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International Journal of Pediatrics and Neonatal Health

Research Article ISSN 2572-4355

Hyperthyroidism of the child in Abidjan (Côte d'Ivoire). Retrospective study of 27 cases

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Abstract

Introduction: Hyperthyroidism is a rare endocrinopathy of various causes, severe and poorly documented in children from Saharan Africa.

Objective: Describe the epidemiological, diagnostic, therapeutic and prognostic aspects of child hyperthyroidism to improved prognosis. Materials and methods: This was a retrospective, descriptive and analytical study carried out in the pediatric department of the University and Teaching Hospital of Treichville from January 2012 to December 2016. It included all children aged 0 to 15 years hospitalized for hyperthyroidism diagnosed on clinical grounds and biological. The variables studied were the epidemiological, diagnostic, therapeutic and issue aspects.

Results: We recorded 24,000 admissions, where 27 cases was of hyperthyroidism, so let say 1 case per thousand admissions. Hyperthyroidism involved 22 girls and 5 boys. Age was between 11 and 15 years in 89% of cases. The main signs were tachycardia (100%), goitre (100%), exophthalmia (89%), weight loss (81.5%), dyspnea (63%) and tremor (44%). T3, T4 levels were above normal in 99% of cases. TSH was low in 96% of the cases. The causes were Graves-Basedow disease (81.4%), toxic adenoma (11.1%), multinodular goitre (3.7%) and thyroiditis (3.7%). Synthesis of antithyroid drugs was marked by remission (52%), discharge against medical advice (33%) and death (15%). The age of more than 10 years (P = 0.031) and the synthetic antithyroid attack dose ≥ 1 mg / kg / day (P = 0.023) were significantly associated with remission.

Conclusion: The hyperthyroidism rare pathology of the child, affects especially the teenager with a female predominance. Graves-Basedow disease remains the most common etiology. The treatment is based on synthetic antithyroid drugs (ATS). Thyroidectomy is a therapeutic alternative. To improve the forecast, we needs a close cooperation between the pediatrists, the endocrinologists and the surgeon-pediatrists

Keywords: Child, Hyperthyroidism, Exophthalmos, Basedow's Disease, Cote d'Ivoire

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Citation: Richard Azagoh-Kouadio et al. (2018), Hyperthyroidism of the child in Abidjan (Côte d'Ivoire). Retrospective study of 27 cases. Int J Ped & Neo Heal. 2:3, 38-42.

Received: February 24, 2018

Accepted: March 05, 2018

Published: March 28, 2018

Introduction

Hyperthyroidism is an endocrinopathy characterized by hypersecretion of thyroid hormones T3 and T4. The prevalence in children varies between 0.5 and 2% of the world population [1]. In Africa sub-Saharan, particularly in Côte d'Ivoire, the incidence of this condition is poorly understood at the national level. However hospital series performed in internal medicine departments [2, 3] have reported cases in adolescents. These pediatric cases demonstrated a delayed diagnosis, at the stage of cardiovascular and neurological complications, with the consequent difficulty of management. And yet, discovered and cared early, the prognosis of hyperthyroidism becomes excellent. How to bring the pediatrician to early recognize the hyperthyroidism of the child in a medical environment characterized by the prevalence of infectious diseases? To answer this question, we undertook this work whose objective was to describe the main epidemiological, diagnostic, therapeutic and evolutionary aspects of the hyperthyroidism of the child for the improvement of prognosis and professional practice.

Patients and methods

Patients

This was a retrospective, descriptive and analytical study conducted in the pediatric ward of the University Teaching Hospital of Treichville

from January 2012 to December 2016. The study population consisted of children aged 0 to 15 years hospitalized during the the study. Included were all medical records of patients who had hyperthyroidism diagnosed on clinical grounds (signs of thyrotoxicosis with or without ocular signs, a goiter or nodule) and / or biological (free T3 ≥ 8.3pmol / Free T4≥19.4 pmol / L, TSH ≤0.25 µIU / ml). Not included were children who had hyperthyroidism with an unusable medical record and those whose diagnosis was not confirmed by biology.

Methods

The children in the study were examined for signs of thyrotoxicosis with or without ocular signs, goiter, or thyroid nodule. At the end of the clinical examination, the suspected hyperthyroidism was confirmed by the assay of thyroid hormones free T3, free T4 coupled if possible to Thyroid Stimulating Hormone (TSH). Hyperthyroidism was defined as a free T3 level higher than the normal reference value (4.0 - 8.3 pmol / ml) and a free T4 level higher than the normal reference value (10.6 - 19, 4 pmol / L) associated with a Thyroid Stimulating Hormone (TSH) level below the normal reference value (0.25 - 5 µIU / ml). Other paraclinical examinations required to assess the impact of hyperthyroidism or to identify the etiology included ECG, ultrasound of the thyroid, and standard skeleton of the skull centered on the sella turcica. Once the diagnosis was made, the child was given carbamizole, a synthetic antithyroid drug sometimes associated with a beta-blocker, an anxiolytic, or surgery. Clinical and para-clinical examination data were recorded in the child's medical record. Medical records were used to populate the standardized survey form with the study variables. These variables were hospital frequency, sex, age, clinical signs, paraclinical signs, treatment received and treatment progress. To carry out the study, we requested and obtained the authorization of the Scientific Medical Director of the establishment. In addition, the survey card used was anonymous and guaranteed the confidentiality of the information collected in the files of the children selected for the study. The collected data were captured and analyzed on the SPSS 11 computer software. The analysis was descriptive. It consisted in determining the numbers, calculating averages and proportions. For the comparison of proportions we used the Chi-square test with a significance level below 5%.

Results

Epidemiological aspects

We recorded 24,000 admissions during the study period, of which 27 cases of hyperthyroidism was a hospital frequency of one case per thousand admissions. Hyperthyroidism involved 22 girls and 5 boys. The average age was 147 months (range 64 to 180 months). The 11 to 15 age group accounted for 89% of the cases. The mother had adverse socioeconomic conditions in 92.6% of cases. All cases lived in rural areas and drinking water was poor in iodine. The history of the 27 children is marked by familial goiter in all cases (27/27, 100%), the death of a parent (13/27, 48%), a family conflict (8/27; 6%), a lack of affection (6/27, 22%).

Diagnostic aspects

The average time of consultation was 8.6 months (extreme 4 and 18 months). The main functional and physical signs are presented in Table I. The goiter was homogeneous in 81.5% of cases and nodular in 18.5%. Exophthalmos was bilateral in 85.2% and unilateral in 3.7% of cases. In 97% of cases there was a clinical picture of adiastole. Blood levels of free thyroid hormone T3 and free T4 were abnormally high in 99% of cases. TSH was abnormally low in 96% of cases. Thyroid ultrasound in 19 children revealed in 84% of cases a hypertrophied, spherical, homogeneous and hypoechoic gland. There was very intense hypervascularization of the Pulsed Color Doppler gland with maximal systolic velocities (MSV) greater than 100 cm / s (often 150 cm / sec) in the lower thyroid artery and a lowered resistance index. The electrocardiogram performed in all patients showed sinus tachycardia in 100% of cases and atrial fibrillation in 14.8%. The causes classified by age are presented in Table II.

Therapeutic and evolutionary aspects

All patients received synthetic antithyroid drugs. Eleven (11) children or 41% have had a thyroidectomy. The evolution under synthetic antithyroid was marked during hospitalization by remission (52%), discharge against medical advice (33%) and death (15%). Follow-up after hospitalization of the 14 cases in remission showed in the third year that 9 (64%) children were still in remission and 5 (36%) relapsed. Age greater than 10 years (P = 0, 031) and the peak dose of synthetic antithyroid drug ≥ 1 mg / kg / day (P = 0.023) were significantly associated with remission.

Functional signs	Enrollment (%)	Physical signs	Enrollment (%)
Palpitation	22/27 (81,5)	Tachycardia	27/27 (100)
Weight loss	22/27 (81,5)	Bilateral exophthalmos	23/27 (85)
Dyspnoea	17/27 (63)	Homogeneous diffuse goiter	22/27 (81,5)
Polyphagia	14/27 (52)	Sign of the stool	12/27 (44)
Tremor	12/27 (44)	Thyroid Breath	10/27 (37)
Nervousness	12/27 (44)	Mentor of hands	7/27 (26)
Insomnia	12/27 (44)	Nodular Goiter	5/27 (18,5)
Thermophobia	8/27 (30)	Thrill	3/27 (11)
Motor diarrhea	7/27 (26)	Prebital myxedema	1 /27(3,7)
Hypersudation	7/27 (26)	Eyelid retraction	1 /27(3,7)
Dysphonia	2/27 (7)	Unilateral exophthalmia	1 /27(3,7)
Dysphagia	2/27 (7)	"coffee with milk" stain	1 /27(3,7)

Table I: Functional and physical signs of childhood hyperthyroidism in Abidjan

* Secondarily Toxic Multinodular Goiter.

Etiologies	< 6 ans Enrollment (%)	6-10 ans Enrollment (%)	11-15 ans Enrollment (%)	Total (%)
Graves-Basedow disease	1(4)	1 (4)	20 (74)	22 (81)
Toxic adenoma	0	1 (4)	2 (7)	3 (11)
GMNT*	0	0	1 (4)	1 (4)
Subacute thyroiditis	0	0	1 (4)	1 (4)
Total	1(4)	2(7)	24 (89)	27 (100)

Table 2: Etiologies of childhood hyperthyroidism in Abidjan

Discussion

The aim of the study is to describe the main epidemiological, diagnostic, therapeutic and prognostic aspects of the child's hyperthyroidism for the improvement of the prognosis. It emerges from this work that hyperthyroidism accounted for 1 case per thousand admissions and mainly concerned the girl aged 11 to 15 years. The clinical manifestations are varied and Grave-Basedow disease (81% of cases) is the main cause. The evolution under antithyroid treatment of synthesis is marked by the remission in 52% of the cases. Lethality is high, 15% of cases. However, these results must be qualified because the work is mono-centric and retrospective. In fact, important biological data such as the antithyroid antibody assay, iodine and iodine levels have not been performed. This would have made it possible to specify the iodine status of patients and the potential role of iodine deficiency. However, the clinical and biological context was sufficient to carry the diagnosis. Despite the limitations described above, the work raises the following points of discussion at the level of the main epidemiological, diagnostic, therapeutic and evolutionary aspects.

Epidemiologically

The hospitalization frequency of 1 case per 1000 admissions that we report is less than those of 2 and 9.9 per thousand respective of Wemeau and al. in France [1] and Sidibé and al. in Mali [4]. This difference can be explained not only by the methodological bias related to hospital studies but also by the lack of knowledge of the disease by some practitioners, the absence of a specialized health structure in rural areas and the high cost of hormonal assays which does not allow for the diagnosis of the disease. Always have the positive diagnosis. The study does not report cases of neonatal hyperthyroidism probably due to the fact that screening for hypothyroidism in the neonatal period is not yet systematic in Côte d'Ivoire. The study reports 22 girls (81%) and 5 boys (19%) with an average age of 147 months (extreme: 64 and 180 months). The predominance of this condition in girls has already been reported by other authors in the literature [1, 5]. It rarely starts before the age of 10 years with a high frequency in adolescents and young adults [5]. All the children in the study lived in rural areas with modest living conditions and a history of familial goiter. The majority came from western Côte d'Ivoire, a mountainous region where the iodine content of drinking water (<2 µg / kg) and cassava (<5 µg / kg) kg) is very low [6]. Cassava contains cyanogenic glycosides whose cyanide hydrolysis in the gastrointestinal tract and then in thiocyanate in the liver inhibit the uptake of iodides by the thyroid, thus creating the conditions for hyperthyroidism [4].

At the diagnostic level

The average consultation time is 8.6 months (4 and 18 months) with the main reasons for admission are weight loss (59.3%), behavioral disorders (44.4%), behavioral disorders are often mistakenly considered as neurotic or reactive to a disturbed family situation. In the study, 13 children experienced psycho-emotional shocks due to death of parents, 8 children for family disputes and 6 children for lack of affection. These behavioral signs, at the forefront of the study, are sources of misdiagnosis; so that hyperthyroidism is recognized late in the complication stage as reported in other series [4, 5, 7, 8]. In labor, 77.8% of patients show signs of dyspnea, dysphonia, dysphagia and bilateral exophthalmos compressions in our study. The delayed diagnosis explains why 89% of the patients of the study are discovered between 11 and 15 years with an average age of 12 years. The parents' indigence, ignorance, the therapeutic route with traditional healers, lack of qualified human resources are all factors that could also explain this delay diagnosis. In the study nearly 41% of children have a statural advance in the study. Meziani et al. [9] reported a rate of 75%. The first cause of hyperthyroidism in the study is Graves-Basedow disease (81.5%). This finding has already been made by other authors in the literature [10-11]. In the literature, Grave-Basedow disease accounts for 10 to 15% of thyroid pathologies in children [12]. It is an autoimmune disease, as evidenced by the presence in the affected subjects of anti-thyroperoxidase (anti-TPO Ac) and anti-thyroglobulin (anti-TG) antibodies [13, 14]. However, the absence of these antithyroid antibodies characteristic of the disease does not eliminate the diagnosis [15]. HLA subjects (HLAA1, HLAB8, HLA DR3) are subject to Graves-Basedow disease. The risk of developing this condition is multiplied by 2.4 and by 5.2 in the HLA-B8 and HLA-DR3 subjects [16, 17]. In the study, the presence of a "coffee with milk" skin spot associated with lameness, bone pain with scoliosis and early development of breast tissue in a 9-year-old girl with Graves' disease in the study, evokes Mc Cune-Albright syndrome [18]. The assay of anti-thyroperoxidase autoantibodies to confirm this hypothesis has not been realized due to the insufficiency of the technical plateau. For those children with Graves-Basedow disease, cardiothyrosis is in the foreground. They all show paroxysmal tachycardia complicated by fibrillation in 14.8% of cases. This cardiac complication has already been reported by Osman and al. [19]. The toxic adenoma (11.1%), second cause in the study, is a benign tumor, usually monoclonal. It can be linked to somatic activating mutations of the TSH receptor or the alpha subunit of the G protein [20]. In the literature, the frequency of toxic adenoma is variable according to the studies, 10.5% in the study of Sidibé and al. [4] in Mali and 16.7% in M'Badinga and al. [21] in Congo. Secondarily toxic multinodular goitres (GMNT) represent 3.7% of cases. This rate, comparable to that of M'Badinga and al. (2.8%) in the Congo [21], is half of the 7.6% reported in Cameroon by Nouedou and al. [22]. In this nosology of goitre, the somatic activating mutations of the TSH receptor have been described; they are distinct from one nodule to another within the same goitre [20]. This situation, which is very rare in children and adolescents [5], is the main cause of hyperthyroidism in elderly patients, occurring on pre-existing goiter with one or more nodules becoming self-supporting. The study

reports 3.7% subacute thyroiditis. In Mali, Sidibé and al. [4] reported a rate of 2.6%. In the study, the only case of thyroiditis had a fever with respiratory signs suggestive of a viral infection. The insufficiency of the technical platform did not make it possible to isolate the virus in cause.

Therapeutic and evolutionary plan

In the study, the antithyroid synthesis used is carbamizole (Neomercazole) for cost and availability reasons. In Côte d'Ivoire radical treatment by radioiodine (131) (131I) is not yet available. This therapeutic attitude has also been used by other authors [23, 24, 25] because carbamizole inhibits hormone synthesis by blocking the activity of thyroperoxidase. Synthetic antithyroid is associated with betablocker and sometimes anxiolytic. Betablocker is used to slow the heart in case of palpitations (81.5%). And anxiolytic to treat nervousness (44%) or irritability too important (44%). For all patients in the study, euthyroidism was obtained after 8 months of regular treatment. Remission is achieved in 52% of cases with such factors significantly associated, age greater than 10 years (P = 0, 031) and the dose of the antithyroid synthesis ≥ 1 mg / kg / day (P = 0.023). The rate of remission, 52%, that we report in the study is in the range of 50 to 75% reported in adults in the literature [26, 27]. This remission is observed much earlier in the girl in our series. This fact has already been reported by Glaser [28] in California, USA. This is related to the small volume of goitre and weight in relation to height without weight loss in girls [29]. In the study, 11 euthyroid patients underwent surgical treatment to prevent relapse. The possibility of relapse under well-conducted medical treatment is around 40% in the literature [30]. The option of surgery, as a preventive modality, was also the choice of Nouedou et al. [20] in Yaoundé, Cameroon. The parents' indigence, the cost of treatment and the duration of treatment are all factors that explain the discontinuation of treatment found in 5 patients in the study.

Conclusions

Hyperthyroidism is a rare endocrinopathy common in girls. The diagnosis is late in children and Graves-Basedow disease is the main cause. Antithyroid synthesis allows remission in the majority of cases with however frequent relapses hence the need for regular monitoring of the patient. Improving the prognosis of patients requires multidisciplinary management including the pediatrician, the pediatric surgeon and the endocrinologist.

Ethical considerations

We obtained the ethical approval from the National Ethics Committee for Health Research (CNER), Ministry of Health Côte d'Ivoire (Arrêté n° 164 MSP/ CAB)

Competing interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Funding

We were not financing for this study

Contribution of the authors:

All authors contributed intellectually to the writing and editing of the manuscript.

Acknowledgments: Aholi Wognin Jean Michel, head of the Computer and Statistical Unit of the Pediatric Department of the Treichville University Hospital

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