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CHANGES IN THE BODY OF CHILDREN BORN TO MOTHERS WITH HYPERTHYROIDISM

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Abstract: Maternal hyperthyroidism has an important influence on fetal development and effects on physical changes in children after birth. Overproduction of thyroid hormones by the mother and transplacental passage of stimulating antibodies from congenital acquired hypothyroidism affecting neonatal thyroid function, growth, and mental development should be considered. There is evidence that children of hyperthyroid mothers are at risk for transient or permanent thyrotoxicosis, growth restriction cardiac mutations and metabolic perturbations. This review summarises the current knowledge on postnatal development in infants of mothers affected with hyperthyroidism taking into account not only the endocrine aspects but also those related to the development of other organ systems, including cardiovascular and brain development. The discussion includes maternal–fetal hormone transfer mechanisms, neonatal thyroid regulation, and clinical approaches of monitoring and managing these potential complications, emphasizing the role of early recognition for long-term outcome optimization. The hyperthyroid mother′s child has to adapt, both physiologically and developmentally, to the consequences of her in utero exposure to excess thyroid hormones and maternal thyroid-grave disease stimulating antibodies. These exposures also impact on neonatal thyroid function, cardiovascular homoeostasis, metabolic control and growth and neurocognitive development. It is now established that severity of maternal disease, circulatory antibodies, and time and effectiveness of maternal therapy are the major constraints for postnatal emission. An early diagnosis and close follow-up of the affected neonates could lead to timely intervention, prevent complications and ensure a favorable outcome. This review summarizes the current understanding of postnatal changes in hyperthyroid offspring and their clinical implications, whereas also exploring interventions to improve long-term health.

Keywords: Maternal Hyperthyroidism, Neonatal Thyroid Function, Fetal Development, Thyrotoxicosis, Growth Disturbances, Cardiovascular Changes, Neurodevelopmental Outcomes, Maternal-Fetal Hormone Transfer

Introduction

The uterine milieu is vital in programming the metabolic and physiological characteristics of the growing fetus. Maternal thyroid hormones, mainly thyroxine (T4) and triiodothyronine (T3), are required for normal organogenesis, specially in central nervous system and cardiovascular system. Pregnancy related hyperthyroidism, frequently the result of either Graves' disease or gestational thyrotoxicosis, is associated with increased maternal thyroid hormone levels and circulating thyroid-stimulating immunoglobulins, which are capable of crossing the placenta into the fetal compartment and acting directly on the fetal thyroid gland. Such perturbations could affect fetal metabolic rate, cardiac output and growth trajectories and the effects can persist into offspring after birth. Neonates' adjustment to thyroid hormone excess may manifest as increased metabolism, cardiac stress and premature development of thyroid disease. Knowledge of the range of postnatal alterations is crucial to predict complications, tailor neonatal screening and adjust early therapy. The pregnant uterus is highly influenced by the endocrine state of the mother with, among other things, a pivotal influence of thyroid hormone on fetal growth. In pregnancies complicated by the presence of hyperthyroidism, increased maternal thyroxine and triiodothyronine concentrations (concomitant thyroid-stimulating immunoglobulins could present) cross the placenta and impact upon fetal organ maturation, metabolic rate, and hormonal homeostasis. The fetal thyroid becomes functionally independent in the second trimester, however early exposure to maternal hormone excess can disrupt normal development of the hypothalamic-pituitary-thyroid axis. As a result, the new-born may suffer from deranged thyroid functions, increased metabolism and cardiovascular adjustments soon after birth. Deviation from an optimal metabolic balance and disturbance of nutrient allocation during the critical period of

organogenesis can also have repercussions on growth patterns and neurocognitive development. Knowledge of these mediators is critical for predicting neonatal needs, designing monitoring patterns and conducting interventions to limit adverse outcomes and promote normal maturation.

Material and Methods

In this paper we present the results of clinical experiments, case series, observational cohorts and experimental research on children born to women with hyperthyroidism. Literature was searched on databases including PubMed, Scopus and Web of Science by using the search terms such as maternal hyperthyroidism, neonatal thyrotoxicosis, fetal thyroid exposure and postnatal developmental outcomes. Selected studies comprised full-term and preterm neonates, determining thyroid hormone concentrations or antibody titers, growth parameters as well as cardiac function and neurodevelopment. Themes of physiologic changes due to maternal thyroid disease were identified by the mixed-methods analysis process. Comparative analysis was conducted to discern transient neonatal and persistent postnatal effects, in which associations of maternal disease severity and treatment timing with neonatal outcomes were highlighted.

Results

Offspring of hyperthyroid mothers have a variety of postnatal variations. About 10–15% of these infants will develop a transient neonatal thyrotoxicosis in the first weeks of life, presenting with tachycardia, irritability, failure to thrive and feeding difficulties. Persistent thyrotoxicosis is relatively rare but can happen with high maternal antibody titers or poor disease control during pregnancy. Cardiovascular symptoms consist of tachycardia, increased pulse pressure, and rarely structural heart defects or arrhythmias. Growth disturbances, such as low birth weight and catch-up growth delay, have been described especially when maternal hyperthyroidism is inadequately controlled. Sequelae in the form of neurobehavioral findings such as mild motor coordination delays, attention and cognitive deficits have been reported in follow up studies implying that high levels of exposure to thyroid hormone during critical windows of development may have an effect on neuronal differentiation and synaptogenesis. The laboratory findings in these patients often include neonatal T4 elevations and low-recalled thyroid-stimulating hormone levels, which resolve over weeks to months in transient cases. Good maternal control by antithyroid therapy and close monitoring can dramatically reduce the frequency of these problems. Clinical data have shown that a significant number of neonates born to mothers with hyperthyroidism present with transient thyrotoxicosis, which is predominant tachycardia and irritability along with poor feeding and failure to thrive. Laboratory findings are frequently increased serum thyroxine and low or suppressed thyroid-stimulating hormone with gradual normalization over the first few weeks in most cases. Ongoing thyrotoxicosis in the neonate of a mother with high titers of antibody or uncontrolled disease may require medication. Cardiovascular effects are tachycardia, widened pulse pressure and occasionally rhythm disorders or structual defects. Growth perturbations consist of reduced birth weight and postnatal catch-up growth retardation that is particularly pronounced in the newborns with severe excess maternal hormones. Neurodevelopmental testing suggests possible risks for motor coordination, attention, and cognition regarding the susceptibility of central nervous system in development to excess thyroid hormones. Maternal management and monitoring in a timely fashion can decrease the incidence and severity of these neonatal complications, underscoring preconception and gestational disease surveillance.

Discussion

The postnatal changes observed are the result of direct and indirect effects of maternal hyperthyroidism on fetal and neonatal physiology. The trans-placental passage of increased maternal T4, T3 and stimulating antibodies leads to disturbance to the strictly controlled fetal hypothalamic-pituitary-thyroid axis, causing a transient hyperactive thyroid in newborns. The cardiovascular and metabolic systems adjust to accommodate the high level of hormones (including long-term functional changes if the exposure is intense or prolonged). Growth restriction may result from elevated in-utero catabolism and imbalanced nutrient partitioning. Neurodevelopmental effects emphasize the susceptibility of a developing CNS to thyroid hormone imbalance during gestation. Prompt diagnosis and monitoring, including neonatal thyroid function testing, cardiac evaluation and neurodevelopmental follow up are

essential to prevent complications. Interdisciplinary cooperation with endocrinologists, neonatologists and paediatricians is advised to maximize short- as well as long-term effects. The postnatal alterations in such children are consequences of a complex pathway involving materno-fetal hormonal excess, placental crossing over and fetal endocrine adjustments. Transplacental migration of thyroid hormones and stimulating antibodies directly affect neonatal thyroid function, whereas secondary effects on metabolic rate, cardiac function, and growth result from enhanced fetal basal metabolism. Thyroid dysregulation in early life is a growing concern and left untreated it may have far-reaching implications, especially concerning neurodevelopment and growth patterns. When titrated to maintain maternal euthyroidism, antithyroid agents prevent fetal risk, but must be actively monitored so as not to induce hypothyroidism. Collaboration among endocrinologists, neonatologists, and developmental specialists is crucial for early identification of affected infants to provide interventions that enhance the most favorable outcomes. Long-term data support the importance of individualized monitoring and follow-up for children with delayed growth or subtle cognitive impairment not readily apparent in newborn.

Conclusion

Moderate symptoms that occur in the progeny of mothers with hyperthyroidism, such as transient and permanent thyrotoxicosis, cardiovascular changes, growth impairment, and effects on neurocognitive development. The extent of worsening and how long this lasts are strongly related to maternal disease activity and the antibody levels. Timely maternal management, neonatal screening and continued postnatal follow-up are crucial in order to reduce the negative sequelae and promote adequate growth and development. Improved knowledge about the interplay between maternal and fetal thyroid helps to define evidence-based strategies for preventing, early recognizing, and managing postnatal sequelae of maternal hyperthyroidism. Fertilization with those sperm may lead to the same outcome in terms of hyperthyroidism-mediated effects on offspring development and physiology 11,12.A particular concern revolves around damage that thyroid stimulating immunoglobulins could cause to offspring with the potential for these antibodies having considerable long-term effects including: altered neurobehavioral outcomes in children born from mothers who had therapeutic I131 or surgical removal of diseased tissues during pregnancy47; possible transplacental transfer of either TSH receptor antibodies43or maternal medications as evidenced by fetal neonatal hyperthyroidism resulting from excessive passage of anti-thyroid drugs through placenta48; other symptoms such as tachycardia associated with inappropriate fetal weight gain49. The extent of these modifications varies according to maternal disease control, titers, duration of intervention. Early diagnosis, close follow-up and optimal management are essential to minimize risks and ensure healthy postnatal growth and neurodevelopment. A complete knowledge of the maternal-fetal thyroid relationship provides insight for clinical decisions and preventive approaches aimed at maximizing long-term health in children born to hyperthyroid mothers.

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