CLINICAL AND PATHOLOGICAL OBSERVATIONS AND TREATMENT OF CONGENITAL GOITRE IN KIDS

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Abstract

Clinical, pathological and biochemical findings were described in stillborn and live kids affected with congenital goitre. The observations involved 5 stillborn kids with goitre, 5 stillborn kids without goitre, used as control, and 7 live kits with goitre. Grossly, the thyroid glands were visible and palpable in both dead and live kids. Histopathologically hyperplastic goitre was observed in 3 kids and colloid goitre was diagnosed in 2 kids. Plasma T3, T4, FT3 and FT4 levels were determined in survived kids. T3 and FT3 levels were very high and T4 and FT4 levels were found to be very low. Alive kids treated with Levothyroxine sodium showed a marked reduction in the size of the thyroid glands after two month treatment and their hormone levels were close to the normal ones. Twins or triples were observed to be predisposed to congenital goitre. All the stillborn kids were twins or triplets and were usually found dead. On the other hand, single born kids survived and showed normal growth rate.

Key words: kid, congenital goitre, pathology, thyroid hormones, treatment.

The synthesis of thyroid hormones are unique among the endocrine glands because the final assembly of the hormones occurs extracellularly within the follicular lumen. Thyroglobulin is a high molecular weight glycoprotein synthesized in successive subunits on the ribosomes of the endoplasmic reticulum in follicular cells (7). Non-neoplastic and non-inflammatory enlargement of the thyroid gland, commonly known as goitre, can develop in all domestic mammals, birds and other submammalian vertebrates. The major pathogenic mechanisms responsible for the development of thyroid hyperplasia include iodine-deficient diets, goitrogenic compounds that interfere with thyroxinogenesis, excess of dietary iodine, and genetically determined defects in the enzymes responsible for biosynthesis of thyroidal hormones. All these mechanisms result in inadequate thyroxine synthesis and decreased blood concentrations of thyroxine (T4) and triiodothyronine (T3). This is detected by the hypothalamus and pituitary gland, stimulating an increase in thyroid stimulating hormone (TSH) production, which results in hypertrophy and hyperplasia of follicular cells of the thyroid (7, 8). The goitre is caused by the thyroid gland enlargement as it tries to produce the thyroid hormones needed by the animal. Thyroid hormones T3 and T4 are very important for maintaining control over metabolism. Shortages or excesses of T3 or T4 have very pronounced effects on the affected animal (9).

Most cases of congenital hypothyroidism are associated with multiple late-term abortions, stillbirths or early postnatal deaths (5, 9). Of the animals born alive, some are weak and partly hairless with subcutaneous oedema of head and neck. Animals born by dams being on iodine deficient diets are more likely to develop severe thyroid hyperplasia and have clinically evidence of hypothyroidism (8). In most cases, the only gross lesion evident in aborted or neonatal animals is a bilateral enlargement of the thyroid glands. Because of the variation in the size and appearance of normal thyroid glands, histopathology must be used to confirm goitre in most cases (7). The enlargement may be due to thyroid tissue hyperplasia or to an increased amount of colloid distending the follicular lumens (9). Primary goitre is caused by deficient dietary iodine intake. Secondary goitre is caused by interference with dietary uptake of water with high content of calcium, nitrates, goitrogenic plants (Brassica sp. and some clovers), and, in rare cases, of excessive amount of iodine (6).

The objective of this study is to gain more information on pathological findings and thyroid hormone levels in kids with congenital goitre for which limited information is available. A possible treatment of kids, showing goitre deficiency of T4 and FT4, with Levothyroxine sodium, which is commonly used in man, was also studied.

Material and Methods

The thyroid glands of 5 stillborn kids with goitre were pathologically examined. All the animals were multiple foetuses and one of the cases involved triplets, while the other involved twins. The thyroid
glands of 5 stillborn kids (one case twins and one case triplets) without clinical goitre were used as control. All the kids come from villages near Burdur. They were reared in small groups (two or three) or as single animals in the backyard like pet animal, not in a herd. For that reason they were fed human food (for example cabbage) very often.

During necropsy tissue specimens were fixed in 10% neutral-buffered formalin solution for histopathologic examination. Formalin fixed tissues were processed routinely, sectioned at 4 µ and stained with haematoxylin and eosin (HE). Then the tissue sections were evaluated microscopically. Blood samples were collected from 7 survived kids with goitre from the jugular vein with the use of heparin as an anticoagulant and plasma samples were sent for biochemical analyses. T₃, T₄, FT₃ and FT₄ analysis were performed using Elecsys 2010 equipment and reagents.

The survived kids were treated with Levothroxine sodium (Levotiron tablet - 0.1 mg - Abdi İbrahim Company). This medicine was administered per os in a dose of 0.05 mg/d/kid for 1 month, and then in a dose of 0.1 mg/d/kid for farther month. The T test from the SPSS statistical programme was used to determine the significance of differences in the T₃, T₄, FT₃ and FT₄ levels in plasma before and after treatment.

Results

Thyroid lobes in stillborn kids with congenital goitre were symmetrically enlarged at birth due to an intense, diffuse hyperplasia. The subnormal growth rate was also seen in these kids and absence of normal wool development was observed in 2 of them. While the kids born as twins or triplets were usually dead, kids born as single generally survived. Only 1 alive kid was twin and co-twin was stillborn. The survived kids had completely normal growth rate, normal wool development and appearance except bilateral swelling of the thyroid glands (Fig. 1). Slight shortage of forelimbs due to bone abnormality was observed in 1 kid. Congenital goitre was diagnosed macroscopically and histopathologically in all 5 foetuses showing severe bilateral swelling of the thyroids (Fig. 2). Macroscopically, thyroid measurements ranged from 7.5x5x1.5 cm to 6.1x4.3x1.2 cm, both lateral lobes and isthmus were uniformly or lobularly enlarged without any nodular lesions nor cystic follicles in the affected gland, weighing more than 36 g. They were firm to the touch and their surface as well as the cut surface were of reddish brown or dark red colour.

![Fig. 1](image1.jpg)

Fig. 1. One-month-old survived kid with congenital goitre.

![Fig. 2](image2.jpg)

Fig. 2. Stillborn twin kids with congenital goitre.

Microscopically, hyperplastic goitre was diagnosed in 3 triplet kids, while colloid goitre was observed in 2 twins. At the hyperplastic goitre cases intense hypertrophy and hyperplasia of follicular cells lining thyroid follicles, with the formation of papillary projections in to the lumens of collapsed follicles, containing little or no colloid, were observed (Fig. 3). The follicles were seen irregular in size and shape because of varied amounts of lightly eosinophilic and vacuolated colloid. The lining epithelial cells were columnar with deeply eosinophilic cytoplasmcs and small hyperchromatic nuclei that were often situated in the basal part of the cells. The follicles were lined by single or multiple layers of hyperplastic follicular cells in most of the follicules. At the colloid goitre cases follicles were progressively distended with densely eosinophilic colloid. The follicular cell lining the macrofollicles were flattened and atrophic. The interface between the colloid and luminal surface of follicular cells was smooth and lacked the characteristic endocytotic vacuoles of actively secreting follicular cells. Histologic examination of the thyroid glands from control kids revealed normal glandular architecture characterized by spherical colloid-filled follicles lined by cuboidal cells.
Before treatment the size of the thyroid glands was changing from 6.1x4.3x1.2 cm to 7.5x5x1.5 cm. After 2 month treatment thyroid glands became smaller (2.8x1.2x0.5 cm to 3.2x1.5x0.8 cm), but they were still bigger than normal glands. The levels of T₃, T₄, FT₃ and FT₄ before and after treatment are shown in Table 1. While T₃ and FT₃ levels were much higher than normal, T₄ and FT₄ were much lower than normal before treatment. The level of these hormones became more or less normal after 2 months of the treatment. Statistical analysis results of hormone levels before and after treatment showed that differences were found to be significant (P<0.001).

<table>
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<th>No. of kid</th>
<th>T₃ nmol/l</th>
<th>T₄ nmol/l</th>
<th>FT₃ pmol/l</th>
<th>FT₄ pmol/l</th>
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<td>18.24*</td>
<td>31.98*</td>
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<tr>
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<td>48.22**</td>
<td>11.73**</td>
<td>18.31**</td>
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<td>11.92**</td>
<td>19.52*</td>
<td>33.01*</td>
<td>3.01*</td>
</tr>
<tr>
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<td>9.72**</td>
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<td>18.31*</td>
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<td>43.75**</td>
<td>13.25**</td>
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* before treatment; ** after treatment

**Discussion**

Hyperplastic goitre is an enlargement of the thyroid gland resulting from hyperplasia of thyroid follicular cells. Follicular cells synthesise and secrete thyroglobulin, which combines with iodine to form the metabolically active thyroid hormones - triiodothyronine and thyroxine. These hormones are then stored as colloid in the lumen of the follicles. Low plasma T₃ and T₄ concentrations induce secreting of neurohypophyseal peptide thyroid-releasing hormone (THR) from the hypothalamus, which stimulates the release of TSH from the pituitary gland. Under the stimulation of TSH, the follicular cells endocytose the follicular colloid and release T₃ and T₄ into systemic circulation. Prolonged stimulation by TSH causes hypertrophy and hyperplasia
of follicular cells, and hyperplastic goitre (7). Colloid goitre represents the involutionary phase of diffuse thyroid hyperplasia (8). Both hyperplastic and colloid goitre were observed in this study. While hyperplastic goitre was diagnosed in twins, colloid goitre was observed in triplets. The results are similar to the findings of previous studies (7-9, 11, 13, 15).

Assane and Sere (2) reported that the thyroxine plasma level was higher in single than in twin lambs. Multiple foetuses (twins or triplets) were observed to be predisposed to congenital goitre. All stillborn cases were multiple foetuses, one of the cases in this study involved triplets, while the other involved twins. The possible cause of this predisposition can be attributed to severity of iodine deficiency in multiple foetuses. Because single foetuses reared by the same owner were observed to be healthy. Although various domestic animals can be affected with goitre, it is common in lambs and calves that goitre is frequently associated with such perinatal diseases as abortion, stillbirth, alopecia, mixoedema or birth of weak young (7, 13). While mixoedema and hair abnormalities were observed in some foetuses, others were of normal appearance in this report.

Thyroid hormones (T3 and T4) are secreted by the thyroid and have a strong influence on the metabolism of carbohydrates, proteins and lipids by favouring intestinal absorption of glucose and deposition in muscular and adipose tissue. They increase essential amino acid absorption, reduce plasma cholesterol and increase absorption of low density lipoproteins (1).

The halogen iodine is an indispensable nutrient that is an essential component of thyroid hormones. It has no other function. Largely ingested as iodides, it is rapidly transported to the thyroid gland, where it is oxidized by tyrosine to form monoiodothyrosine, diiodothyronine, triiodothyronine (T3), and tetraiodothyronine (T4; thyroxine). Thyroglobulin or colloid, is the storage form of these hormones (9). Takahashi et al. (14) reported low serum T4 levels and high serum T3 levels in calves with congenital goitre. Similar findings were observed in this study.

In addition to simple deficiency, a number of dietary substances exist, referred to as goitrogens, which interfere with various steps in iodine metabolism and thyroxine synthesis and release. The effect of goitrogens, which are analogous to iodine deficiency, can be mediated through interference with the uptake of iodine by the thyroid, interference with oxidation of iodate to iodine by thyroid peroxidase and its subsequent organification, interference with hormone secretion, increase metabolism of thyroid hormone, and interference with monodeiodinase, which converts T4 to T3. As seen in Table 1, although the T3 levels were very high, T4 levels were lower compared with normal in this study because of the iodine deficiency due to goitrogenic food intake.

The normal mean value of the plasma T3 level is 0.74 - 1.12 nmol/L and T4 level is 56.8 - 73.35 nmol/L in small ruminant (1, 4). Normal level of FT3 (3.67-5.11 pmol/L) and FT4 (13.38 - 18.53 pmol/L) were reported by the authors (4). Andrewartha et al, (3) reported that less than 50 nmol/l of thyroxine concentration was a very important sign of goitre. In the present study we also observed similar findings. Thyroxine levels were 17.31 - 19.95 nmol/L and were found to be very low. Differences in thyroid hormone levels before and after treatment were also found to be statistically significant.

Iodine deficiency is easily diagnosed if goitre is present but the occurrence of stillbirths without obvious goitre may be confusing (6). It is therefore important to submit the thyroid glands for histopathological examination in all cases of late term abortion, stillbirth, or neonatal death.

The thyroid stimulating hormone promotes the release of thyroxin from the thyroid gland. It also increases the rate of binding the iodine within the thyroid. The release of thyroxin serves as a general metabolic control, with higher levels of thyroxin producing an increased metabolic rate. Goitre can be brought about by either hyper- or hypothyroid conditions. The most common cause in animals is a deficiency of iodine, making the animal hypothyroid. Many foodstuffs have goitrogenic effects and inhibit the activity of the thyroid. Vegetables such as cabbage, soybeans, lentils, linseed, peas, peanuts and all of the cruciferous (mustard-like) plants possess goitrogens such as thiocyanate and goitrin which is especially prevalent in the Brassica family. They interfere with the process of trapping iodine by the thyroid, and their effects can be counteracted by increasing levels of iodine in the ration (7). Goitre is caused by iodine deficiency in utero due to grazing goitrogenic plants by dam (10). The cause of the goitres in the goat kids examined in this study was determined to be food-related iodine deficiency. In all cases the pregnant does had been fed goitrogenic plants like cabbage by their owners. We advised to owners to add potassium iodate to the feed if the dams are fed cabbage when they are pregnant. No congenital goitre case was observed after this treatment. Wither (15) also reported similar treatment in cattle.

Levothyroxine sodium is commonly used to treat goitre in humans, especially if the T4 level is low (12). It is also used in hypothyroidism in dogs (16). This medicine was found effective for goat goitre with low T4 level but it is very important to analyse the blood thyroid hormones level before treatment. After the kids started to eat a normal feed, the treatment should be stopped. This medicine was found to be useful not only to increase the T4 and FT4 levels but also to decrease T3 and FT3 contents.

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References


