Submitted: 24.01.2023
Accepted: 26.01.2023
Early publication date: 27.03.2023

Endokrynologia Polska
DOI: 10.5603/EP.a2023.0017
ISSN 0423–104X, e-ISSN 2299–8306

Liquid levothyroxine in the treatment of myxoedema coma

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Key words: *hypothyroidism; myxoedema coma; liquid levothyroxine*

Myxoedema coma, also known as myxoedema crisis, is the most serious complication of untreated or highly inadequately treated hypothyroidism. Its most common symptoms include decreased mental status, hypothermia, and multiple organ disorders, mostly involving the cardiovascular and nervous system. Myxoedema coma is a life-threatening condition; therefore, early treatment initiation is extremely important. The recommended treatment involves intravenous administration of thyroid hormones, but due to infrequent occurrence of myxoedema coma, intravenous levothyroxine (LT4) is not always immediately available in Polish conditions (direct import, short expiration date of the drug). Thus, liquid levothyroxine administered through a gastric tube seems to be a good alternative.

This article presents 3 cases of patients with myxoedema coma and severe hypothyroidism who received liquid LT4 (Tirosint-SOL) [1–4] and achieved an increase in serum free thyroxine and resolution of the life-threatening condition associated with thyroid hormone deficiency.

Case 1

A 67-year-old woman hospitalized in the intensive care unit (ICU) for over a month was connected to a ventilator for respiratory failure in the course of SARS-CoV-2 infection. She was unconscious, had respiratory and circulatory failure, massive peripheral oedema, and progressive multiple organ dysfunction. The patient was transferred to the palliative care unit for patients with no prognosis for recovery. The patient had a history of schizophrenia, hypertension, and hypothyroidism diagnosed many years earlier.

Despite administering LT4 tablets at a dose of 100 μg/d through the gastric tube, the thyroid-stimulating hormone (TSH) level was 57.2 μU/mL (reference range: 0.27–4.2 μU/mL) and the free thyroxine (FT4) level was 5.41 pmol/L (reference range: 12–22 pmol/L). Low bioavailability of LT4 tablets administered by gastric tube in a critically ill patient with massive oedema and malabsorption was considered the cause of poor hormonal compensation.

The medication was switched to liquid LT4 at a dose of 150 μg/d administered through the gastric tube. After 2 weeks of treatment, TSH was 22.5 μU/mL, free triiodothyronine (FT3) was 2.85 pmol/L (reference range: 3.1–6.8 pmol/L), and FT4 was 9.84 pmol/L. The patient's condition was still serious, but it improved — she was conscious, able to answer simple questions, and was breathing partially on her own supported by passive oxygen therapy.

After another 2 weeks, further improvement in laboratory results (TSH — 18.6 μU/mL; FT3 — 3.63 pmol/L; FT4 — 14.5 pmol/L) was observed.

After another week, the patient was disconnected from the ventilator, and treatment with liquid LT4 at a dose of 125 ug/d was continued. In a follow-up assessment at 3 weeks, the TSH value was 1.57 uIU/mL. The patient was transferred from the ICU to rehabilitation ward.

Case 2

A 69-year-old man was admitted urgently to the endocrinology department from the emergency unit due to myxoedema coma. The patient had been less communicative for 2 days and lost consciousness on the day of admission.

At the beginning of hospitalization, the patient's condition was serious; he had respiratory failure, bradypnea, and shallow breathing with periodic apnoea up to 30 s. He was conscious but unable to communicate logically; he was very sluggish, and his speech was slurred and unintelligible. Physical examination showed systemic oedema and pale, dry, cold skin. His blood pressure was 138/57 mm Hg with a subsequent drop to 70/40 mm Hg,

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Case 2

Date	FT3 [pmol/L] N:3,1-6,8	FT4 [pmol/L] N:12,0-22,0	TSH [µIU/mL] N:0,270-4,200	Dose of liquid LT4 [µg/day]
01.05	< 0.95	< 0.42	29.88	200
02.05	1.16	2.58	17.80	200
04.05	1.48	6.24	-	200
06.05	1.82	8.30	18.90	125
09.05	1.71	8.54	-	125
10.05	1.97	9.58	-	125
16.05	1.96	10.5	18.80	125

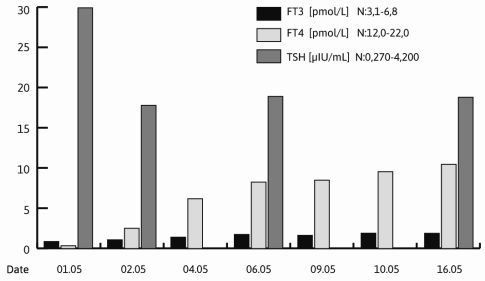

Figure 1. *Changes in thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) concentrations during the treatment with liquid levothyroxine in patient 2*

pulse about 50/min, temperature 33.2°C, and blood oxygen saturation (SpO_2) — 91–95% on oxygen therapy of 2 L/min through a nasal cannula. Laboratory results were as follows: TSH — 29.88 uIU/mL, FT4 < 0.42 ng/dL, FT3 < 0.95 pg/mL, cortisol level within the reference range (although inadequately low for the severity of the patient's condition), and high anti-thyroid peroxidase antibodies (aTPO). Moreover, hyponatraemia and hyperlipidaemia were detected. Chest X-ray revealed pulmonary congestion. Electrocardiography (ECG) showed sinus bradycardia (about 50 beats/min), AV 1 block, intermediate electrical axis, and intraventricular conduction disturbances without fresh ST-T ischaemic changes.

Due to unavailability of intravenous LT4, liquid LT4 was administered at a dose of 200 µg with hydrocortisone cover. Norepinephrine infusion was used to stabilize circulation.

After 5 days, the following results were obtained: TSH — 18.9 uIU/mL, FT3 — 1.82 pmol/L, FT4 — 8.3 pmol/L, and sodium — 144 mmol/L [reference range: 136–145mmol/L]. After another 10 days of the treatment, FT3 was 1.96 pmol/L, while FT4 was 10.5 pmol/L (Fig. 1).

The patient's general condition also improved. Treatment with liquid LT4 at a dose of 125 µg/d was continued.

Case 3

A 75-year-old woman with Graves' orbitopathy was admitted to the ICU after resuscitation due to a sudden cardiac arrest following orbital decompression surgery. The patient's condition was serious; she was unconscious, intubated, and mechanically ventilated. The patient had a history of hypothyroidism after ^{131}I therapy, atrial fibrillation, hypertension, type 2 diabetes, chronic coronary syndrome, chronic heart failure, chronic obstructive pulmonary disease, systemic atherosclerosis, mitral and tricuspid valve regurgitation.

Multidisciplinary integrated treatment was initiated (analgosedation, mechanical ventilation, cardiovascular stabilization). The patient was fed enterally, and this route was used to administer LT4 at an initial dose of 175 µg/d. Due to increasing clinical and laboratory features of hypothyroidism, the dose was increased, and then, in the absence of a satisfactory outcome, the therapy was switched from tablets to liquid LT4 at a dose of 200 µg/d. After the switch, thyroid hormones increased, TSH decreased, and finally, metabolic normalization was achieved. Despite the treatment, the patient could not be disconnected from the ventilator and was transferred to a long-term care facility.

In the presented cases of patients with myxoedema coma, rapid improvement of thyroid function was achieved after implementation of enteral liquid LT4. Considering not only the effectiveness [2–4] but also the number of ready-to-use doses and convenience of administration [5] in the aforementioned life-threatening situations, we suggest that liquid LT4 should be available in hospital pharmacies.

Acknowledgements
The authors would like to thank Proper Medical Writing and IBSA Poland Sp. z o. o. for their support in the preparation of this manuscript.

Funding
No funding was available.

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