A randomised controlled trial of iodine supplementation in preterm infants

Clinical Trials Number: NCT00638092
www.npeu.ox.ac.uk/I2S2  www.euthyroid.org
Part 1

We invite you to participate in a research project which we believe to be of potential importance. To help you understand what the research is about, we are providing you with the following information, which we want to be sure you understand before you decide whether to participate. Be sure to ask any questions you have about the information which follows, and we will do our best to explain, and to provide any further information you require. Part 1 tells you the purpose of this study and what will happen to you if you take part, and part 2 gives you more detailed information about the conduct of the study.

What is the purpose of the study?

Thyroid hormones are required for the normal development of the brain and other organs. Babies with low thyroid hormone levels perform less well in tests of brain function later in life. In many premature babies a disorder of thyroid hormone production has been found where thyroid hormone levels are low. The levels may remain low for a few weeks or months after birth and, unlike adults, cannot be raised by treating the babies with more thyroid hormone. We need to know very much more about this condition and how the premature baby handles thyroid hormones differently, so that new treatments can be developed for premature babies.

Iodine is required by the body to make thyroid hormones, and is found naturally in foodstuffs and milks, including breast milk. We add iodine to the intravenous feeding solutions your baby will require. The levels of iodine in these intravenous feeding solutions and in the milks, both formula and breast, may be too low for the needs of premature babies. We would like to know if giving a small increase in iodine to premature babies will help them make more thyroid hormones. To do this we need to compare babies having our usual solutions with babies who are having additional iodine.

Why have I been invited?

You and your baby have been invited to take part in this study because your baby has been born prematurely. We are inviting 1700 mothers and babies to take part in this study.
Do I have to take part?

Participation in this study is entirely voluntary and you are free to refuse to take part or to withdraw from the study at any time without having to give a reason and without this affecting either your or your baby’s future medical care. A copy of this information sheet and consent form will be given to you to keep.

What will happen if I agree to take part?

If you agree to take part in this study, your baby will be assigned either to receive a daily iodine supplementation (in the form of sodium iodide) plus the standard intravenous feeding solution, or to receive an equivalent daily volume of sodium chloride (the placebo) plus the standard intravenous feeding solution. Whichever group your baby is in, your baby will be receiving some iodine as it is already present in the intravenous fluids and milks.

The extra sodium iodide added as part of this study is very small. All infants have the same chance of being assigned to the usual or the increased iodine intake group. Neither you nor the doctors and nurses will know which group your baby was allocated to until the end of the study. Your baby will receive a daily supplement until your baby is the equivalent of 34 weeks gestation (i.e. if your baby had stayed in the womb until week 34).

Blood samples for thyroid hormone tests are needed from your baby on days 7, 14 and 28 after birth, and again at the end of the period of daily supplementation. Babies in the Neonatal Unit require many routine blood tests and the thyroid hormone tests will be done at the same time whenever possible.

While your baby is in the Neonatal unit we shall record their progress on a specially designed form; for instance we will record whether they were sick and what medications they were prescribed; thereafter and until their second birthday we shall record episodes of major illness or events that may be relevant to their development.

We would also like to see your child again when they are around their second birthday to assess how they are progressing using some standard developmental tests. A researcher will record by filling in some forms, how your child responds in a variety of situations. For example, to
the sound of a bell, the rolling of a ball, a picture book and with building blocks. This assessment might last about 1½ hours. Please note that some assessments will be monitored for quality control purposes and will be viewed by a member of the trial team. If you wish to have a copy, you can arrange this during your assessment. The information that we might be able to get by doing follow up assessments of infants in this study is potentially very valuable and we might wish to contact you and your child beyond the 2 year follow up. To do this, information that is held by the NHS and records maintained by The NHS Information Centre and the NHS Central Register may be used to help contact you and provide information about your health status. It is possible, for example, that we might contact you and your child at around 5 years of age in order to do further assessments and we should be grateful if you would give consideration to this at this stage.

**Expenses and payments**

When you bring your child for the follow-up assessment we shall reimburse your travel costs.

**What are the possible discomforts and risks for my baby taking part?**

Taking blood samples is potentially a painful procedure which can result in bleeding and bruising at the injection site. However we will ensure that as far as possible the blood samples to be taken for this study will be obtained at the same time as samples which are taken for the routine care of your baby.

**What are the side effects of any treatment received for my baby taking part?**

The only side-effects that we are aware of from the administration of Sodium Iodide supplement occurs if too much is administered. We have eliminated the risk of excessive overdose by limiting the amount of Sodium Iodide that is provided in each dose vial. Overdoses of Sodium Iodide can cause the thyroid gland to switch off and shutdown the
production of thyroid hormone. However this only happens where very much larger doses, well above the dosage here, are administered to preterm babies.

**What are the possible benefits of your baby taking part?**

Adding iodine to babies feeding solutions might help premature babies make more thyroid hormones, which might help them to perform better in tests of brain function later in life.

**Part 2**

**What if relevant new information becomes available?**

If any new information about sodium iodide and supplementation of infant nutrition becomes available during the trial the implications of the information for your baby will be discussed with you.

**What will happen if I don’t want to carry on with the study?**

If you decide to withdraw your baby from the study, you will be asked whether certain procedures related to the study may be continued. You are still free to withdraw your baby at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your baby receives.

**What happens in the event that I have a complaint arising out of my baby’s part in this study?**

If your baby has been harmed by taking part in this study, you may have grounds for legal action and seek compensation through the Research Sponsor, the University of Oxford, who has appropriate insurance-related arrangements in place. If your baby is harmed and it's due to any clinical treatment then the NHS indemnity arrangements will apply. If you wish to complain about any aspect of the way you or your baby has been treated you may use the normal National Health Service complaints procedures, the Patient Liaison Manager at your hospital will advise you about this.
Your rights

The doctors and nurses involved in this study will give you information and answer any questions you have. If more information is required you can contact your consultant in the Neonatal Unit or speak to the Neonatal Research Nurse assisting with this trial who will be available most days in the Neonatal Intensive Care Unit, and will be happy to discuss any concerns you may have regarding your baby’s participation in the trial.

Will my taking part in this study be kept confidential?

The information we obtain about your baby in this study will be given a special study number (i.e. anonymised) that will be linked to your baby’s identity on a separate password-protected computer file. This means that your baby’s identity will only be known to the members of the research teams in Oxford and Dundee. Your baby’s information will be sent to the coordinating centre, at the National Perinatal Epidemiology Unit in Oxford and stored securely, where it will be kept indefinitely. The data will also be stored in the Department of Public Health, University of Dundee who are leading the research programme and analysing the data.

The UK Regulatory Authority who authorise clinical trials such as this one may also review the research and medical records of patients who take part in clinical trials to ensure the trial is being run in compliance with regulations. Your baby’s information will also be made available to a special committee made up of experts in neonatal care and in running trials, whose role is to monitor this study to determine its ongoing relevance and safety issues. In addition, representatives from the Research Sponsor may look at relevant data for the purpose of audit and monitoring.

What will happen to the blood samples taken from your baby?

Your baby’s blood will be spotted onto an absorbent card, sometimes called a Guthrie card. A Guthrie card blood sample will be collected for this trial on four occasions. The amount of blood required for each Guthrie card is about 0.25ml, which means for the complete study about 1ml (one fifth of a teaspoonful) will be needed. The Guthrie cards will
be sent to Amsterdam for analysis as they routinely analyse the range of thyroid hormones that we need for this study. The confidentiality of your baby’s sample is assured in the same way as it is under the UK congenital hypothyroid screening programme.

If the level of thyroid hormone of your baby is such that further medical care is desirable then both you and your doctor will be informed. After discharge home your baby will continue to be reviewed as part of routine clinical care. We will contact you again when your baby is about 2 years old to arrange a convenient time and place to assess the development of your child.

**What will happen to the results of the research study?**

At the end of the study, a summary will be available on the web site www.npeu.ox.ac.uk/I2S2 or you may request a hard copy from your neonatal unit. The findings from the study will eventually be published in a medical journal. Your anonymity is assured, as individual patients will not be identifiable.

**Who is organising and funding the research?**

The Medical Research Council is supporting this study and the University of Oxford is sponsoring this study.

**Who has reviewed the study?**

This study has been reviewed by a NHS Research Ethics Committee which has responsibility for scrutinising proposals for medical research on humans, in accordance with the requirements of the Clinical Trials Regulations. In this case, the reviewing Committee was the Fife & Forth Valley Research Ethics Committee who has raised no objections from the point of view of medical ethics. However it is a requirement that your baby’s records in this research, along with any relevant medical records, be made available for scrutiny by the UK Regulatory Authority.

Thank you for taking the time to read this information sheet.
Further information and contact details

General information about the research can be found at: www.npeu.ox.ac.uk/I2S2

Specific information can be obtained from:

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