surface on the anterior axillary line over an area where liver dullness was elicited by percussion. Normal ^{131}I thryoid uptake values at 2 hours, 24 hours and 48 hours in our centre have been found to be 13.3 $\pm$ 6.5 percent; 38.7 $\pm$ 13.8 percent and 41.1 $\pm$ 13.2 percent, respectively. Normal PBI^{131} value at 48 hours has been found to be 0.099 $\pm$ 0.063 percent of the administered dose per litre of the plasma.

CORRELATION BETWEEN P. B. I.^{131} VALUES AND EXTERNAL LIVER COUNTS

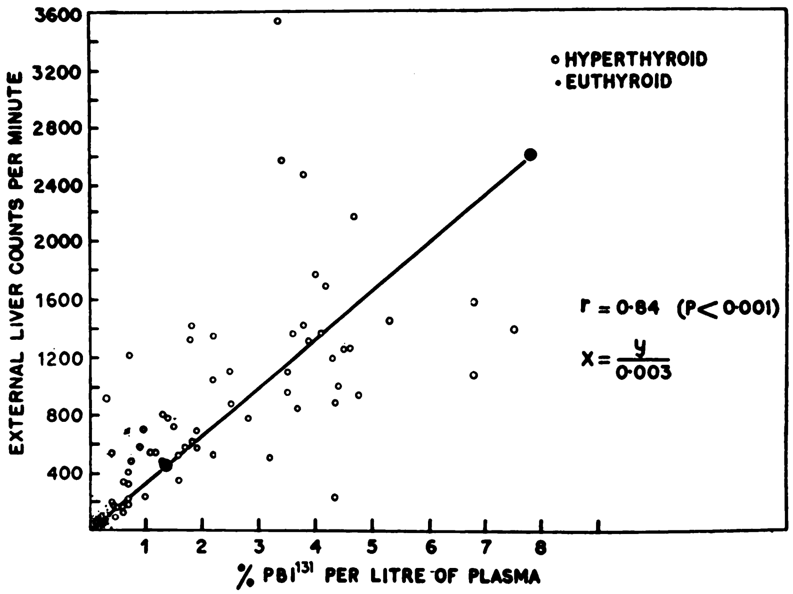

Fig. 1. Shows line of regression. Most of euthyroids are clustered at the beginning. Correlaton coefficient-r.

CORRELATION BETWEEN P. B. I.^{131} VALUES AND EXTERNAL LIVER COUNTS

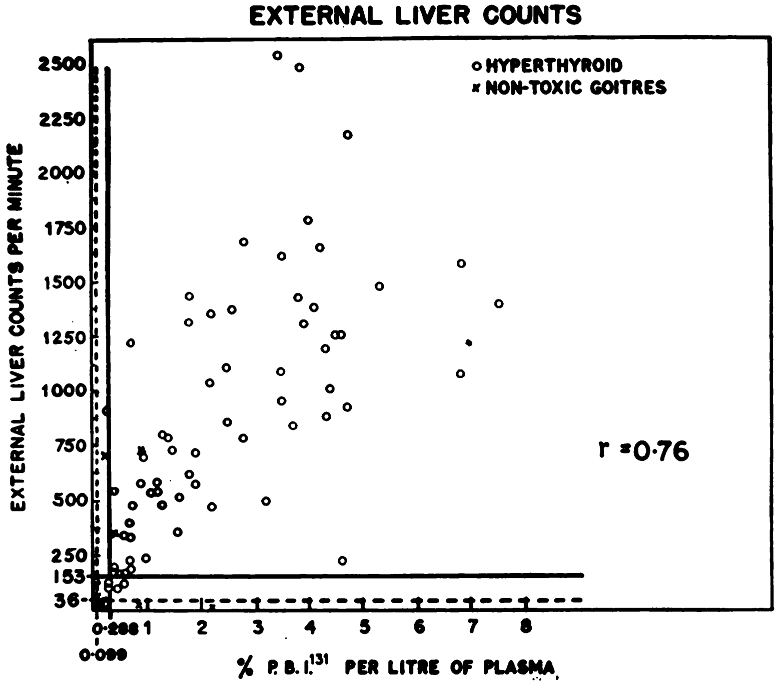

Fig. 2. Shows the mean normal percent of P.B.I^{131} value (0.099%) and mean normal external liver counts (36 cpm) as interrupted lines. Continuous lines show maximum limits (3 SD) of above normal values.

RESULTS

Fig. 1 shows the liver counts of 141 patients plotted against their respective plasma PBI^{131}. The analysis of the correlation between plasma PBI^{131} and the external liver counts was done by the Grouped Frequency Method. The correlation coefficient between these two parameters was found to be 0.84 (P less than 0.001). The equation for the regression line shown on the graph is $Y = 0.003 X$.

The mean liver count of the group of 70 euthyroid individuals was 35.7 counts per minute (S.E.4.7). Fig. 1 shows most of the euthyroids in a cluster at the bottom of the line of regression. The corresponding mean liver count in a group of 71 hyperthyroid patients was 935.7 counts per minute (S.E.90). The difference between the mean liver counts of the two groups is statistically highly significant ($t=10.2$).

The mean PBI^{131} at 48 hours in a group of 71 euthyroid individuals is 0.09 percent (S.E. 0.007) of the administered dose per litre of plasma. The corresponding mean plasma PBI^{131} of the group of 70 hyperthyroid patients was 2.39 percent (S.E.0.22). The difference between the mean values of the two groups is statistically highly significant ($t = 9$).

Fig. 2 shows the liver counts plotted against their corresponding PBI^{131} values in a group of 26 patients having nontoxic goitres with high uptake and the same 71 hyperthyroid patients which are shown in Fig. 1. The continuous lines show maximum limits of normal PBI^{131} and normal liver counts (3 SD from the mean) which are 0.29 percent of administered dose per litre of plasma and 153 counts per minute, respectively. The dotted lines show the mean values of these two parameters. The correlation coefficient is 0.76 (P less than .001). Two patients with nontoxic goitres had the PBI^{131} value of 0.85 percent and 2.2 percent, but the liver counts were 50 and 12, respectively. However, one patient with a nontoxic goitre had high liver counts and normal PBI^{131}.

Figure 3 shows the separation of hyperthyroid cases from nontoxic goitre and euthyroid patients by external liver counting and by PBI^{131} value. Ninety-seven percent of euthyroid patients had 153 counts per minute or less over the liver while 100 percent of the euthyroid patients had a PBI^{131} value of 0.29 percent of administered dose per litre of the plasma or less. Ninety-six percent of hyperthyroid patients show more than 153 counts per minute over the liver as against 98 percent of the patients having a PBI^{131} value of more than 0.29 percent of the administered dose per litre of the plasma. Nontoxic goitre patients show the same percentage (81%) of patients having less than 153 counts per minute over the liver and the PBI^{131} value of 0.29 percent of administered dose per litre of plasma. The demarcation lines of 153 counts per minute over the liver and 0.29 percent per litre of plasma have been chosen as they are 3 SD away from mean normal values of liver counts and PBI^{131}.

DISCUSSION

In the study of thyroid function with radioiodine, the estimation of plasma PBI^{131} is an important investigation for differentiating toxic and the nontoxic goitres. The test on which this crucial demarcation depends should be free of overlap between the normal and the abnormal groups and, moreover, should be capable of giving reproducible results in the hands of a technician during routine use.

Plasma PBI^{131} levels are usually estimated either by the protein precipitation method or by a ion-exchange resin method. Doubts have been expressed regarding the protein precipitation technique, though it is not exactly known where the source of error lies (5). Some believe that the error lies in the precipitation of inorganic plasma iodide with the proteins, thereby giving falsely high value for plasma PBI^{131}, while others believe that the plasma PBI^{131} values are falsely low because of the dissociation of the iodine from the plasma during precipitation (6). Resin column studies (7) indicate that as much as 20-30 percent of labeled tri-iodo thyronine and thyroxine may be trapped in the column giving lower PBI^{131} value. In addition cost of resin is always a consideration where the problem of differentiating between high uptake endemic goitre and the toxic goitre is common. Like any other chemical test involving the use of a radioisotope, both the above tests demand scrupulous care to avoid contamination of glassware and chemicals. Furthermore, counting of plasma samples requires an expensive well scintillation counting assembly.

A very good correlation at 48 hours is obtained between PBI^{131} and liver counts, as shown in Fig. 1 and Fig. 2. All thyrotoxic patients, except three, had liver counts above 150. The mean count in the group of euthyroid individuals

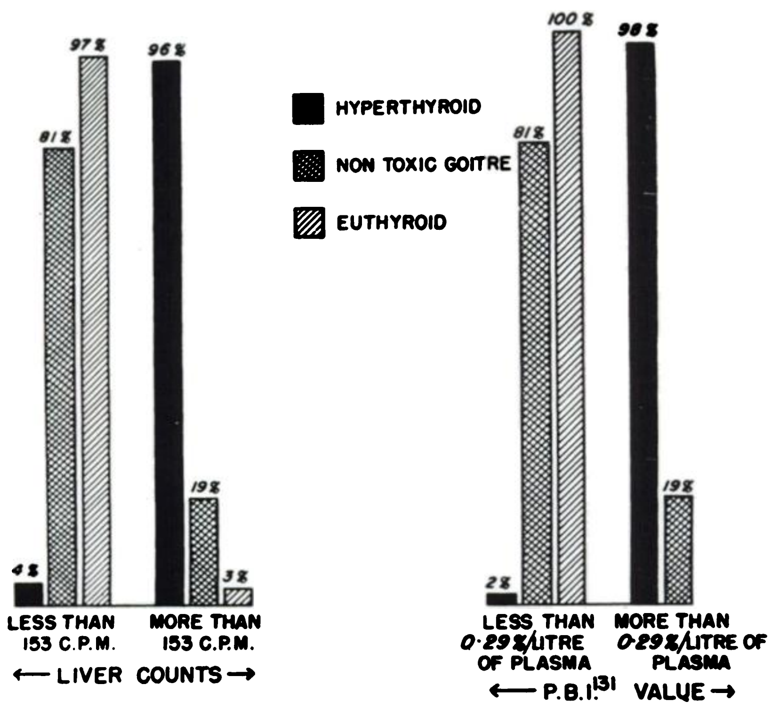

Fig. 3

Fig. 3. Compares the efficiency of separation of euthyroids, nontoxic goitres and hyperthyroids by external liver counting and by $P.B.I^{131}$ estimation. Total number of patients 167 (70 euthyroids, 71 hyperthyroids and 26 nontoxic goitres).

was 35.7 (S.E. 4.7). Liver counts of almost all the thyrotoxics are more than three standard deviations away from the mean normal liver count. Figure 2 also shows a good separation of the toxic and the nontoxic goitres by external counting of the liver.

The liver counting method has the following advantages over the conventional PBI^{131} determination: (i) The technique is simple and requires the same equipment that is used for the thyroid uptake measurement (ii) Additional well scintillation counting equipment is unnecessary (iii) Erroneous results due to contaminated glassware and chemicals are avoided as no chemical processing is needed (iv) The patient is spared the discomfort of venepuncture.

Some limitations of the external counting of the liver as an approximate estimation of the circulating thyroxine are (i) If the patients are not administered an identical dose then the counting rate over the liver will have to be expressed in proportion to the size of the dose (ii) Patients with renal disease who do not rapidly excrete the inorganic iodide may give falsely high liver counts, though we have not seen such a patient (iii) In direct chemical determinations of organically bound ^{131}I, it is possible to distinguish the activity due to inorganic iodide, protein bound iodide and butanol extractable iodide if required, while the external liver counting does not permit such a distinction (iv) As with plasma PBI^{131} estimations, there is an area of borderline overlap with liver counts where it is not possible to separate the toxic from a nontoxic goitre (v) In patients with chronic liver disease like cirrhosis the external liver counts may be effected irrespective of thyroid status.

Figure 3 bears out that external counting of liver at 48 hours after the administration of radioiodine serves the same function as the determination of plasma PBI^{131} levels. To say the least, liver counting is a good cross-check on PBI^{131} estimations, when both are done simultaneously. When so much of the future line of management and treatment of a case of goitre depends on the results of PBI^{131} determination it is prudent to have a cross-check.

SUMMARY

External liver counting clearly distinguishes between euthyroid and hyperthyroid patients ($t = 10.2$); hyperthyroid and nontoxic goitre patients ($t = 11.9$). Individual values for these patients show a good separation between the groups. Correlation coefficient between liver counts and PBI^{131} in euthyroid and hyperthyroid patients was found to be 0.84 and correlation coefficient for hyperthyroid and nontoxic goitre patients was 0.76.

The advantages of external liver counting as an alternative method to plasma PBI^{131} estimations are:

(a) Simplicity of the techniques;
(b) No additional well scintillation assembly needed, and
(c) No errors in results due to contamination of glassware, chemicals, etc.

ACKNOWLEDGEMENTS

We are grateful to Dr. E. E. Pochin of University College Hospital Medical School, London, for his valuable suggestions and helpful criticisms.

REFERENCES

1. Pochin, E. E.: *Medical radioisotope scanning* I.A.E.A. Proceedings, 156, 1959.
2. Pochin, E. E.: *Medical radioisotope scanning* I.A.E.A. Proceedings, 158, 1959.
3. Middleworth, Vain, Turner, J. A. and Lipcomb, A.: Liver function related to thyroxine metabolism. *J. Nucl. Med.* 4:132, 1963.
4. I.A.E.A. Consultants' meeting. British J. of Radiology, 35:205, 1962.
5. Veall, N. and Vetter, H.: Radioisotope scanning in clinical research and diagnosis. Butterworth & Co., 298, 1958.
6. Veall, N. and Vetter, H.: Radioisotope scanning in clinical research and diagnosis. Butterworth & Co., 297, 1958.
7. Raventos, A., Gorson, R. O. and Chamberlain, R. H.: Plasma I^{131} determination and Thyroid I^{131} uptake in the diagnosis of Hyperthyroidism, "problem" cases. *Radiology.* 77:12, 1961.