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Cystic Fibrosis Research News

Title:

Final Results of the Southwest German Pilot Study on Cystic Fibrosis Newborn Screening – Evaluation of an IRT/PAP Protocol With IRT-Dependent Safety Net

Lay Title:

Evaluation of a biochemical cystic fibrosis newborn screening protocol using IRT and PAP

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What was your research question?

For the planned newborn screening programme for cystic fibrosis (CF) in Germany, we investigated whether we can use a test looking at a combination of two proteins found in the blood of people with CF, immunoreactive trypsinogen (IRT) and pancreatitis-associated protein (PAP), to accurately predict whether a newborn baby has CF.

Why is this important?

Children with CF benefit from being diagnosed early. This has been already seen in other western countries with genetic-based newborn screening programmes for CF. These

screening tests diagnose CF by firstly measuring IRT levels and then considering if there are also genetic variants which are common in CF. However, for regulatory reasons in Germany we tested a strategy that did not consider genetic variants and instead was based on biochemical screening with IRT and PAP, a method that was first proposed by a French working group in 2005. It is important for such screening tests that no newborn baby with CF is missed (sensitivity) and as few as possible are wrongly diagnosed as having CF (specificity).

What did you do?

Almost 500,000 newborn babies from South-West Germany were screened for CF from 2008 to 2016. We firstly measured, the level of IRT in the blood in all newborn babies. If IRT was higher than normal, we also measured PAP levels and also tested the blood to see if four genetic variants common in Germans with CF were present. Afterwards, we compared the results of the modified biochemical strategy (IRT and PAP) with those of the genetic screening strategy (IRT and the four most common genetic variants) to see whether the biochemical screening strategy is as good as the genetic-based strategy.

What did you find?

We present these final results, now that the database has been closed; it is four years since the end of the study so that we had a chance to identify as many of the children as possible who may have originally been wrongly diagnosed as not having CF. We found that the sensitivity of the IRT/PAP strategy is similar as that of the genetic-based screening strategy. However, the IRT/PAP strategy was a lot less specific and identified many more healthy newborns as having CF when they didn't.

What does this mean and reasons for caution?

The changes we made to the method increased the sensitivity of the IRT and PAP strategy when compared to the original. However, biochemical screening is not as good as genetic screening, because it diagnoses more healthy newborns who don't actually have CF and the parents of these children are unnecessarily frightened until the diagnosis can be excluded by further testing. However, a study from the Netherlands which was published in 2012 to showed that , the number of these falsely identified healthy newborns can be reduced by combining IRT and PAP screening with the search for CF-typical genetic variants in a third stage.

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What's next?

The findings from this study were incorporated into the German newborn screening programme for CF which was introduced in 2016. The results of the first three years of this screening programme are currently being evaluated to improve its quality further.

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