THE EFFECT OF IODOCHLORO-OXYQUINOLINE
AND IOPANOIC ACID ON THE DETERMINATION OF
PBI AND BEI

By

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ABSTRACT

Our results have confirmed that BEI determination is a more specific method than PBI determination for the estimation of the concentration of thyroxine and other, if any, iodine-containing hormones. Although the administration of iodinated organic compounds sometimes increased the BEI concentration, the latter in this respect was less susceptible than the PBI.

Ingestion of iodoxchloro-oxyquinoline to a small number of healthy volunteers caused both the PBI and the BEI concentration to reach higher values than could be determined by the methods used. Following discontinuation of intake the BEI level required only one week to return to the normal range; the PBI, however, took several weeks. Administration of iopanoic acid (for cholecystography) caused a much greater and more prolonged increase in PBI than in BEI.

Determination of protein-bound iodine (PBI) in the serum is a common and valuable method in the diagnosis of thyroid disorders. It has, however, the well-known drawback that administration of iodine-containing compounds increases the concentration to an unpredictable level, at which it may remain for a long period. Almost one half of the samples that show elevated values in routine analyses at our laboratory come from patients who have taken

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iodine-containing preparations or contrast media. In our experience, the two principal sources of this error are the bowel antiseptic, iodochloro-oxyquinoline (Entero-Vioform®, ICOQ) and the oral bile contrast medium, iopanoic acid (Telepaque®).

The determination of butanol-extractable iodine (BEI), originally introduced for diagnostic use by Man et al. (1951), affords a possibility of a more specific evaluation of thyroxine and its derivatives in the serum. The technique, however, has been considered too laborious and time-consuming for routine use. The simplified procedure of Posner (1961), later modified by Fischer et al. (1964), has brought about an improvement in this respect.

Although numerous data have been published on the influence of iodine-containing compounds on PBI, very little seems to be known about the extent to which they influence the BEI value. While Man et al. (1951) and, later, Pileggi et al. (1961) observed that iodinated organic compounds did in fact influence BEI, they reported no quantitative data apart from the BEI determinations of Pileggi et al. (1961) obtained in a number of sera taken as early as the day after administration of an iodine-containing preparation. We therefore considered it worth while to make a comparative study of PBI and BEI in subjects to whom iodinated compounds were administered. The findings could facilitate the clinical evaluation of cases of thyroid disorders in which iodine-containing preparations have been used.

**METHODS**

Protein-bound iodine was determined by the method of Barker & Humphrey (1950) as modified by Skanse & Hedenskog (1955); BEI, by Ljunggren's (1965) modification of the technique of Fischer et al. (1964). The latter modification was necessary in order to compensate for serum constituents inhibiting the oxidation of cerium in the photometric iodine determination. The BEI value from one healthy subject known not to have taken iodine or any iodinated compound is assumed to equal the subject's PBI concentration; and the BEI concentration in the samples examined is calculated in relation to this standard concentration. It is recognized that this constitutes an approximation, since the inhibitory effect may be different in different sera. However, concentration figures thus obtained by the two methods will be directly comparable. The BEI determination is more laborious and requires greater experience and technical skill than does the PBI.

A dose of 1.5 g (six tablets) ICOQ was administered orally once a day for five days, to each of five euthyroid male volunteers. Serum samples were taken before the test and one day, one week, three weeks and eight weeks, respectively, after intake of the final dose. No side effects were observed. Patients examined by cholecystography were randomly selected from the X-ray department of the hospital. They had received 6 g iopanoic acid by mouth several weeks or months prior to our study. In this group, neither the thyroid gland nor its function was clinically examined. In most cases PBI and BEI were determined in the same samples.
RESULTS AND DISCUSSION

Confirming the results of Man & Bondy (1957) and Postier (1961), we found good agreement between the BEI and the PBI values from euthyroid, hypothyroid, and most of the hyperthyroid subjects.

However, in 40 of 1500 consecutive serum samples delivered to the laboratory for routine analysis, the PBI concentration was higher than 20 µg/100 ml (the upper limit of the method). In 25 of these 40 samples, the BEI concentration, too, exceeded the upper limit. We were unable to get anamnestic data on these 25 cases, since the samples had come from a number of different hospitals and doctors. Of the remaining fifteen samples, BEI was normal or almost normal in seven and moderately increased in eight. Diagnostic data as well as histories with regard to iodinated compounds were obtainable in most of these fifteen cases. They are recorded in Table 1. Most of the patients had either received iodine-containing preparations or suffered from diseases often treated with such preparations. It may be observed that the BEI value was normal in one patient on whom aortography and one on whom urography had been recently performed, whereas all of the four cholecystography patients had an increased BEI value.

Table 1.
BEI values of samples with a PBI concentration above 20 µg/100 ml; diagnosis, type of iodine-containing compound taken, and interval between administration and taking of blood sample.

<table>
<thead>
<tr>
<th>BEI µg/100 ml</th>
<th>Diagnosis or condition</th>
<th>Type of compound or examination</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.2</td>
<td>Operated goiter</td>
<td>Thyroid pills</td>
<td>(During therapy)</td>
</tr>
<tr>
<td>12.3</td>
<td>Goiter</td>
<td>ICOQ</td>
<td>1 week</td>
</tr>
<tr>
<td>6.4</td>
<td>Cardiosclerosis</td>
<td>ICOQ</td>
<td>Brief</td>
</tr>
<tr>
<td>3.3</td>
<td>?</td>
<td>Aortography</td>
<td>2 weeks</td>
</tr>
<tr>
<td>6.1</td>
<td>Diabetes</td>
<td>Urography</td>
<td>1 year</td>
</tr>
<tr>
<td>13.3</td>
<td>Hypernephroma</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>12.2</td>
<td>(Ashma) Pulm. emphysema</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>8.3</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>11.1</td>
<td>Susp. hyperthyroidism</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>5.9</td>
<td>Anaemia</td>
<td>Urography</td>
<td>(Same day)</td>
</tr>
<tr>
<td>6.5</td>
<td>Neurasthenia</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>12.8</td>
<td>Fever</td>
<td>Cholecystography</td>
<td>1 week</td>
</tr>
<tr>
<td>8.6</td>
<td>Gastric carcinoma</td>
<td>Cholecyst. &amp; urography</td>
<td>6-2 weeks</td>
</tr>
<tr>
<td>10.1</td>
<td>Susp. hyperthyroidism</td>
<td>Cholecystography</td>
<td>1 week</td>
</tr>
<tr>
<td>9.4</td>
<td>Obstipation</td>
<td>Cholecystography</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>

ICOQ = iodochloro-oxyquinoline.
The results from the ICOQ group are demonstrated in Fig. 1. One day after intake of the last dose, both PBI and BEI were beyond the determinable range. One week later, the BEI values had become normal (except for one which reached 8.7 $\mu$g/100 ml), whereas the PBI value was still considerably high. After three weeks, the PBI concentrations were still high, while the BEI values had returned to the original levels. At eight weeks, one subject had dropped out, but in the remaining four, the PBI values were within the normal range, though still about 1 $\mu$g/100 ml higher than the initial level. There were inter-individual differences in the effect of the contaminant on the two tests. This was probably due to the presence of different metabolites of ICOQ (Lamberg 1965, personal communication). The rate of normalization of PBI is consistent with that reported by Ogden & Sheline (1959) and Thorén (1960).

The results from the cholecystography patients are illustrated in Figs. 2 and 3. Seven of the 14 patients studied within four weeks after X-ray examination showed high BEI levels, but all of those studied after a longer interval had values within the normal range. The PBI values, on the other hand, did not appear to be normalized until at least seven weeks had elapsed, and even one
Fig. 2.
PBI values of patients who had taken 6 g iopanoic acid by mouth for cholecystography. Abscissa: Interval (in weeks) between administration of the iodine-containing compound and taking of the sample. The arrows above the dots in the upper left corner indicate that the concentration exceeded the limit of the method, 20 \( \mu g/100 \) ml. When two dots are connected by a line, they are from the same subject. Horizontal lines denote the normal concentration range.

Fig. 3.
BEI values of the same samples as in Fig. 2. Legend as in Fig. 2.
of the few samples obtained after a longer period, had a very high PBI concentration. In each of the cholecystography patients with an increased PBI level, BEI was considerably lower. In eight cases, PBI was too high to be determined by the method. Of these eight, BEI was normal in two and moderately increased in the other six (4.0–9.8).

Ten of the samples from the cholecystography patients with increased PBI values were also examined by means of a modification of the tri-iodothyronine resin absorption test (Levin, to be published). No evidence of hyperthyroidism was found in any of these patients. A discussion of these results will be published later.

REFERENCES


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