iSEARCH Study – Lay summary of results

This is a summary of the main results from the iSEARCH Study: Can intrapartum Sildenafil Citrate safely avert the risks of contraction-induced hypoxia in labour? iSEARCH – a pragmatic multicentre Phase III randomised controlled trial.

There were 3257 participants from 13 hospitals in Australia who participated in this study. We greatly appreciate the contribution of all the iSEARCH participants, their families and the hospital staff involved.

What was the trial about?

In Australia, nearly 1 in 4 caesarean sections are performed due to suspected fetal distress, which occurs when the placenta can't supply enough oxygen and nutrients during labour. The main solutions for fetal distress are emergency caesarean sections or instrumental vaginal births, both carrying significant risks.

The iSEARCH study aimed to assess whether Sildenafil (which has been shown to increase blood flow to the uterus and placenta) compared to placebo reduces the risk of operative birth for fetal distress in women in term labour and improves outcomes for the mother and baby.

3257 participants were randomly placed into two separate groups, with an equal chance of receiving either the sildenafil or the placebo.

What were the effects of the treatment?

Sildenafil did not demonstrate any additional benefit in reducing the risk of operative birth.

What were the side-effects of the treatment?

There were no differences between the two groups with regards to prespecified side effects potentially related to sildenafil nor any other serious outcomes. Specifically, there were no cases of maternal mortality, intrapartum stillbirth or neonatal death in either group. One case of persistent pulmonary hypertension occurred in the sildenafil group compared to three cases in the placebo group.

Were there any serious side-effects?

No, there were no unexpected serious adverse events were reported.

How will the results help patients and doctors in future?

The results of the iSEARCH trial provide important insights for both patients and doctors. Although the use of sildenafil during labour at term did not show a reduction in operative births due to fetal distress, the findings highlight the need for continued research in this area.

The findings emphasise that while promising results from earlier studies were not replicated, alternative approaches and careful monitoring of fetal well-being during labour remain crucial.

Can these results explain why my baby had a particular outcome?

This study assessed sildenafil's effect on women in labor at term. The results showed no difference between the sildenafil and placebo groups. Because of this it was not possible to explain why an individual baby had a particular outcome.

If you were involved in the study and would like to discuss any part of the study further, please contact your local iSEARCH doctor at the hospital where your baby was born who will be happy to speak with you.

What will the researchers do next?

The investigators will be investigating if placental function before labour contributes to a baby becoming distressed in labour. Longer term neurodevelopmental outcomes will also be examined.

Where can I find out more about the trial?

The iSEARCH study has been published in:

Journal of the American Medical Association (JAMA): https://jamanetwork.com/journals/jama/article-abstract/2835126

You can also find out more from the following websites:

- https://ctc.usyd.edu.au/our-research/research-areas/neonatal-and-perinatal/active-trials/isearch/
- https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=380796&isReview=true

Thank you again for taking part in this important work.

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