



# CHILDREN'S & WOMEN'S HEALTH CENTRE OF BRITISH COLUMBIA

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## **SUBJECT INFORMATION AND CONSENT FORM**

### **Title of Study:**

The effects of droperidol and ondansetron on dispersion of myocardial repolarization in children.

### **Principal Investigator:**

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## **1. INTRODUCTION**

You are invited to have your child participate in this study because he/she is undergoing a procedure that requires a general anesthetic. We are investigating the effect of anti-nausea medications on certain aspects of the heartbeat.

## **2. YOUR PARTICIPATION IS VOLUNTARY**

Your child's participation is entirely voluntary, so it is up to you to decide whether or not to have your child participate. Before you decide, it is important for you to understand what the research involves. This consent form will tell you about the study, why the research is being done, what will happen to your child during the study and the possible benefits, risks and discomforts.

If you do decide to have your child participate, you will be asked to sign this form. You are still free to withdraw at any time and without giving any reasons for your decision.

If you choose not to be involved or to withdraw your child from the study, you do not have to tell us why. The medical care that your child will be receiving will not be any different or less than the care he/she would normally receive. Please take time to read this information and ask any questions that may help you understand the study before you decide whether to be in the study or not.

### 3. BACKGROUND

**Your child is undergoing an operation that is associated with a significant risk of post-operative nausea and vomiting (PONV). As part of the normal, routine care that your child receives, we will give them medicines to reduce the likelihood of PONV occurring.** Your child's anaesthetist will talk to you about this in detail if you wish. We are interested in the effect of these anti-sickness medicines on your child's heartbeat.

The heart is a muscle and each time it contracts it results in a heartbeat. Before the next heartbeat, the muscle must, like any other muscle, relax. There are some rare diseases, called long QT syndromes, in which control of heart muscle relaxation is abnormal. Patients with such diseases are at risk of sudden death under certain circumstances, which include having an anesthetic.

Because these conditions are very rare, we know less than we would like to about which medicines are the safest to use in their presence. We therefore want to look at the **effect of two** different anti-nausea medications, on relaxation of heart muscle in children with **NORMAL** hearts. This will provide information on which to base recommendations for anti-nausea medications in patients with the abnormalities mentioned above.

### 4. WHY IS THIS STUDY BEING DONE?

**The answer to this question is rather complicated & requires some more background information. We know, from adult studies, that both drugs (and, indeed, many other drugs) have small effects on the heart's electrical activity for a few minutes after injecting them. The effect is to make the heart take a fraction of a second longer than normal to relax. Although we can measure these changes, they do not affect the healthy heart's normal function because the normal heart has the ability to cope with such small changes – this is called 'reserve'. However, a small number of children and adults have genetic changes that result in their hearts already taking longer than normal to relax. A few of these people get severely abnormal heartbeats, which may cause them**

to faint or even die suddenly. These people have a condition called long QT syndrome. However, there are many very mild forms of the condition & neither the people affected, nor their doctors, can tell that they have it. Although these people are completely asymptomatic, & will probably remain so all their lives, nevertheless, they have less 'reserve' to cope with additional disturbances to the way their hearts relax. If these seemingly normal people, with reduced reserve, are given medicines that further delay the heart's relaxation mechanisms, they may be at increased risk of abnormal heartbeats. Our research is aimed at identifying whether drugs given by anaesthetic doctors have any effect on the heart's relaxation mechanisms &, if so, how much. In this way, we can better decide which drugs to use & which to avoid in the future, when it is likely to become easier to detect people who have the mild forms of long QT syndrome.

Both ondansetron and droperidol have been given to hundreds of thousands of people to reduce their risk of nausea & vomiting after surgery & there is no evidence that either of them increase the risk of abnormal heartbeats, even though, as described above, they both briefly slow the heart's relaxation by a tiny amount. At much higher doses than we use, droperidol can cause significant delays to heart relaxation and there have been some reports of it causing, or contributing to abnormal heart rhythms at these higher doses. For this reason, droperidol carries a "black box" warning issued by the Federal Drug Agency requiring its manufacturers to warn physicians of this fact & recommend close monitoring of the heart rhythm in any patient given droperidol, even at the much lower doses used to prevent nausea & vomiting. There has been much debate about this warning amongst anaesthetists, as many feel that the risk is being overplayed & that patients may actually be denied a proven effective treatment for a common & distressing problem. A second reason for undertaking this study, therefore, is to accurately measure the very small effect these drugs are having on the heart's relaxation, using a new, more reliable test. We expect to use our results to reassure doctors and patients that the benefits of using these medicines far outweigh any risk of abnormal heartbeats. In order to be clear about the risks & benefits of droperidol, they are listed here, along with some everyday risks for comparison:

- Risk of post-operative nausea and vomiting after this type of surgery without treatment: 50-70%
- Risk of post-operative nausea and vomiting after this type of surgery with treatment: 20-30%
- Risk of dying in a car accident each year: 1 in 8 000
- Risk of dying in a home accident each year: 1 in 11 000
- Risk of being in a railway accident each year: 1 in 140 000

- **Estimated risk of life-threatening heartbeat disturbance from droperidol: 1 in 600 000**

## **5. WHO CAN PARTICIPATE IN THE STUDY?**

In order to participate in the study, your child must be aged 3 - 10 years.

## **6. WHO SHOULD NOT PARTICIPATE IN THE STUDY?**

Children with long QT syndrome, a family history of long QT syndrome, or on certain medicines that affect the heartbeat cannot be invited to participate in this study. In addition, children must be in general good health to be involved. Your child's anesthetist will make this judgment.

## **5. WHAT DOES THE STUDY INVOLVE?**

We will take a heart tracing (an ECG) just before your child goes to sleep. We will then take another tracing 5 minutes after the anesthetic has started. The study will then be finished.

Having an ECG involves placing some stickers on the arms, legs & chest. These are then attached to some wires, to record the tracing. It is painless & harmless.

In this study, the anti-nausea drugs ondansetron and **droperidol** are put through the **intravenous (IV)** line **once your child** is asleep. Whether your child receives just ondansetron, just droperidol, a combination of both, or no anti-nausea medicines will be selected randomly (like a flip of the coin, where neither the investigators nor you would choose). The doses of all drugs used are within the normal dose range that your child would receive if not in the study. After that, the study is finished and the anesthetist will use his/her usual technique to keep your child asleep during the operation.

The study therefore requires an extra five minutes *before* your child goes to sleep to take the first heart tracing, and five minutes *after* your child is asleep for the second heart tracing.

**If your child does not take part in the study, he/she will not have the ECG traces recorded. However, the anaesthetic medicines received will be identical. The anti-sickness medicines that are routinely used are droperidol, ondansetron and another drug called dexamethasone. Your anaesthetist will choose to give two of these medicines, keeping the third one in reserve in case your child is sick in spite of the attempt to prevent this.**

## **6. WHAT ARE THE POSSIBLE HARMS AND SIDE EFFECTS OF PARTICIPATING?**

There are no significant risks from having an ECG.

**The drugs ondansetron and droperidol are recognized, routine medicines for preventing and treating nausea & vomiting. There is a third drug that is also frequently used, called dexamethasone. In our usual practice at BCCH, children undergoing the operation that your child is going to have receive two of these three drugs. If these do not work, the third one is given. The two we use most commonly are ondansetron and dexamethasone, with droperidol as our reserve. Therefore, the study intervention does not increase the usual (very low) risk of anesthesia. The intervention conducted in the study is part of normal and standard practice at BCCH. Like all drugs, they may have side effects. These are typically minor and short-lived and, because we are giving the drugs whilst your child is asleep, your child is extremely unlikely to notice them if they occur. Droperidol can make you feel sleepy on its own. As described earlier, the makers of droperidol warn physicians of the small risk of abnormal heart rhythms. The risk is estimated to be approximately 1 in 600 000. We routinely monitor the heartbeat continuously during and immediately after an anaesthetic – it is a standard part of anaesthetic care. As an additional safety measure, we will record a third heart tracing, in recovery, for all children in the study, to confirm that it remains normal.**

The 5-minute interval between the two heart tracings does not increase anesthetic time as, under normal circumstances, there is always a gap between going to sleep and starting the procedure. This time is used to put on monitors, set up equipment, etc. This gap is of variable length, but is very commonly at least 5-10 minutes. For this study we need a 5 minute gap before starting your child's procedure.

We are doing this study in children with normal hearts and we expect your child's heart tracings to be normal. However, in the highly unlikely event that we find an abnormality on the heart tracing, we would discuss it with a children's heart specialist at BC Children's Hospital and we would tell you about it, to arrange any necessary follow-up.

## **7. WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?**

Your child will not directly benefit from participation in this study. The information we get from the study will be used to advise anesthetists on the effect of droperidol and ondansetron on heart muscle relaxation and which concentration to use in future situations in patients with or at risk of long QT syndromes.

## **8. WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT TO PARTICIPATE?**

Your child's participation in this research is entirely voluntary. You may withdraw your child from this study at any time. If you decide to enter your child in the study and withdraw at any time in the future, there will be no penalty or loss of benefits to which you and your child are otherwise entitled, and your child's future medical care will not be affected.

If you choose to enter the study and then decide to withdraw at a later time, all data collected about your child during his/her enrolment in the study will be retained for analysis. By law, this data cannot be destroyed.

## **9. WHAT HAPPENS IF SOMETHING GOES WRONG?**

By signing this consent form you are in no way waiving your or your child's **legal rights** or releasing the investigator or anyone else from their legal and professional responsibilities.

## **10. CAN MY CHILD BE ASKED TO LEAVE THE STUDY?**

The study doctor(s)/investigators may decide to discontinue the study at any time, or withdraw your child from the study at any time, if they feel that it is in your child's best interests.

## **11. WHAT WILL THE STUDY COST ME?**

There will be no additional cost to you for your child's participation in the study. You will not be charged for any research procedure. You or your child will not receive any remuneration/reimbursement for participation.

## **12. WILL MY CHILD'S PARTICIPATION IN THIS STUDY BE KEPT CONFIDENTIAL?**

Your child's confidentiality will be respected. No information that discloses your child's identity will be released or published without your specific consent to the disclosure.

Research records and medical records identifying your child may be inspected, in the presence of an Investigator or his or her designate, by representatives of the UBC Research Ethics Board, for the purpose of monitoring the research. However, records which identify your child by name or initials will be kept in a locked cabinet and will not be allowed to leave the Investigators' offices. Copies of relevant data, which identify your child only by code number, may be required by regulatory agencies. However, your child will not be identified by name, initials, or date of birth as part of this study data.

**13. WHO DO I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY DURING MY CHILD'S PARTICIPATION?**

If you have any questions or desire further information about this study before or during your child's participation, you can contact Dr. Whyte at 604-875-2711.

**14. WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT MY CHILD'S RIGHTS AS A SUBJECT DURING THE STUDY?**

If you have any concerns about your child's treatment rights as a research subject, please contact the Research Subject Information Line at the University of British Columbia Office of Research Services at 604-822-8598.

**15. CONSENT TO PARTICIPATE**

I have read or have had read to me all of the above. I have had enough time to consider entry to the study. All of my questions have been answered to my satisfaction. I understand that my child's participation is entirely voluntary and that he/she may refuse to participate, or I may withdraw my child from the study at any time.

The parent(s)/guardian(s) and the investigator are satisfied that the information contained in this consent form was explained to the child to the extent that he/she is able to understand it, that all questions have been answered, and that the child assents to participating in the research.

I acknowledge having received a signed and dated copy of this consent form for my own records.

Name of Subject: \_\_\_\_\_

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Printed name of subject's parent / Legally acceptable representative	Signature	Date
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Printed name of witness	Signature	Date
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Printed name of principal investigator/ Designated representative	Signature	Date
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