



Wolff-Chaikoff effect in a newborn: is it an overlooked problem?

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Abstract Hypothyroidism is a serious endocrine disorder emerging from deficient production of thyroid hormone (thyroid gland agenesis or dysgenesis, or inborn metabolic defects of thyroid hormone production) or a defect in thyroid hormonal receptor activity. Prevention of iodine organification by means of using iodine-containing drugs or solutions is a protective mechanism for the body and is known as the Wolff-Chaikoff effect. This effect blocks thyroid hormone generation and is often transient, with thyroid hormone synthesis recovering in a few days or weeks. We present a neonate with transient thyroid dysfunction resulting from topical exposure to iodine-containing antiseptic solution. Our aim was to increase awareness that the use of antiseptic iodine solutions in neonates may result in transient hypothyroidism through the Wolff-Chaikoff effect and should be considered after the use of iodine-containing solutions or drugs.

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Insufficient thyroid hormone production can be the result of thyroid agenesis, dysgenesis, inborn metabolic defects of thyroid hormone production, or deficiency of thyroid-stimulating hormone (TSH)/thyrotropin-releasing hormone secretion. If diagnosis and treatment are delayed, mental and motor development will be severely impaired. Although prolonged jaundice, a large posterior fontanel, prolonged gestation, and umbilical hernia could be signs of congenital hypothyroidism, clinical findings are not obvious in the neonatal period, making screening tests essential for early diagnosis [1].

The most common causes giving rise to transient hypothyroidism include the presence of thyroid antibodies

caused by maternal autoimmune thyroid disease (Graves or Hashimoto) and exposure of the mother to antithyroid drugs (eg, propylthiouracil, methimazole) or iodine-containing solutions and other compounds (eg, lithium, amiodarone). Blockage of thyroid hormone synthesis as a result of iodine exposure is a protective mechanism for the body and is known as the Wolff-Chaikoff effect [2]. This effect blocks thyroid hormone generation and is often transient, with thyroid hormone synthesis recovering in a few days or weeks. Because congenital hypothyroidism requires lifetime thyroid hormone replacement and because hypothyroidism caused by the Wolff-Chaikoff effect is almost always spontaneously reversible, the identification of causes leading to transient hypothyroidism is essential. Here, we present a newborn whose thyroid functions were transiently repressed because of topical use of iodine-containing antiseptic solution during and after an umbilical cord hernia operation.

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1. Case

A newborn girl with a gestational age of 40 weeks was delivered to a 28-year-old healthy woman after an uncomplicated pregnancy. She was the first child of nonconsanguineous parents with no family history of thyroid or any other autoimmune disease. Her weight and length were at the 50th percentile, and she was brought to our hospital in his second postnatal hour with umbilical cord hernia. The patient's history revealed an abdominal protrusion detected by intrauterine ultrasonography in the seventh month of pregnancy. She was operated on the second postnatal day for umbilical cord hernia. During the operation, the abdominal and inguinal areas were scrubbed with the iodine-containing antiseptic solution for disinfection, and this process was continued once a day for 4 days postoperatively. During follow-up, the baby did not show any pathologic weight loss, and her physical examination was normal except for jaundice appearing on the seventh postnatal day.

Hemolysis was not noticed in the peripheral smear of the patient, and laboratory analyses provided the following results: hemoglobin, 15.5 g/dL; hematocrit, 43%; red blood cell count, $4.82 \times 106/\text{mm}^3$; white blood cell count, $10,700/\text{mm}^3$; and thrombocyte count, $314,000/\text{mm}^3$. Except for high levels of indirect bilirubin (total/direct bilirubin levels, 13.6/0.54 mg/dL), no pathologic findings could be detected in the biochemical analysis of the patient. The patient's blood group was O Rh+, the mother's blood group was A Rh+, and the direct Coombs' test was -. Sepsis workup was within the reference range, and a blood culture was negative. Blood and urine amino acids were normal, and reducing sugar in urine was negative. No treatment was given because the bilirubin did not reach higher levels. Indirect bilirubin levels decreased during follow-up and reached the normal level on the 12th day.

On the seventh postnatal day, thyroid function tests revealed normal triiodothyronine (T_3), together with low values of total thyroxine (T_4), free T_4 , and free T_3 , whereas TSH and urinary iodine excretion were increased. The

mother's thyroid function tests were normal and the thyroid antibodies were negative. In addition, family history of thyroid disease or any other autoimmune disease was also negative. Because of high urine iodine levels before starting treatment, a second serum was drawn for thyroid function tests and revealed normal serum TSH and thyroid hormone levels. During the 2-year follow-up, the patient was euthyroid with normal mental, motor, and physical development. The thyroid hormone values and urinary iodine levels of the patient can be seen in Table 1.

2. Discussion

The case presented here is a neonate who was operated on because of umbilical hernia on the second day of life and where slight indirect hyperbilirubinemia was observed on the 7th day.

The clinical findings are not obvious in the neonatal period. However, prolonged jaundice in association with umbilical hernia, as in our case, could be the warning signs of congenital hypothyroidism. That condition must be ruled out in a healthy newborn infant who has indirect-reacting hyperbilirubinemia beyond the first few weeks, whenever neonatal screening is not available. Thyroid-stimulating hormone screening for congenital hypothyroidism had not been performed in this baby because this is not a routine procedure in our country.

The actual function of thyroid gland is the synthesis of thyroid hormones (T_3 and T_4). Iodine deficiency or excess can both provoke disorders in thyroid functions [3,4]. Thyroid complications can result from excess iodide as in thyrotoxicosis, or hypothyroidism can be seen after iodine supplementation. In iodine-induced thyrotoxicosis, hyperthyroidism may occur several years after the initiation of iodine excess. On the other hand, in case of an excess of iodine, hormone generation is repressed through inhibition of iodine organification in thyroid gland. Prevention of iodine organification using iodine-containing drugs or solutions is a protective mechanism for the body and is known as the Wolff-Chaikoff effect [2].

It has been suggested that iodine exposure is the most common cause of neonatal transient hypothyroidism. The suppression of the thyroid by excess iodine in neonates may occur because of maternal or neonatal exposure [5]. Neonates are particularly sensitive to iodine excess because their skin is especially permeable, the iodine trapping process in the thyroid gland is very active, and the iodine renal clearance is low. In many cases, neonatal transient hypothyroidism is attributed to neonatal exposure of iodine-containing drugs or topical iodine-containing antiseptics (10% povidone-iodine solution) used routinely. It has been suggested that evaluation at birth of urinary iodine excretion in every newborn with high TSH could help in predicting a good prognosis, because hypothyroidism caused by the Wolff-Chaikoff effect is mostly spontaneously reversible [6].

Table 1 The thyroid function tests and urinary iodine amounts of the patient on the 7th day, 15th day, and at 2 years of age

	First measurement (PN 7th day)	First control (PN 15th day)	Second control (2 y)
TT ₃ (ng/mL)	2.66	1.60	1.56
TT ₄ (nmol/L)	6.28	91.34	9.3
FT ₃ (pg/mL)	<0.260	3.78	3.92
FT ₄ (pmol/L)	<0.300	15.23	13.5
TSH (mIU/L)	80.12	3.22	3.96
Iodine in urine (µg/L)	450	135	–

PN indicates postnatal; TT₃, total T₃; TT₄, total T₄; FT₃, free T₃; FT₄, free T₄.

It is not clear whether transient neonatal hypothyroidism (TNH) should be treated. Many reports in neonates with transient hypothyroidism concluded that transient hypothyroidism caused by the Wolff-Chaikoff effect is almost always reversible, even if short-term T₄ replacement therapy may be suggested [7,8]. In the study of Bartalena [9], 11 cases (17%) of hypothyroidism were found in the offspring (10 detected at birth and 1 in utero), resulting from 64 pregnancies in which amiodarone was given to the mother. Hypothyroidism was transient in all cases, and only 5 infants (45%) had been treated short term with thyroid hormones. In the study of Smerdely [10], the thyroid function of very low-birth-weight infants admitted to neonatal intensive care units where topical iodinated antiseptic agents were used was compared with infants where no iodinated agents were used. Low serum T₄ level and high thyrotropin concentrations were detected in 9 of 36 babies exposed to iodine, and L-T₄ treatment was started in 20% of the babies (decision to treat was based on clinical signs of hypothyroidism or the results of the routine newborn screening program) until the time of discharge from hospital. Thyroxine replacement therapy had been discontinued in all but 1 infant (because of persistent abnormalities in thyroid function) by discharge in this study. In conclusion, they suggested that there is little evidence for the efficacy or necessity of treatment of transient neonatal hypothyroidism, and they did not advocate it on the basis of this study. They also state that further studies are needed to address this issue.

Thyroid function tests were repeated a week later in our case before considering treatment, because of high urine iodine levels despite hypothyroidism and revealed normal thyroid function tests. The significance of TNH on psychomotor development in infants remains unknown, but a delay in the diagnosis and treatment of primary hypothyroidism causes severe neurologic and intellectual impairment. Markou et al [7] suggested that patients who develop transient iodine-induced hypothyroidism must be followed long term because many will develop permanent

primary hypothyroidism. The presented baby is now 2 years old with normal growth, development, and thyroid function tests.

This case was meant to emphasize that iodine-containing antiseptic solutions used in neonates may cause transient hypothyroidism because of the Wolff-Chaikoff effect, and that the routine use of iodine antiseptics in newborn infants should therefore be avoided. Even though this effect is usually transient and disappears in days or weeks, short-term hormone replacement treatment and long-term follow-up can be necessary in some cases once the iodine exposure is removed, as in our patient.

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