Pregnancy & Neonatal Management Guide for Long QT Syndrome (LQTS) TYPES 1 & 2

SEPTEMBER 2018

BC Inherited Arrhythmia Program (BCIAP) and Cardiac Obstetrics (COB) Clinic

BCIAP

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‘High Risk’ LQTS Patients*

Any LQTS patient meeting one or more of the following criteria is designated ‘high risk’ throughout this document:

- Resting QTc >500 ms (in the absence of reversible QT prolonging factors)
- Previous cardiac arrest
- Implantable Cardioverter Defibrillator (ICD) in place
- *Previously documented* high burden of non-sustained ventricular tachycardia or ventricular ectopy

Potential Triggers of LQTS Cardiac Events**†

QT-Prolonging Drugs

It is important for LQTS patients to **avoid** taking QT-prolonging drugs. Some of these medications are commonly used during pregnancy, delivery, and postpartum[1,2] such as certain anesthetics, certain antibiotics, oxytocin, domperidone for lactation.

- Visit www.crediblemeds.org or download the **CredibleMeds Mobile App** for the full list of drugs to avoid.

Sudden Auditory Arousal

Note that sudden loud noises may trigger cardiac events, particularly in LQTS type 2 associated with mutations in the *KCNH2* gene.

† *Only triggers relevant to this document are listed. For expanded information on LQTS triggers, see Schwartz PJ and Ackerman MJ.*[3]

Initial Visit (preconception or first prenatal visit)

Genetic Counselling

Given hereditary LQTS is usually autosomal dominant, when one parent is affected there is a 50% chance of recurrence in each pregnancy. In rare cases where both parents are affected with LQTS, the risk to each child is 75%. If not already done, affected individuals can be referred to the **BC Inherited Arrhythmia Program (BCIAP)** for genetic counselling and consideration of genetic testing.

Pregnancy Management Plan

For women affected by LQTS, pre-conception/early pregnancy counselling should be provided and a management plan for the pregnancy and postpartum period established.

- Assess risk status and effectiveness of current management (including beta-blocker medication—see below).

Beta-blockade

The most common pharmacologic treatment for LQTS is beta-blocker medication to reduce the risk of cardiac events and sudden cardiac death.[3,4]

- Dosage and choice of beta-blocker should be individualized based on clinical status (heart rate, evidence of symptoms, tolerance, etc). The goal is to minimize risk of life-threatening arrhythmia and maximize medication adherence, with a resting heart rate <100 bpm.
- Exercise stress testing may be helpful in assessing adequacy of beta-blockade.
- The cardiologists and obstetricians associated with the BCIAP and Cardiac Obstetrics (COB) clinic most often use nadolol[5,6] or bisoprolol[7,8] to treat pregnant women with LQTS. Nadolol should be used preferentially in **high risk*** women.
  - *Metoprolol is not advised* as it is not as effective for LQTS.[9]
- Beta-blockers are unlikely to increase the risk of congenital anomalies in the fetus above the background rate.[4,10-12] However, it is recommended that all women take 0.4 mg (400 micrograms) of folic acid every day, beginning at least three months before conception and throughout pregnancy to reduce the chance of congenital anomalies in the fetus.[13]

Refer to Specialty Clinics

Refer all pregnant women to the BCIAP, who will optimize management and provide genetic counselling. **High risk* women should also be referred to the Cardiac Obstetrics (COB) Clinic** at St. Paul's Hospital in Vancouver.

- Initiate referral *as early as possible* to facilitate booking and coordination of appointment. Please send dating scan along with referral, if available.
- **BCIAP referral form:** www.cardiacbc.ca/Documents/BCIAP%20Vancouver%20referral%20form.pdf
- **COB Clinic referral form:** www.heartcentre.ca/professionals/referrals
- The multi-disciplinary COB team will develop an individualized cardiac-obstetrical care delivery plan for the high risk patient, including advice on beta-blocker management/titration, management of symptoms, and labour and delivery planning. The care plan will be communicated to the primary health care provider and delivery team.

*See definition, page 2

Ongoing Pregnancy

Although the majority of women with LQTS do not experience cardiac events during pregnancy,[14,15] **beta-blockers should be continued throughout pregnancy for prevention of cardiac events**.

Increased risk for fetal intrauterine growth restriction (IUGR) has been reported with maternal beta-blocker use,[16] but it is unclear whether this is a result of underlying maternal health conditions predisposing to IUGR (for example, hypertension or maternal heart disease). Although few studies have assessed women with primary arrhythmia on beta-blocker therapy, one study supports an associated risk for IUGR,[17] and a more recent study also suggests lower birth weight and earlier delivery of infants of women with LQTS being treated with beta-blockers.[4]

Maternal Assessment

- Record **maternal heart rate**, **blood pressure**, and **beta-blocker dosage and type** on the prenatal record at every prenatal visit, to aid with dosage/titration decisions and communication with specialists when needed.

Beta-blocker Titration

- Beta-blocker dosage may need to be increased through the latter stages of pregnancy due to increasing blood volume and drug excretion; however, caution should be exercised because side effects with higher doses may lead to non-adherence.
- Beta-blocker side effects include postural hypotension, fatigue, depression and worsening of reactive airways disease. There is clear overlap of these side effects with symptoms reported during pregnancy, so consultation with both cardiac and obstetric experts may be warranted to interpret symptoms and adjust medications.

Fetal Evaluation

The following is suggested, and can be performed locally:

- Routine detailed ultrasound scan at 18 to 20 weeks
- Repeat ultrasounds at 28 to 32 weeks and 36 weeks gestation.
  - If concern with fetal growth is identified at any stage, a follow-up scan is recommended in two weeks' time, as well as referral to local obstetrician (or discussion with COB clinic for those **high risk*** patients being followed by COB clinic).
- In some cases of hereditary LQTS, the fetus may present with severe bradycardia or other arrhythmias.[18] If persistent fetal bradycardia or other fetal arrhythmia is noted, referral to Obstetrics/Maternal Fetal Medicine is indicated.

Pre-labour Anesthesia Consultation

- Initiate referral to anesthesiologist/anesthetist to plan for safe analgesia and anesthesia in labour and delivery (also see Drake E et al[1]).

*See definition, page 2

Labour & Delivery

Care providers should be aware that **most deliveries occur without event** and can usually be carried out at local hospitals. With adequate beta blockade, the maximum heart rate should be blunted, and safe delivery without instrumentation (barring other maternal or fetal indications) should be expected.

Lower fetal heart rates are normal in babies of mothers on beta-blockers, with normal heart rate fluctuation at a lower heart rate range, which does not normally indicate fetal distress.

High risk* women will have been assessed earlier in pregnancy at the BCIAP and COB clinic to determine optimal delivery management and location.[19,20]

- **Home deliveries are <u>not</u> advised.**
- **Ensure resuscitation equipment** including an external defibrillator is available in or nearby the delivery suite.
- **Pain management** should be readily available, and planned early epidural should be considered.
- **Nurse in a calm, quiet environment.****
- Although **second stage pushing** could increase the heart rate, it is generally thought to be safe with adequate beta-blockade.
- Decisions regarding **epidural and assisted delivery** should be made based on obstetrical indication; these interventions are rarely indicated for LQTS status.[1]

<u>Avoid</u> circumstances that could increase the risk for ventricular arrhythmias, such as:

- **Electrolyte imbalance**
  - Check **serum K^+ and Mg^{2+}** levels on all patients at the time of admission, and manage accordingly.
- **Excessive bleeding,** which is concerning because of the associated tachycardia, while hypotension limits the ability to give beta-blockers.
  - Rapid restoration of blood volume should be considered in the setting of a hemorrhage in both high and low risk LQTS cases.

(Circumstances to Avoid – Continued)

- **QT prolonging drugs** and certain anesthetics**[1,2]
  - Oxytocin is on the list of drugs to avoid in LQTS. There is no known increased risk with routine IM injection; however, prolongation of the QTc has been reported with IV infusion. In the case of an oxytocin infusion, the patient's status should be monitored carefully (preferably one-to-one nursing), since the combination of hemorrhage and an oxytocin infusion could increase the risk for cardiac events. In a patient that requires higher doses of oxytocin, intermittent ECGs may be considered to monitor the QTc.
    A QTc >500 ms should be discussed with an Electrophysiologist. If consult is needed, please contact the on-call cardiologist/ Electrophysiologist available locally or contact St. Paul's Hospital (604-682-2344) and ask to speak to the on-call Electrophysiologist.
    IV beta-blockers may be considered, however it is important to note that intrapartum IV beta-blockers may increase the risk of hypoglycemia in the neonate (see page 6).

**See definition, page 2

The Neonate

Neonates who were exposed to beta-blockers in utero may be at-risk for postnatal symptoms of beta-blockade and hypoglycemia.[12,21]

For those infants exposed to maternal beta-blockers in-utero:

- Observe for drowsiness, hypotension and hypoglycemia.
- Screen neonates for hypoglycemia as per the Canadian Paediatric Society guidelines for newborns at risk for hypoglycaemia.[22]
- Mother and baby should stay in hospital (preferably together in the mother-baby suite) 24–36 hours after delivery.

For all infants with a mother *or* father with LQTS, ECGs should be performed at day one and three weeks of life and faxed (high-resolution) to the pediatric heart rhythm specialist on-call at BC Children's Hospital for review:

- Complete '*Request for Neonatal ECG Review*' fax sheet available at **www.cardiacbc.ca/our-services/programs/bc-inherited-arrhythmia-program** and **fax to 604-875-3463.**
- **Along with fax, send e-mail** to both Connie Ens (Cardiology Nurse Clinician **cens@cw.bc.ca**), and Kayla Yard (Clinical Secretary **kayla.yard@cw.bc.ca**) with subject line '*Incoming Neonatal ECG Review*' to alert to incoming fax.

Genetic testing for those infants in families with a known mutation should be offered through a referral to the BCIAP genetic counsellors.

Postpartum

Women with LQTS have an increased risk for cardiac events, including sudden cardiac death, in the first nine months following delivery.[14,15] It is especially important for women to continue taking beta-blockers throughout the postpartum period.

Maternal Assessment

- To ensure adherence to beta-blocker therapy postpartum, maternal assessment with review of symptoms and heart rate is recommended at 1 week postpartum and monthly thereafter until 9 months postpartum.
- Arrange **exercise stress testing** for all women at 3–6 months postpartum to assess adequacy of beta-blockade and assist with beta-blocker titration (if needed). Beta-blockers are typically titrated based on change in peak exercise heart rate (target 15–20% reduction on exercise test).
  - Stress test can be arranged locally in most cases. *Please contact the BCIAP if further information or guidance is needed.*
  - For **high risk*** women followed by the COB clinic, the COB clinic will advise on exercise testing and beta-blocker dosage.

Beta-blocker Titration

For those patients whose beta-blocker dose was increased during pregnancy, a decrease may be needed in the postpartum period.

- Optimal timing of the downward titration will vary between women, but generally starts around 3–6 months postpartum.
- Women should ultimately be returned to their pre-pregnancy optimal therapy and dosing.
- For **high risk*** women followed by the COB clinic, the COB clinic will advise on optimal beta-blocker titration.

Breastfeeding

Beta-blockers as a group are excreted in breast milk and there is potential for beta-blockade in nursing infants. However, few adverse effects have actually been reported in nursing infants.

- None of the beta-blockers commonly used for LQTS by the BCIAP are contraindicated in breastfeeding; however, exposed infants should be monitored for features of beta-blockade. In some cases, extra public health nurse visits might be considered.
- Choice of maternal beta-blocker must take into account both the stability of the mother and the risk of beta-blockade in the infant. Although there may be excretion of the beta-blocker into breast milk, changing the type of maternal beta-blocker after delivery because of theoretical risk is generally not advocated due to the risk of destabilizing the mother.
- **Domperidone**, commonly used to stimulate lactation, is on the list of QT-prolonging drugs[†] and is contraindicated in LQTS patients.

[†]*See potential triggers, page 2*

Contact Information

Cardiac Obstetrics Clinic:
St. Paul's Hospital
Room 5051, 1081 Burrard Street
Vancouver, BC V6Z 1Y6
PHONE: 604-806-8520
FAX: 604-806-8800
EMAIL: **pach@providencehealth.bc.ca**
www.heartcentre.ca/services/cardiac-obstetrics

BC Inherited Arrhythmia Program:
www.cardiacbc.ca/our-services/programs/bc-inherited-arrhythmia-program

Adult patients – Vancouver site:
St. Paul's Hospital
211-1033 Davie St.
Vancouver BC V5N 1E1
PHONE: (604) 682-2344 ext. 66765
FAX: (604) 806-9474

Adult Patients – Victoria site:
Department of Medical Genetics
Victoria General Hospital
1 Hospital Way
Victoria, BC V8Z 6R5
PHONE: (250) 727-4461
FAX: (250) 727-4295

Pediatric BCIAP site:
Heart Centre – BC Children's Hospital
1F41, 4480 Oak St Vancouver, BC V6H 3V4
PHONE: (604) 875-2295
FAX: (604) 875-3463

Motherisk Helpline
(information about beta-blocker exposure during pregnancy & breastfeeding)
PHONE: 1-877-439-2744; 416-813-6780
http://www.motherisk.org/

The Canadian SADS Foundation
(patient-friendly information & support group)
PHONE: (905) 826-6303
Info@SADS.ca
https://sads.ca

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Additional reading:

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