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R. Wahl
M. Breidt
E. Kallee

Iodide supplementation: 200 μg daily or 1 500 μg weekly?

Zusätzliche Versorgung mit Iodid: 200 μg täglich oder 1 500 μg wöchentlich?

Summary 25 euthyroid volunteers were divided into two groups. Each participant of group A received 200 μg iodine in the form of diiodotyrosine per day for a period of eight weeks, i.e. 7 x 200 μg iodine/week. Each participant of group B received 1 500 μg iodide once a week for a period of eight weeks. In addition to the basal excretion of iodine with the collected urine, the excretion values in group A amounted to 67 % of the applied dose in the eighth week. In group B, the excretion values amounted to 65 % of the applied dose in the eighth week. Hence, no significant difference between both groups was found.

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Prof. Dr. med. R. Wahl (✉) · E. Kallee
Medizinische Klinik und Poliklinik,
Abt. IV Eberhard-Karls-
Universität Tübingen
Otfried-Müller Str. 20
72076 Tübingen

Dr. med. M. Breidt
Städt. Krankenhaus Esslingen
Hirschlandstr. 97
73730 Esslingen

Zusammenfassung 25 schilddrüsengesunde Probanden wurden in zwei Gruppen aufgeteilt. Jeder Teilnehmer in Gruppe A erhielt 8 Wochen lang 200 μg Iod täglich in Form von Diiodtyrosin, also insgesamt 7 x 200 μg/Woche, in Gruppe B 1 500 μg Iodid einmal pro Woche. Die wöchentliche Iodausscheidung im Urin betrug in Gruppe A zusätzlich zur basalen Ausscheidung in der 8. Woche ca. 67 % der durch Tabletten aufgenommenen Iodmenge von 7 x 200 μg/Woche. In Gruppe B betrug die renale Iodausscheidung in der 8. Woche ca. 65 % der durch Tabletten aufgenommenen Iodmenge. Zwischen beiden Formen der Iodzufuhr besteht somit kein bedeutender Unterschied.

Key words Iodine – urinary iodine – iodide substitution – goiter prevention – iodide tablets

Schlüsselwörter Iod – Uriniod – Substitution mit Iodid – Kropfprophylaxe – Iodidtabletten

Abbreviation index *d* = day · *h* = hour · μ*g* = microgram · *n* = number of cases

Introduction

The Federal Republic of Germany is an area with endemic prevalence of goitre (3). Iodine deficiency is considered to be the reason for these strumae. In order to prevent endemic goiter, a daily intake of 150–300 μg of iodine is recommended by the WHO or 180–200 μg by the „Deutsche Gesellschaft für Ernährung“ (German Society for Nutrition) (13). When using iodised salt in the diet, the intake of iodine with food in most cases does not exceed 100 μg per day (4); therefore extra iodine in tablet form is recommended as a prophylactic measure, especially for children and teenagers. 200 μg per day are regarded as an effective dose in iodide tablets.

3,5-Diiodo-L-tyrosine tablets containing 200 μg iodine to be taken daily or potassium iodide tablets containing 1 500 μg iodide (I^-) to be taken weekly were from Henning, Berlin/Germany. In this study we investigated whether both forms of administration have similar effects.

Materials and methods

a) Test persons and materials:

Test persons were 25 volunteers aged 21 to 47 years from Tübingen and the surrounding area. At the time of the investigation, none of the test subjects suffered from thyropathy or any other metabolic disease. During the last 7 months before the start of the trial and during the time of the study, the donors had no contact with either contrast media or drugs containing iodine. During the 8 weeks of the trial, the volunteers were required not to eat sea fish or any other seafood.

The subjects were divided into 2 groups:

Group A (6 women and 6 men) were given 200 µg of iodine in the form of diiodotyrosine tablets every day. Group B (6 women and 7 men) were given 1 tablet containing 1 500 µg of iodide once a week. The tablets were taken in the morning before breakfast.

Renal iodine secretion was considered to be a satisfactory parameter for assessing the iodine input and output. This does not take into account other pathways of secretion, such as faeces and perspiration. For measuring urinary iodine levels, urine was collected for 24 hours in 2-litre polyethylene flasks. After measuring the volume, approximately 10 ml of the collected urine were put into polyethylene tubes and stored at 4° to 7 °C until used. If a subject could not collect all urine during the 24-hour period, the test person was required to note it down and estimate the missing amount. This was the case in 9 of 558 urinary collections. The urine specimens of group B had to be diluted for iodine analysis on the day the iodide was given.

b) Methods

The total iodine was assessed using a PBI-Autoanalyzer® (Technicon Instruments, Tarratown/New York). The samples were acid-incinerated at 300 °C and the iodine was determined by the Sandell-Kolthoff Ce/As reaction. The samples were measured with and without internal standards in order to adjust for interferences. The variation coefficient of this method was 6 % (n = 20). Details of the method were described by Wahl et al. (14).

Results

The urinary volumes per 24 h totalled 1 377 ± 467 ml in male and 1 420 ± 457 ml in female participants. Serious errors concerning the volume collected can therefore be excluded. The variation coefficient of iodine output averaged 21 % (14 – 26 %) for 5 subjects on 6 successive days.

Test Group A (200 µg iodine daily in form of diiodotyrosine)

Fig. 1 shows the average values of the renal iodine output of two days per week during an intake of 200 µg of extra iodine daily. They include the basal iodine output of 80 ± 22 µg/d as determined in a preceding experiment during 7 days. In the first week, an average of 159 ± 36 µg iodine per day (about 40 % of the supplementary intake) were renally excreted, and in the eighth week an average of 219 ± 48 µg iodine (about 70 % of the artificial input). The basal iodine output averaged 80 ± 22 µg/d in the preceding experiment during 7 days. Eight weeks were obviously not sufficient to reach the sum of the normal daily iodine input of 80 µg plus 200 µg extra iodine intake. In the first week, only a total of 553 µg iodine (ca. 40 %) of the weekly supplementary iodide input of 7 x 200 µg was additionally excreted as compared to 931 µg in the eighth week, i.e. 67 % of the supplementary intake. This increase demonstrates both the pre-existing iodine deficiency and the gradual saturation of the thyroid with iodine.

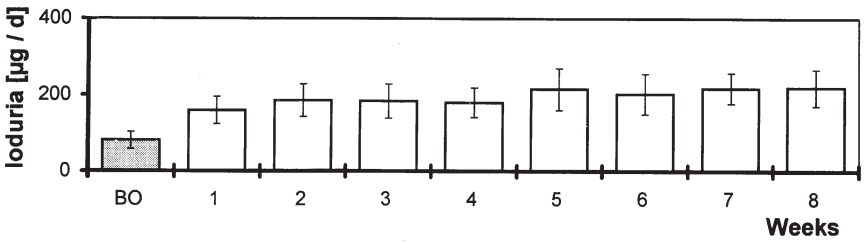

Fig. 1 Iodine output including the basal output (BO) of group A (200 µg iodine in the form of diiodotyrosine/day; n = 12) in the course of two days preceding the main experiments and on the period of the daily intake of 200 µg of iodide within 8 weeks. The basal output was assessed in the course of 7 days preceding the main experiments. Mean values of days 1 and 2 of each week and standard deviations are shown.

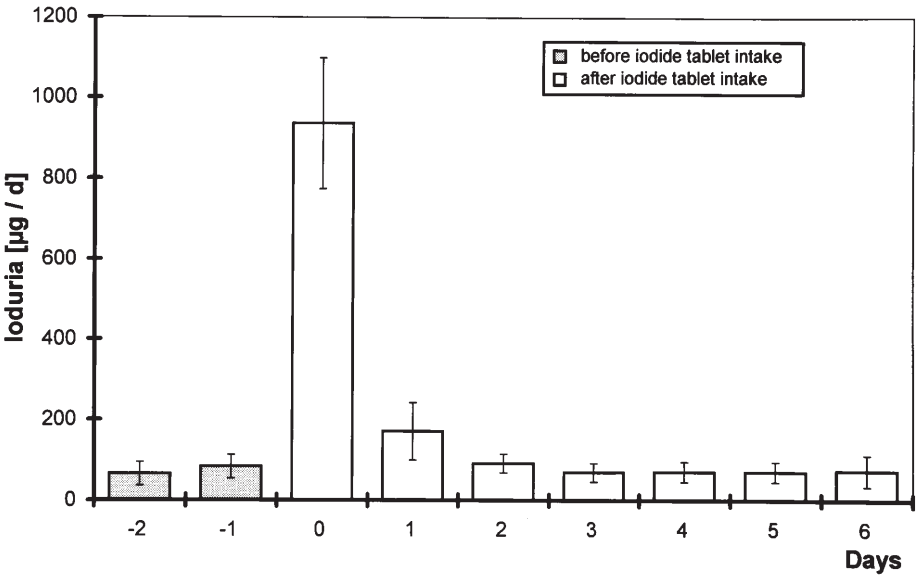

Fig. 2 Iodine output (including the basal output) in the 24 h urine of group B (1 500 µg iodide/week; n = 13) in the days preceding the main experiments (-2 and -1), on the day the first tablet of 1 500 µg of iodide was taken (day 0), and in the subsequent first week. Mean values and standard deviations are shown.

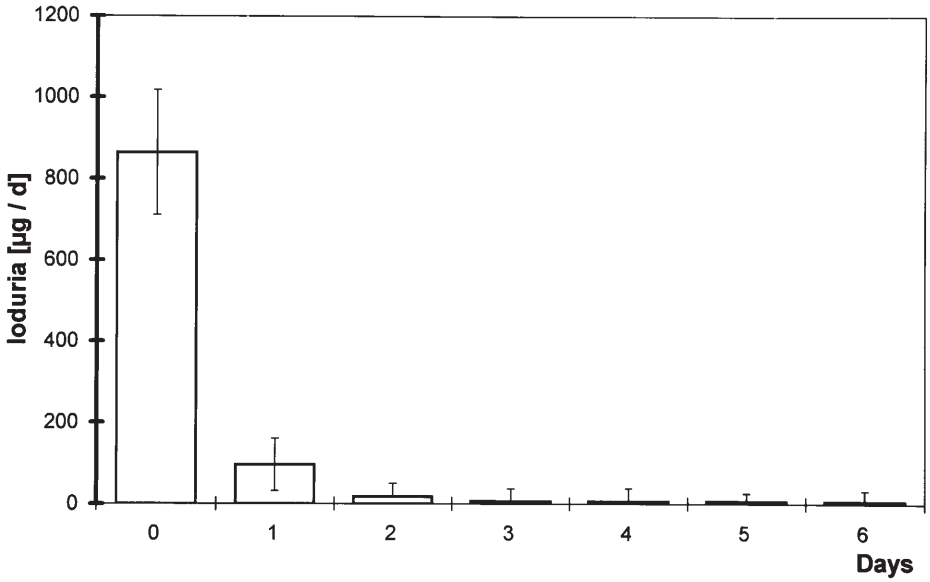

Fig. 3 Iodine output of group B (1 500 µg iodide/week) in the course of one week (first week of this study) after subtracting the average basal iodine output of 74 µg/d. Day 0 shows the average value not only of one week but of all eight weeks on the day of the tablet intake.

Test Group B (1 500 mg iodide weekly)

Fig. 2 shows the iodine output including the basal iodine output before and after taking 1 500 µg of iodide once a week (n = 13). Four days after taking the tablet the values were back to the pre-starting points.

The renal iodine output including the basal iodine output in the course of 8 weeks averaged 74 ± 23 µg/day before taking 1 500 µg and 938 ± 166 µg/day on the day the tablet was taken.

Fig. 3 shows the corrected iodine output per week after subtracting the average basal iodine output of 74 µg/d. These values demonstrate the additional iodine output as a result of taking one tablet per week under the chosen conditions. On the third day, the iodine output was already back to the base-line.

Summing up the corrected iodine outputs one can state that of the supplementary iodine input of 1 500 µg once a week, an average of only 963 µg per week (= 65 %) were excreted in addition to the basal renal iodine output.

(For this average iodine output only the corrected iodine output of days 0 and 1 was considered. According to figure 3 the iodine output after the first two days can be ignored.)

The comparison between the supplementary weekly iodine intake and the corrected iodine output of groups A (an equivalent of 200 µg iodine in form of diiodotyrosine/day or 1 400 µg iodine/week, resp.) and B (1 500 µg iodide/week) during the second half of the trial shows a mean urinary iodine excretion of 67 % in group A and 64 % in group B, respectively.

Discussion

After taking 1 500 µg of iodide, the renal iodine output first increases greatly and thereafter decreases very rapidly. This can be explained as follows: The half-life of the disappearance of iodide from the plasma amounts to approximately 4 hours (10). After absorption of iodide follows an outflux from plasma into the extravascular water space, the latter being about 10–15 times greater than the vascular water space. At the same time, renal iodide excretion starts.

The biological total-body half-life of iodine and the half-life of its extraction from storage in the thyroid is important for establishing an equilibrium between iodine intake and iodine output. The half-life of disappearance of iodide from the thyroid amounts to approximately 40 days (7). Thus, after about 6 weeks, a state of balance between iodine input and iodine output and a replenishment of the thyroid store can probably be expected. This coincides quite well with our observations because starting from week 4 in group A (200 µg iodine daily), the increase of urinary iodine output was reaching a limiting value in an asymptotic fashion. This fact shows at least the transition toward an equilibrium between iodine intake and iodine output. (A stable equilibrium takes probably more time than 8 weeks.)

According to the present results, there is no great difference between taking 1 500 µg iodide once a week and a daily intake of 200 µg iodine in the form of diiodotyrosine. Our results are in contrast to a calculation (5) favouring only a daily dose of 200 µg iodide. But this calculation has been contradicted (2, 7, 12).

The present study coincides well with the study of Saller et al. (11) who measured intrathyroidal iodine stores by means of X-ray fluorescence methods in some patients. These authors found that a regimen of 1 500 µg iodide weekly resulted in a similar iodide incorporation into the thyroid gland as compared to a regimen of 200 µg iodide daily.

Because diiodotyrosine is rapidly absorbed from the gastrointestinal tract combined with rapid and almost complete metabolic degradation by deiodination, diiodotyrosine is a suitable iodine carrier compound for therapeutic purposes (8). In particular diiodotyrosine is not toxic nor is its iodine volatile during storage. Some pharmaceutical quality aspects such as long term pharmaceutical stability make diiodotyrosine seem superior to iodide tablets (8).

Kahaly et al. (6) found no significant differences in urinary iodine between potassium iodide and diiodotyrosine after daily intake of either preparation. Both preparations demonstrate bio-equivalence and are adequate to correct iodine deficiency. In our studies, in both cases, approx. two third of the iodide input are excreted with the urine at any time within the observation period of 8 weeks. Assuming a balance between intake and output of iodine, the difference between the intake of iodide (100 %) and the ioduria (approx. 65 %) is probably caused by storage of iodine in the iodine-deficient thyroids and by retention of thyroid hormones and iodide in the blood and extravascular space. Some parts may also be excreted via faeces and perspiration. Anke et al. (1) ascribe a figure of approximately 30 % of the iodine output as occuring via faeces, including organically bound iodine, but this value was observed at a much lower level of iodine intake. As compared to our results of urinary iodine output an excretion of 30 % with the faeces alone seems to be very high.

Briefly, our study shows that both methods of treatment – 200 µg iodide daily or 1 500 µg once a week – seem to be equivalent in iodide supplementation when comparing the cumulative weekly excretions of iodine after a duration of treatment of 8 weeks. The choice of the treatment can therefore depend on the compliance of the patient. Peters et al. (9) recently showed that a once-weekly dose of 1 500 µg iodide is a reliable means of preventing a recurrence of endemic goiters in at least two third of patients.

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