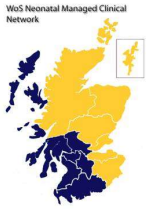
MCN for Neonatology
West of Scotland
Neonatal Guideline



Anti-Ro & Anti-La antibodies

Guideline for the management of babies born to mothers with systemic lupus erythematosus (SLE) and other autoimmune disorders

This document is applicable to all medical, nursing and midwifery staff caring for the newborn in hospital or community. It is intended as a guide to the management of babies born to mothers with anti-Ro or anti-La antibodies. Note that some babies may develop neonatal lupus without a diagnosis having been made in the mother. The guideline should be used with reference to the relevant pharmacy monographs.

Contents

1. Introduction:

Systemic lupus erythematosus (SLE) is a chronic inflammatory multisystem disease. Most women with SLE have normal fertility, but they are at higher risk of pregnancy complications including hypertension, preterm labour, thrombosis and postpartum haemorrhage. There is a higher incidence of miscarriage and fetal loss especially in women with co-existing antiphospholipid syndrome (presence of lupus anticoagulant and anticardiolipin antibodies).

Neonatal lupus — Neonatal lupus is a passively acquired autoimmune disease that occurs in about 2 percent of babies born to mothers with anti-Ro/SSA and/or anti-La/SSB antibodies. It is caused by passage across the placenta after about the 20th week of pregnancy of anti-Ro/SSA and/or anti-La/SSB antibodies to intracellular ribonucleoproteins. Antibody levels are reported by the lab in GG&C. Approximately 50% of women who give birth to a baby with the neonatal lupus syndrome do not have a diagnosis of lupus or any other autoimmune disease (eg Sjögren's syndrome) at the time of their pregnancy despite the presence of anti-Ro/SSA or anti-La/SSB antibodies. Around half of these mothers will go on to develop autoimmune disease, and they should all therefore be referred to a rheumatologist for assessment postnatally.

Signs of neonatal lupus include a red, raised rash on the scalp and around the eyes. The rash almost always resolves by six to eight months of age following clearance of the maternal antibodies and the majority (90 percent) of these infants do not subsequently develop lupus.

Infants may also demonstrate transient abnormalities of liver function and generalised or selective reduction in cellular blood components, e.g., anaemia, reduced white cell count and/or thrombocytopenia.

The most common cardiac manifestation of neonatal lupus is complete heart block, which occurs in approximately 2 percent of newborns whose mothers have anti-Ro/SSA or anti-La/SSB antibodies. Complete heart block may rarely be associated with cardiomyopathy secondary to endocardial fibroelastosis (EFE), and is irreversible.

Women with known anti-Ro/SSA or anti-La/SSB antibodies will undergo weekly monitoring of the fetal heart rate using *Doptone*, starting from 18 weeks of pregnancy. Four weekly ultrasound scans will be undertaken from 20 weeks of gestation onwards, aiming to detect fetal heart block at an early stage to allow monitoring of fetal cardiac function and alert the neonatal/cardiology team to the potential need for a pacemaker after birth.

There is at present no proven treatment for fetal heart block prior to birth. There have been reported cases of reduction in the degree of heart block and reversion to sinus rhythm after maternal steroid therapy but dexamethasone is not recommended as prophylaxis to prevent fetal congenital heart block (1). Neither has intravenous immunoglobulin been established as an effective preventative treatment (2). A ventricular heart rate of <55 beats per minute, reduced left ventricular function, hydrops, presentation earlier in pregnancy and reduced cardiac function are risk factors for fetal and neonatal death. Antenatal treatment with an alpha-sympathomimetic drug is not routinely employed due to the risks to the maternal health (3,4).

If a mother gives birth to a baby with neonatal lupus, her risk of having a child with neonatal lupus in a subsequent pregnancy is 16-18%. Several maternal therapies have been trialled in a bid to prevent CHB in a further pregnancy, however evidence is lacking.

2. Management of the asymptomatic baby

Cord bloods:

FBC and differential WBC

Clinical examination soon after birth – if heart rate $\geq$ 80 beats per minute and baby clinically stable, he/she should remain with mum.

ECG prior to discharge.

The ECG should be discussed with a neonatal consultant prior to baby's discharge.

Feeding advice:

Breastfeeding is recommended for most women with SLE as there is no increased risk of neonatal lupus related to breastfeeding. Note that most medications enter breast milk to some extent:

- Diclofenac or ibuprofen can be used, but aspirin should be avoided.
- If NSAIDs are not tolerated, dihydrocodeine may be used with caution as higher doses may lead to drowsiness, or rarely, respiratory depression.
- Prednisolone can be taken in low doses up to 40 mg/day.
- Chloroquine, hydroxychloroquine and heparin appear to be safe while breastfeeding.
- Azathioprine and cyclosporine enter breast milk in very low concentrations and their continued use can be considered on a case by case basis. This should have been discussed with mother prior to delivery and a plan documented in the handheld records and/or maternal Badger.
- Cyclophosphamide and methotrexate should be avoided during breastfeeding.

Follow up – out patient clinic 2-3 weeks. The family should be advised to contact the neonatal unit for earlier review if baby develops a rash, or if there are any other concerns.

Advice should be given to parents to avoid the baby being exposed to direct sunlight (complete (*i.e.* Factor 50 or greater) sunblock plus a hat).

Management of babies whose mothers have been treated with TNF inhibitors and other immunosuppressive biological therapy

(e.g.: Infliximab, Belimumab, Rituximab)

Whether infants can receive a live vaccine will depend on the drug involved and how long it was continued for in pregnancy. A plan should be made with an appropriate specialist and the mother during pregnancy. For infants exposed to immunosuppressive biological therapy in utero or through breastfeeding, risk vs benefit of administering a live vaccine should be determined on an individual patient basis. Discuss with pharmacy, an Infectious Diseases specialist or the Public Health team.
The British Society of Rheumatology and the British society of gastroenterology provide the following guidance(which may conflict with manufacturers' and national guidance):

BSR Guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids

In summary:

- Delaying giving live vaccines until 6 months of age is advised for most biologic immunosuppressive agents (Green Book)
- Rotavirus vaccine is safe to give and can be considered after discussion with the parents.
- Manufacturers' of Infliximab advise avoiding live vaccines until 12 months of age in infants exposed in utero or through breastfeeding unless infant levels are undetectable. Consideration should be given to measuring infant levels at 6months of age if there is high need for a live vaccine e.g. BCG before 12 months of age.

3. Management of the symptomatic baby

3.1 Congenital heart block

As noted above, the congenital heart block associated with neonatal lupus is considered a form of passively acquired autoimmune disease in which maternal autoantibodies to Ro (SS-A) and La (SS-B) cross the placenta and injure the previously normal fetal heart. While the non-cardiac manifestations of neonatal lupus are generally transient, and resolve with clearance of maternal antibodies from the infant's circulation at several months of age, damage to the conduction system and myocardial disease are irreversible.

Neonatal lupus is usually diagnosed in the presence of a slow heart rate discovered in a fetus or newborn in the absence of associated structural cardiac abnormalities. *In utero*, the peak onset of the diagnosis of bradycardia is between 18 and 24 weeks of gestation, corresponding to about six weeks after effective placental transport of maternal IgG antibodies begins. The precise mechanism is unknown. The degree of heart block may vary from first degree to third degree block, but most cases diagnosed *in utero* present with at least second degree or more advanced block. There is a high mortality rate, particularly in fetuses diagnosed with hydrops. Of all cases that are recognised with congenital heart block, the majority will have a pacemaker placed before reaching adulthood.

Babies identified to have a slow heart rate (<80 bpm) should be transferred to the neonatal unit for a baseline ECG to confirm the rhythm and a 24 hour ECG recording should be undertaken. The baby should be discussed with paediatric cardiology on-call team prior to transfer to the postnatal ward, to allow outpatient follow up to be arranged. Infants with a mean heart rate < 55 bpm, or any other abnormal cardiac findings should admitted urgently to the NICU, discussed with the on-call neonatology consultant and referred to cardiology as soon as possible. Even with a heart rate of < 55bpm, most neonates will be asymptomatic but if there are signs of low cardiac output, an intravenous infusion of isoprenaline may help to increase the heart rate temporarily before a pacemaker is inserted. Isoprenaline may be sourced from NICU at RHC.

3.2 Pancytopenia

Pancytopenia is rare but isolated thrombocytopenia more common. Most cases will resolve spontaneously over 4 – 6 months with disappearance of maternal antibody; treatment of severe thrombocytopenia or pancytopenia will be symptomatic. Intravenous immunoglobulin may be helpful. Significant abnormalities of the blood count should be discussed with a consultant.

All babies with blood dyscrasia or skin rash should be referred to rheumatology

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