MCN for Neonatology
West of Scotland
Neonatal Guideline

Neonatal Thyrotoxicosis

Management of babies born to mothers with a history of hyperthyroidism (Grave's Disease)

This document is applicable to all medical, nursing and midwifery staff caring for the newborn in hospital or community. The guideline should be used with reference to the appropriate pharmacy monographs and obstetric guidelines for the management of pregnant women with thyroid disease.

Introduction

Neonatal Thyrotoxicosis is usually the result of thyroid stimulating antibodies passing from the mother to the fetus towards the end of pregnancy. Thyroid Receptor Antibodies (TRAbs) occur in women with Graves' disease (GD) and are usually the cause of this condition. The prevalence of Graves' disease in pregnancy is around 0.2% and the incidence of overt thyrotoxicosis in their offspring has been estimated to be between 1% and 12.5%. The maternal TRAbs freely cross the placenta particularly towards the second half of pregnancy. The thyroid in the fetus is fully developed by 7 weeks gestation with thyroid hormone synthesis beginning at 10 to 12 weeks gestation. By 25 weeks gestation the thyroid is almost fully functional so transfer of TRAbs to the fetus can cause in utero and/or postnatal hyperthyroidism.

Much more rarely hyperthyroidism may occur in infants born to mothers with Hashimoto's thyroiditis or where there are activating mutations of the Thyroid Stimulating Hormone (TSH) receptor. These causes are too uncommon to warrant routine screening of infants unless there is a family history of hyperthyroidism in a previous infant.

It is important to remember that neonatal thyrotoxicosis will not be detected by the Newborn Bloodspot Screening Programme. The UK programme screens only for high TSH to identify congenital hypothyroidsim. It does not measure T4 and low levels of TSH are not reported.

Identifying Babies at risk of hyperthyroidism

Any infant whose mother has a current or past history of hyperthyroidism is potentially at risk of neonatal thyrotoxicosis. 'At risk' infants should be identified by maternal history and the measurement of TRAbs in the mother during pregnancy. Current maternal thyroid function may be misleading as the mother may still have circulating thyroid receptor antibodies, despite being euthyroid or hypothyroid, if she is currently receiving treatment with anti-thyroid medication or following thyroid ablative therapy (surgery or radioactive iodine).

NB. mothers with thyroid disease frequently have Thyroid Peroxidase (TPO) antibodies reported – these are not a risk factor for hyperthyroidism in the neonate and do not require any neonatal investigations

High risk mothers

- Current thyrotoxicosis on antithyroid medication (Carbimazole or Propylthiouracil)
- Previous thyrotoxicosis treated with radioactive iodine or thyroid surgery
- Any mother with positive TRAbs

Low risk mothers

- Previous thyrotoxicosis treated only with antithyroid medication. Mother now euthyroid **and** off anti-thyroid treatment.
- Mothers with negative TRAbs

Negligible risk

- Maternal hypothyroidism (unless due to surgery or radioactive iodine - *see above*)

All mothers with a current or past history of thyrotoxicosis (high and low risk groups) should have their antibody titres measured at booking. If positive these should be repeated later in pregnancy (antibody titres often fall toward the end of pregnancy). *See obstetric guideline*
If thyroid antibodies are detected (TRAb >2 U/L) then this should be indicated in the 'paediatric alert' section of the maternal notes. Paediatric staff should be informed as soon as the baby has delivered.
N.B. Where there is a history of thyrotoxicosis in the mother but no TRAb titres are available the baby should be managed as 'High Risk' .
No further action is required for the negligible risk group or for the low risk group if thyroid antibodies are not detected at booking.

Management of babies at risk of hyperthyroidism

NB. Only babies whose mothers have TRAbs > 2 U/l require investigation (or those for whom no TRAb measurement is available from the current pregnancy)

Infants with Neonatal Thyrotoxicosis may present at birth and the remainder usually become symptomatic over the first 10 days of life. These infants may be critically unwell therefore clinical assessment for signs of thyrotoxicosis and initial investigations should be performed very shortly after birth.

- Confirm maternal TRAb titres >2 U/L during current pregnancy, if no TRAb results available send infant TRAB titres and treat infant as high risk.
- Ask if there is a family history of **neonatal** thyroid disease.
- Examine for features of neonatal thyrotoxicosis. *See below*.
- Send following investigations (ideally from cord blood and ensure sample is labelled and request form states cord blood – this will allow lab to distinguish between maternal and infant results.)
    - freeT4, TSH, TRAb (requires a **minimum of 1ml** in lithium heparin).
    - Infant TRAb, results will be available within 7 – 10 days

N.B. in the first few days of life it is common to find that TSH and free T4 are **both** raised. This is a normal acute phase response and is **not** hyperthyroidism. TSH is **suppressed** in thyrotoxicosis (TSH <0.2milliunits/L).

Normal reference ranges: TRAb <1 U/L, fT4: 6-30picomol/L, TSH: 0.2-15 milliunits/L

Subsequent management is based on the results of these initial investigations

Normal Thyroid Function and absent/low (baby's) TRAb levels.

NB. *TRAb levels are performed on a weekly basis, the day will depend on how many samples received that week. It may be possible to have a TRAb level within 24-48 hours of sending sample depending on when the analysis is run that week. The labs anticipate that all results should be availabe within 7- 10 days. In the situation of no TRAb levels being available follow up as below (infants with Normal TFTs and raised TRAb)*

- Follow up as outpatient at 10-14 days. No further investigation unless symptomatic.
- Prior to discharge, parents should be advised of the features of neonatal hyperthyroidism *see below* and advised to contact the unit if symptomatic.

Normal Thyroid Function but (baby's)TRAb > 2 U/L or unknown

- Repeat fT4 and TSH on day 3-5 and again at day 10-14 to detect later onset hyperthyroidism. Prior to repeating bloods check results of infant TRAb titres and if <2 U/L bloods not required, almost all will be back prior to day 10.
- Prior to discharge, parents should be advised of the features of neonatal hyperthyroidism *see below* and advised to contact the unit if symptomatic.
- Infants with TRAb > 2 are at risk of late onset hyperthyroidism as TRAbs remain in the infant circulation for up to 6 weeks, there have been reports of development of hyperthyroidism as late as day 45. Therefore infants with normal thyroid function but raised TRAb should be followed up at 4 weeks and 2-3months to ensure no signs of late onset hyperthyroidism.

Abnormal Thyroid Function

- If fT4 >30 **and** TSH < 0.2, **or** there are symptoms or signs of hyperthyroidism then the baby is potentially hyperthyroid and should be discussed urgently with the duty Neonatal Consultant as pharmacological treatment may be required. Liaison with a consultant paediatric endocrinologist should be considered for babies with thyrotoxicosis.

- Occasionally infants whose mothers have been on antithyroid medication may be hypothyroid.

Treatment of neonatal thyrotoxicosis

Drug therapy

Monotherapy with carbimazole may be sufficient in an asymptomatic infant with biochemical evidence of hypoerthyroidism. However in a symptomatic infant concurrent therapy with propranolol and/or iodine may be required.

- **Carbimazole** - 250 micrograms/kg/dose 3 times daily until euthyroid. Higher doses, up to 1mg/kg/day, may be required if the infant is in thyrotoxic crisis. Carbimazole reduces the uptake of iodine by the thyroid and blocks thyroid hormone synthesis by preventing the organification and coupling of iodothyronine residues. It does not inhibit the release of pre-formed thyroid hormones and may take a number of weeks to render the infant euthyroid. Agranulocytosis may occur during treatment with Carbimazole.

- **Propranolol** - 250–500 micrograms/kg/dose every 6–8 hours initially adjusted according to response. Propranolol helps control symptoms caused by adrenergic stimulation. In addition, it inhibits deiodination of T4 to T3.

- **Lugol's Iodine solution (Aqueous Iodine Oral Solution)**
  – 0.05 ml, 3 times a day for 1 week.
  Lugol's Iodine is used in infants with haemodynamic instabillity. It helps rapidly block thyroid hormone synthesis, blocks thyroid hormone release and promptly reduces free thyroid hormone concentrations. The effects are temporary and co-administration of carbimazole is essential.

Monitoring
The aim of treatment is to abolish hyperthyroidism without causing hypothyroidism. Treatment must be titrated against the clinical response. Propranolol may be stopped once clinically euthyroid.

TFTs
These should be measured at regular intervals aiming to achieve T4 measurements in the normal range. fT4 – 6 - 30 pmol/L and a TSH level between 0.05 - 5mU/L
N.B. TSH may remain suppressed for 2-3 weeks even with adequate therapy

FBC
Carbimazole may cause agranulocytosis in 0.03% of patients. The FBC should be measured after 1 week of treatment. This should be repeated at any stage if there are suggestive symptoms (fever, mouth ulcers, rash).

Prognosis
The half life of TRABs is about 12 days. Treatment may therefore be required for 8-12 weeks. Following successful cessation of carbimazole there is usually no need for further follow-up

Features of Neonatal Hyperthyroidism / Thyrotoxicosis

Head and Neck

- Goitre
- Periorbital Oedema
- Exopthalmos

CNS

- Irritable
- Jittery
- Poor sleeping
- Microcephaly – head <5th centile

CVS

- Tachycardia
- Arrhythmias
- Flushing
- Sweating
- Hypertension

GI

- Increased appetite
- Diarrhoea / vomiting
- Excess weight loss
- Hepatosplenomegaly

Other

- Bruising + petechiae due to thrombocytopaenia
- Jaundice

Other Documents

Endocrine Society Guideline (2012) – **"Management of Thyroid Dysfunction during Pregnancy"**

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