Guideline

Women and Babies: Management of Infants of Mothers with Thyroid Disease

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Functional Sub-Group: Clinical Governance
Corporate Governance

Summary: Describes the management of infants of mothers with thyroid disease with specific reference to screening for neonatal thyrotoxicosis

National Standard
- Standard 1: Governance for Safety and Quality in Health Service Organisations
- Standard 9: Recognising and responding to the deterioriating patient.

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Management of Infants of Mothers with Thyroid Disease

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Management of Infants of Mothers with Thyroid Disease

INTRODUCTION

The risks addressed by this policy:

Clinical risk of undiagnosed thyrotoxicosis in infants of mothers with Graves’ Disease

The aims / expected outcome of this policy

Infants of mothers with Graves’ Disease will be appropriately screened for thyrotoxicosis and those found positive will be appropriately and promptly managed.

POLICY STATEMENT

The goal of this guideline is to familiarise midwifery, medical and nursing staff to the risks for infants of mothers with Graves’ Disease, to ensure they will be appropriately screened for thyrotoxicosis and those found positive will be appropriately and promptly managed.

PRINCIPLES / GUIDELINES

Infants of mothers with Hashimotos thyroiditis

Infants of mothers with Hashimoto’s thyroiditis are at low risk of transient hypothyroidism from thyroid blocking antibodies (incidence estimated at 1:180000), and rarely of thyrotoxicosis from coexistent thyroid stimulating antibodies. Most infants with transient hypothyroidism born to mothers with Hashimoto’s thyroiditis are identified by routine neonatal thyroid TSH screening.[1] There is conflicting advice on whether it is necessary to perform additional thyroid function tests on infants of mothers with Hashimoto’s thyroiditis [1, 2]. Until evidence is presented to the contrary, infants of mothers with Hashimoto’s thyroiditis should not have specific thyroid function screening apart from the routine NSW Newborn Screening Programme TSH measurement on day 3 or 4.

Infants of mothers with Graves’ Disease

Neonatal thyrotoxicosis is rare condition caused by the transplacental passage of TSH receptor antibodies (TRAB) from mothers with Graves disease or, very rarely, Hashimotos thyroiditis. TRABs may continue to be present in the maternal blood stream even after ablation of the thyroid gland with surgery or radioiodine. Neonatal thyrotoxicosis secondary to TRABs is a transient disorder, limited by the clearance of maternal antibody from the baby’s circulation. Rarely, thyrotoxicosis may be due to inherited activating mutations in the TSH receptor.

Incidence: The reported prevalence of Graves’ disease in pregnant women is approximately 0.2%. Although it is usually stated that only 11.5% of their offspring will have overt hyperthyroidism, higher incidences have been reported (5%-12.5%). A further 3% of babies of
mothers with Graves’ disease have biochemical thyrotoxicosis in the absence of symptoms.[2]

**Risk Factors:** The main risk factor for development of neonatal thyrotoxicosis is the presence and titre of TRABs in the maternal blood stream. Neonatal thyrotoxicosis is rare in mothers with normal TRAB titres.[3,4] It had been proposed that risk increases with higher TRAB titres and a higher risk threshold of 5 times the upper limit in your laboratory.[4] These cut offs are not specific and neonatal thyrotoxicosis can occur at lower TRAB levels.

In the recent case series of Besancon et al, none of the babies whose mothers had normal TRAB titres developed neonatal thyrotoxicosis while 21% (7 of 33) of those whose mothers had raised TRAB levels developed neonatal thyrotoxicosis, (all biochemical without symptoms). All these 7 cases were associated with TRAB levels more than 2x the upper limit of normal for their laboratory.[3] In the RPA laboratory <1 IU/L is normal, 1-2 IU/L is equivocal and >2 IU/L is high. We will stratify into higher and lower risk on the basis of a TRAB level of >2 IU/L.

**Prevention:** Infants of mothers with Graves’ disease during pregnancy who are appropriately managed with antithyroid medication will usually have infants who are asymptomatic, although they are still at risk of biochemical hyperthyroidism (T4 >35 pmol/L). [5]

**Consequences:** Fetal thyroid tissue function is established by 12 week gestation and by 25 week is almost functionally mature.

**Effects on pregnancy:** Although data are sparse, pregnancies affected by maternal hyperthyroidism may be at increased risk of:Miscarriage[6] Stillbirth[6] Intrauterine growth restriction[7] Preterm labor and other pregnancy complications including pregnancy induced hypertension and thyroid crisis[7]

**Fetal effects:** the fetus may develop goitre, tachycardia, hydrops associated with heart failure, growth retardation, craniosynostosis, increased fetal motility and accelerated bone maturation.

**Neonatal effects:** In the neonate, overt symptoms and signs usually occur in the first few days of life and may last for 3-6 months, proportional to the clearance of maternal IgG [8]. However, overt thyrotoxicosis has been reported to occur as late as 45 days [8], delayed by the presence of transplacentally transferred maternal antithyroid drugs or blocking antibodies. Affected neonates may have irritability, restlessness, goitre, excessive weight loss, failure to regain birth weight, diarrhoea, sweating, flushing and eye signs including peri-orbital edema, lid retraction and proptosis.[7, 9-11]. Initial sinus tachycardia can progress to tachyarrhythmia and congestive cardiac failure[12]. Systemic[13] and pulmonary hypertension may be present[14, 15]. Neonatal thyrotoxicosis is reported to have a mortality of 16-25%[10, 16]. Most infants have a goitre. Advanced bone age, craniosynostosis, and microcephaly may be evident in both the fetus and newborn.

**Symptoms and signs of neonatal thyrotoxicosis:**
- Restlessness
- Tachycardia
- Poor feeding and occasionally extreme hunger
- Excessive weight loss
- Diarrhoea

**Long term outcome:** Neonatal Graves’ disease tends to resolve spontaneously within 3-12 weeks as maternal immunoglobulins are cleared from the circulation but subsequent development may be impaired although data are sparse. The developmental outcome for infants of mothers with treated hyperthyroidism is generally within the normal range and similar to a matched control group[17].
Screening for Neonatal Thyrotoxicosis: (see flow chart)

Infants at risk of congenital hyperthyroidism (Maternal Graves disease, family history of activating mutations in TSH receptor) should have the following screening based on their underlying risk:

Infants at high risk for neonatal thyrotoxicosis:

Defined on the following criteria:

- Maternal third trimester TSH Receptor Antibody (TRAB) titres > 2 IU/L or unknown.
- Concerns about fetal thyrotoxicosis, e.g., fetal tachycardia, growth restriction.

These babies should have:

- JMO/NNP review for clinical signs of neonatal thyrotoxicosis shortly after birth e.g., IUGR, tachycardia or goitre. If clinical concern, check early day 1 TFTs.
- There should be a further JMO/NNP review prior to discharge, either on the newborn baby check or as an extra review.
- **End of week 1 thyroid function screening test.**
  - If the baby is still in hospital on day 5, TFTs should be checked then.
  - For all babies going home prior to day 5, they should be booked in for outpatient review and TFTs on day 5-7 with the consultant second on when the baby was born. If this does not fit with the consultant's usual clinic day, an appointment will need to be arranged on another day but make sure the 2nd on consultant can see them when the appointment is arranged.
  - If the above TFTs are normal and the mother is not on any antithyroid medication, no further investigation is needed.
  - If the above TFTs are normal but the mother is on antithyroid medication, further clinical review and repeat TFTs by the second neonatologist should be arranged for between day 10 to 14.

Infants at low risk for neonatal thyrotoxicosis:

defined as those with Maternal TRAB antibodies <2 IU/L and no concerns about fetal thyrotoxicosis.

- These babies do not need any screening investigation apart from the normal NBST but TFTs should be checked if there are any clinical concerns about thyrotoxicosis.

Any results that may be consistent with thyrotoxicosis (e.g., T4 > 35 pmol/L, TSH < 3 IU/L) should be discussed with the supervising neonatologist or Fellow.

Treatment:

Thyroid functions tests suggest hyperthyroidism (T4 > 35 pmol/L, TSH < 3 IU/L) then discuss with the supervising neonatologist or Fellow who will decide whether to initiate the following management:

1. Contact the on call Endocrinologist at either Sydney Childrens Hospital (93821111) or Childrens Hospital Westmead (98450000)
2. The treatment of thyrotoxicosis is supported by case reports in the literature and is consistent with the treatment of hyperthyroidism in other populations of patients. Thyrotoxicosis in the newborn may be treated with either:
• Propylthiouracil (PTU): 5-10 mg/kg/day in three divided doses. PTU inhibits the synthesis of thyroid hormones by blocking the oxidation of iodine in the thyroid gland and synthesis of thyroxine and triiodothyronine. Peak concentration occurs within 1 hour of ingestion. The major drug interaction is the enhancement of anticoagulant activity.

• Or Carbimazole: 0.5-1.5 mg/kg/day as a single daily dose: As the drugs block the synthesis but not the release of thyroid hormones, a clinical response to thionamides may not occur until the thyroid hormone stored in the colloid is depleted. Therefore

• Iodide solution, which suppresses thyroid hormone synthesis and has a prompt effect in inhibiting the release of thyroid hormones, may be used in conjunction with case reports in the literature of their use.

3. Either: Saturated potassium iodide (KI) (48 mg iodine per drop) given in a dose of 1 drop daily, or Lugols solution (5% KI; about 8mg iodine/drop) in a dose of 1 to 3 drops daily.

4. Beta-Blockers are effective in controlling symptoms caused by adrenergic stimulation, in particular, cardiovascular symptoms associated with tachycardia or tachyarrhythmia. In addition, they inhibit deiodination of T4 to T3. Use:

5. Propranolol 0.27-0.75 mg/kg 8 hourly. This may be administered orally or slow intravenous injection (over 10 minutes). The goal of therapy is reduction in heart rate to safe levels (Potential side effects include hypoglycaemia, bradycardia, and hypotension, so babies require close monitoring.

6. Specific treatment for cardiac failure may be required, for example Digoxin and Diuretics.

7. Severely thyrotoxic babies may be treated with prednisolone [19] which suppresses deiodination of T4 to T3 and compensates for hypercatabolism of endogenous glucocorticoids induced by T3 and T4. The dose of prednisolone is 2mg/kg/day.

8. Other general measures:

• Sedatives may also be helpful in managing irritability and restlessness.
• Monitor for hyperthermia and aim to achieve a neutral thermal environment.
• Assess fluid balance infants may have increased fluid requirements secondary to increased transepidermal water losses associated with hyperthermia and losses associated with diarrhoea.
• Assess growth, infants may need increased caloric intake to ensure normal growth.
Does the mother have Graves’ Disease e.g autoimmune thyrotoxicosis?

- Review TSH receptor antibody (TRAB) levels during pregnancy.
  - Antibodies >2 IU/L or
  - unknown antibody titres or
  - Suspected Fetal Thyrotoxicosis*

High Risk of Thyrotoxicosis
- MO/NNP review after birth
- Are there clinical signs of thyrotoxicosis? (e.g goitre, tachycardia, IUGR)

Check early TFTs

TFTs suggest thyrotoxicosis (high T4, T3, low TSH)?

Mother on antithyroid medication?

Outpatient review with second on neonatologist at 10-14 days. Repeat TFTs

Consult with Neonatologist re further management and involvement of Endocrinology.

Normal clinical review and NBST at 48 to 72 hours.

Low Risk of Thyrotoxicosis
- MO/NNP review prior to discharge.
- If inpatient on day 5, check TFTs.
- Otherwise book into 2nd on Consultant outpatients day 5-7 for review and TFTs.

Consult with Neonatologist re further management and involvement of Endocrinology.

TFTs suggest thyrotoxicosis (high T4, T3, low TSH)?

Reassure and discharge
REFERENCES


