



ORAL PATHOLOGY IN OVERT THYROID DISEASES

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Thyroid hormones play an important role in the metabolic functions, regulation of growth and body development, including that of the oral cavity. Deficiency or excess of these hormones may have implications in the oro-dental pathology. Oro-dental pathology in patients with congenital hypothyroidism includes changes of hard and soft tissues. The hard structures changes include vertical facial growth, small size of the jaw, delayed eruption of primary and permanent dentition, structural dental alterations (open apex permanence, short root appearance and large pulp chambers secondary to slow dentin formation), enamel alterations and malocclusion. Changes of the soft structures of the oral cavity include hypertrophy of the lips, macroglossia (generated by subcutaneous mucopolysaccharides accumulation that can cause dental deformities), “geographic” tongue and salivary glands enlargement. In patients with overt hypothyroidism the most common oro-dental manifestations are: delayed teeth eruption, poor periodontal health, altered tooth morphology, increased bleeding and decrease wound healing, macroglossia while in overt hyperthyroidism we may find increased susceptibility to caries and periodontal disease, maxillary and mandibular osteoporosis. Both the endocrinologist and the dentist need to be familiar with the oro-dental implications of thyroid diseases and must have a good communication to maintain patient’s oral health.

Key words: congenital hypothyroidism, overt hypothyroidism, overt hyperthyroidism, oral cavity pathology.

INTRODUCTION

Thyroid hormones play an important role in the metabolic functions, regulation of growth and development including that of the oral cavity. Deficiency or excess of thyroid hormones may have implications in the oro-dental pathology. Thyroid deficiencies are a common endocrine disorder. Epidemiological studies revealed that the prevalence of thyroid disorders varies depending on the etiopathogenic form. The incidence of congenital hypothyroidism is estimated at 1 newborn in 3.500–4.000 births¹. The disease generates significant changes in the oral cavity in the absence of early diagnosis and treatment. The spontaneous overt hypothyroidism is more common in women than men and the prevalence ranges 0.6 and 12 per 1000 women and 1.3 and 4 per 1000 men. The prevalence of hyperthyroidism (the most common causes are Graves' disease and toxic multinodular goitre) in women ranges

between 0.5 and 2% and is estimated to be 10 times more common in women than men¹.

CONGENITAL HYPOTHYROIDISM

Congenital hypothyroidism is a disease characterized by thyroid hormone deficiency present at birth. This condition, similar to other thyroid diseases, seems to be more prevalent between females than males with a ratio of almost 2 to 1. The etiology of the disease includes primary (dysgenesis of gland or alteration of hormonal synthesis), secondary (deficiency of thyroid stimulating hormone-TSH) or peripheral (defects of thyroid hormone transport, metabolism or action) causes. The most common neonatal signs and symptoms are lethargy, prolonged jaundice, hypotonia, protuberant abdomen with umbilical hernia, constipation, large fontanelles, macroglossia².

Screening, diagnosis and management of congenital hypothyroidism. Strategies for detecting congenital hypothyroidism have been introduced in many countries. Consensus guidelines of the

European Society for Pediatric Endocrinology on screening, diagnosis and management of congenital hypothyroidism recommend TSH determination as it is the most sensitive test for the diagnosis of primary congenital hypothyroidism. Blood sample is usually collected by heel prick, spotted on filter paper and transmitted to specialized laboratories. A value of TSH ≥ 40 mU/L requires the early initiation of specific therapy; if concentration of TSH is ≤ 40 mU/L, it is recommended to determine the venous concentration of free thyroxine (FT4); if FT4 level is below norms, treatment should be started with thyroxine supplementation. Imagistic methods of diagnosis (scintigraphy, ultrasound) may be useful for the definitive diagnosis of congenital hypothyroidism. After diagnosis confirmation, treatment should be initiated no later than two weeks of life with levothyroxine, initial dose of 10–15 $\mu\text{g}/\text{kg}/\text{day}$ ³.

Oro-dental pathology in patients with congenital hypothyroidism include changes of hard and soft tissues. Hard structures changes include vertical facial growth, small size of the jaws, delayed eruption of primary and permanent dentition, structural dental alterations (open apex permanence, short root appearance and large pulp chambers secondary to slow dentin formation), enamel alterations, malocclusion, etc. At the level of soft structures of oral cavity one can notice hypertrophy of the lips, macroglossia, generated by subcutaneous mucopolysaccharides accumulation that can cause dental deformities, geographic tongue and salivary glands enlargement^{4,5,6}. Management of oral pathology in congenital hypothyroidism requires collaboration between dentist and endocrinologist. Under the conditions of early initiation of substitution treatment, no special requirements are necessary for dental treatment except to treat macroglossia and malocclusion⁷. Treatment of macroglossia in patients with congenital hypothyroidism is medical (thyroxine supplementation); in the absence of a favorable response the surgical therapy of congenital macroglossia is recommended according to Núñez-Martínez PM *et al* in three situations: “*the presence of functional deficits (impaired swallowing, articulation of speech, sialorrhea or airway obstruction); dental alterations due to macroglossia; psychological impact due to the physical appearance of the patient, which gives a false impression of mental disability*”⁸. Malocclusion should be corrected with orthodontic therapy⁹. The review of the medical literature showed no specific features of malocclusion treatment in patients with congenital hypothyroidism.

OVERT HYPOTHYROIDISM

Overt hypothyroidism is defined by decrease of thyroid gland function highlighted by a decrease in thyroid hormone production (low FT4 and/or free triiodothyronine-FT3) and TSH levels above upper reference limit¹⁰. Overt hypothyroidism is associated with specific signs and symptoms: dry skin, bradycardia, weight gain, fatigue, intolerance to cold, constipation, slowing of motor activity¹¹. Potential complications of overt hypothyroidism are represented by cardiac diseases, dyslipidemia, infertility, difficulty in conceiving, psychological dysfunction and myxedematous coma¹².

Oro-dental manifestations in patients with overt hypothyroidism include: delayed eruption, poor periodontal health, altered tooth morphology, increased bleeding and decreased wound healing, macroglossia, etc.^{13,14}.

The Clinical Practice Guidelines for Hypothyroidism in adults published in 2012 in the journal *Thyroid*, recommends that monotherapy with levothyroxine is the standard treatment of hypothyroidism. The daily dose of levothyroxine should consider different factors like age, sex and body weight¹⁵. The etiology of hypothyroidism influences the thyroid hormonal replacement dose; patients with total thyroidectomy (surgically induced or by radioactive-iodine ablation) require higher doses than those with residual functioning thyroid tissues¹⁶. Rosenbaum RL and Barzel US have studied the dose of levothyroxine needed for complete replacement in relation to age¹⁷. In the study were included 67 patients with primary hypothyroidism: 23 with average age 75.7 years (group 1) and 44 with average age 48.1 years (group 2). Patients in group 1 needed an average 118 $\mu\text{g}/\text{day}$ whereas the patients of group 2 needed 158 $\mu\text{g}/\text{day}$. The authors concluded that the thyroxine requirement decreases with age, possibly due to a reduction in thyroxine degradation rate¹⁷. Similar results have been reported by Sawin CT *et al*. after analysis of the daily dose of thyroxine needed in order to achieve TSH level within the normal range in 84 patients with primary hypothyroidism, aged between 23 and 84 years¹⁸. In contrast to the previous mentioned studies, Devdhar M *et al* in a study in which they were included 248 patients with primary hypothyroidism (69 men and 179 women) found that differences in daily dose of levothyroxine replacement are secondary to gender and body weight but not age¹⁹. The relationship between sex and levothyroxine

dosage requirement was investigated in several studies. A prospective study performed by Jonklass J which included 50 patients (37 women and 13 men) with total thyroidectomy, the doses were higher in women compared to men²⁰. Similar results were presented by Devdhar M *et al.*: men had a lower dose of levothyroxine replacement than women (1.62 µg/kg vs 1.92 µg/kg)¹⁹. Levothyroxine dosage requirements were investigated in various regimes based on weight, body mass index, lean body mass^{21–25}. Most studies reviewed showed that lean body mass predict optimal thyroid dosing in patients with primary hypothyroidism.

The following conditions must be considered in oral manifestation management of hypothyroidism:

- increased bleeding and decrease wound healing are generated by the presence in excess of mucopolysaccharides which decrease the ability of small blood vessels to constrict. In a review published in 2011 Chanda S and Bathla M entitled “*Oral manifestations of thyroid disorders and its management*” the authors suggest that “*local pressure for extended time will probably control the bleeding from the small vessels adequately*”⁶.
- patients with hypothyroidism may have susceptibility to infections due to decreased activity in fibroblasts⁶.
- cardiovascular disease is a frequent complication of hypothyroidism; antibiotic prophylaxis may be necessary in case of valvular pathology or arrhythmias before invasive procedures^{6, 26}. In case of uncontrolled cardiac disease any invasive dental treatment should be postponed for more than 6–12 months²⁷.
- surgical procedures in patients with hypothyroidism may precipitate the appearance of myxedematous coma. In these conditions it is imperative to discontinue the dental treatment²⁷.

HYPERTHYROIDISM

Overt hyperthyroidism is defined by increase of thyroid gland function highlighted by suppressed TSH with elevated FT4 and/or FT3. Overt hyperthyroidism is associated with specific signs and symptoms including weight loss, tachycardia, tremor, proximal muscle weakness, anxiety, irritability, hyperactivity, heat intolerance. Complications of overt hyperthyroidism are represented by the “thyroid storm” which is a major medical emergency, cardiac abnormalities

(atrial fibrillation, congestive heart failure, etc.), osteoporosis^{28, 5, 29, 20, 31, 32}.

Oro-dental manifestations in patients with overt hyperthyroidism include increased susceptibility to caries and periodontal disease, maxillary and mandibular osteoporosis⁶.

The 2018 European Thyroid Association Guideline for the Management of Graves’ Hyperthyroidism mentions that the reduction in hormone production can be achieved by using antithyroid drug or by the reducing of the thyroid tissue with radioactive iodine or thyroidectomy³³. The main antithyroid drugs are thionamides, respectively methimazole, carbimazole, propylthiouracil. In Romania the most used a antithyroid drug is methimazole. Treatment can be initiated with an initial dose of 10–30 mg/day methimazole, 15–40 mg/day carbimazole or 100 mg every 8 h propylthiouracil. The initial dose of antithyroid drugs can be gradually decreased depending on the improvement of symptoms and specific hormonal determinations³³. The same guide suggests that the optimal duration of antithyroid drug treatment is 12–18 months. Adverse events of treatment with antithyroid drug includes allergic reaction, hepatitis, lupus-like syndrome and agranulocytosis^{33–37}. Patients with recurrence after treatment with antithyroid drug or those who have adverse reactions on therapy can benefit from radioactive iodine or thyroidectomy.

Management of oro-dental manifestations in patients with overt hyperthyroidism should bear mind that antithyroid drugs can generate agranulocytosis with oral infection and hypoprothrombinemia associated with bleeding. Agranulocytosis (absolute neutrophil count $<500 \times 10^6/l$) is a very rare side effect generated by the therapy with antithyroid drugs which affects about 0.5% of patients. Agranulocytosis usually occurs within two months of initiation of the antithyroid drug therapy without age or gender differences, but this complication was proven to be related to dose. Agranulocytosis may install slowly or explosively and can be complicated by severe infections, being potentially fatal. Most infections interest the oropharyngeal region. In the most common situation, clinical diagnosis at presentation are acute pharyngitis and other infections in the oral cavity. The buccopharyngeal mucosa may present erythema, ulceration or necrosis; periodontal, periapical and oral mucosa infection usually aggravate quickly. Based on this side effects, patients need to stop medication and consult a specialist doctor especially in case oropharynx

infection with fever^{5, 38-42}. Treatment of agranulocytosis induced by antithyroid drugs require administration of intravenous broad-spectrum antibiotics, glucocorticoids and granulocyte colony stimulating factor^{40, 43-45}. In this state dental treatment is not a priority.

Patients with hyperthyroidism have a greater risk of bleeding after invasive dental treatment. Propylthiouracil has anti-vitamin K properties than can cause hypoprothrombinemia with bleeding⁵. Patients with hyperthyroidism and hypertension require longer duration of local pressure to stop bleeding⁶. In case of signs and symptoms of thyrotoxicosis epinefrine is contraindicated. In a previous mentioned review by Chanda S and Bathla M, the authors point out the fact that patients with hyperthyroidism have increased levels of anxiety and surgery can precipitate a thyrotoxic crisis and mention that “*Epinephrine is contraindicated, and elective dental care should be deferred for patients who have hyperthyroidism and exhibit signs or symptoms of thyrotoxicosis*”⁶.

CONCLUSION

The oral cavity is affected by the deficiency or excess of thyroid hormones. Both the endocrinologist and the dentist need to be familiar with the oro-dental complications of thyroid diseases and must have a good communication to maintain patient's thyroid and oral health.

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