Furosemide increases thyroid uptake of radiiodine in an anuric patient: First observation

To the Editor: Earlier studies demonstrated unexpected decrease of radiiodine (131I) renal excretion in patients adherent to low-iodine diet before 131I treatment while receiving furosemide [1,2]. This effect seems specific for humans, since it was not confirmed in a study on mice treated with low-iodine diet [3]. Other researchers [4-7] observed increase of 131I uptake to thyroid tissue or thyroid remnants, in patients receiving either furosemide or other diuretics after 131I. However, this increase in 131I uptake could be either due to increased radioactivity in blood, probably a simple diffusion of radioactivity from blood to thyroid, or to increased transport of 131I across thyroid cell membrane, stimulated by diuretics [8, 9]. Observations on a patient as described below suggested a clue to the above mechanism of increased 131I thyroid uptake.

This was a male patient, 34 years old, anuric, suffering from terminal renal failure and hemodialyzed thrice weekly for four hours per session, from June 2010 till today, November 2011. He was diagnosed as having papillary thyroid cancer metastatic to local and regional lymph nodes (pT3N1aMx). After total thyroidectomy, the patient was submitted to whole-body scintigraphy with 111MBq of 131I (using γ-camera e.cam, dual-head, variable angle, Siemens Medical Solutions, USA), which showed an area of radiiodine accumulation at the left side of thyroid bed (2.4% of the administered 131I was fixed to this area at 24h). In order to achieve complete thyroid ablation, 1.95GBq of 131I were given to the patient after being for 15-days on a low-iodine diet and having plasma TSH 45mIU/L. The patient’s consent for the whole procedure was obtained.

With an aim to remove unbound 131I from the patient’s body, the patient was hemodialyzed twice, 24h and 48h after the administration of 131I with separate and controlled collection of radioactive waste solutions. Thus, 73% of the administered 131I dose was eliminated, as calculated after measurements of radioactivity of the dialysis waste solution and in blood and by a survey-meter at 2-meters distance from the patient. Seventy-two hours after administration of 131I, whole-body scintigraphy was made using the same gamma camera. One zone of intense 131I accumulation was found in the thyroid bed, at the projection of right thyroid lobe.

About 18h from the radiiodine administration the patient experienced an episode of high blood pressure (160/100mmHg), and was given by accident (considering his anuric state) an intravenous injection of 20mg furosemide, the drug which is routinely used for treatment of hypertensive emergencies, due to its direct vasodilating and diuretic effect [10, 11]. Although the patient’s blood pressure dropped to 130/80mmHg, and no deterioration of patient’s health was noted, this event was reported to the hospital Quality Assurance Committee. In order to follow effects of furosemide on 131I, after obtaining consent from the patient nine 2mL samples of venous blood were drawn from the cubital vein at 15min intervals, till nine samples were collected and simultaneously radioactivity in the neck region was measured by a survey meter with pancake probe, leaning on the thyroid region. Obtained values of radioactivity were expressed as percentage of initial radioactivity of blood and thyroid region, recorded before administration of furosemide (Table 1 and Fig. 1).

As early as 15min after the administration of furosemide the drop of radioactivity was recorded in the blood and increase of radioactivity was noted in the thyroid region. All remaining 7 measurements of blood and thyroid radioactivity showed gradual decrease in blood radioactivity and increase in thyroid region (Table 1 and Fig. 1). Using Pearson’s test, we found high reverse correlation (r=-0.968) radioactivity in between changes in blood and in the thyroid region, with high statistical significance (P<0.001).

### Table 1. Radioactivity over thyroid region and blood radioactivity

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Thyroid region radioactivity (μR/h)</th>
<th>% of initial</th>
<th>Δ%</th>
<th>Blood radioactivity (cpm/mL)</th>
<th>% of initial</th>
<th>Δ%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>28080</td>
<td>100.0</td>
<td>0.0</td>
<td>134235</td>
<td>100.0</td>
<td>0.0</td>
</tr>
<tr>
<td>15</td>
<td>29070</td>
<td>103.5</td>
<td>+3.5</td>
<td>128748</td>
<td>95.9</td>
<td>-4.1</td>
</tr>
<tr>
<td>30</td>
<td>29270</td>
<td>104.2</td>
<td>+4.2</td>
<td>128040</td>
<td>95.4</td>
<td>-4.6</td>
</tr>
<tr>
<td>45</td>
<td>29780</td>
<td>106.1</td>
<td>+6.1</td>
<td>125059</td>
<td>93.2</td>
<td>-6.8</td>
</tr>
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<td>125744</td>
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<td>-6.3</td>
</tr>
<tr>
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<tr>
<td>120</td>
<td>29900</td>
<td>106.5</td>
<td>+6.5</td>
<td>125389</td>
<td>93.4</td>
<td>-6.6</td>
</tr>
</tbody>
</table>
Taking into account the above and the fact that the patient had terminal chronic renal failure with anuria, the interference of furosemide on the excretion of $^{131}$I form the kidneys could be excluded. Increased radioactivity in the thyroid region indicated increased blood flow through the thyroid bed due to vasodilation effect of furosemide. Direct stimulation of $^{131}$I uptake by the thyroid cells or inhibition of basolateral efflux of $^{131}$I through unspecific chloride channels could have been caused by furosemide. This is in accordance with results of others, who proposed specific stimulative action of furosemide on NaI symporter (NIS) or pendrine anion symporter (PDS) in rat [4] and human thyreocytes [5], and also an inhibitory action on chloride channels in vascular tissue [12]. The observed decrease of blood radioactivity could not be explained only by shift of $^{131}$I from blood to thyroid gland, since $^{131}$I pool in blood is much larger than in the thyroid gland. There could also be, certain transfer of $^{131}$I from blood to other tissues driven by the vasodilating action of furosemide, but this remains to be confirmed.

However, it still remained unsolved whether furosemide action on thyroid tissue is dependent on pre-treatment low-iodine diet. Studies on patients who were not compliant with low-iodine diet could clarify this issue.

In conclusion, in a male 34 years old, with papillary thyroid carcinoma, anuric with chronic renal failure, increased $^{131}$I uptake by the thyroid gland could be due to mechanisms related to the injected furosemide.

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Bibliography

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Figure 1. Radioactivity vs. time in thyroid region and blood