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Early diagnosis and epilepsy prevention: Results of the EPISTOP study

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Studies have shown that early diagnosis of TSC has been linked with improved outcomes, and doctors have recently learned how to diagnose TSC prenatally (before a child is born) more easily.

7 in 10 infants living with TSC develop seizures until 24 months of age. Early seizures are associated with speech delay, intellectual disability, and autistic behaviour. 8 in 10 of prenatal infants and infants with TSC have cardiac rhabdomyomas (growths on the heart), which can be identified through cardiac tomography (a type of x-ray technique).

Researchers have been trying to find ways to identify, manage and/or treat symptoms of TSC in newborns and infants, to improve outcomes in later life.

In 2011, Prof Sergiusz Jóźwiak published results showing the preventative treatment of children under 2 years of age with abnormal activity on EEG with vigabatrin (everolimus) 100-150mg/kg. EEG stands for electroencephalogram – a test that records brain activity. During the test, small sensors are attached to the scalp which pick up electrical signals produced by brain cells when they send messages to each other.

The results showed that in the group treated with preventative vigabatrin:

- There were a lower number of infants with infantile spasms and drug-resistant epilepsy
- There were a higher number of seizure-free infants at the age of 24 months
- Infants had a higher IQ score at 24 months
- 0% of infants had moderate, severe and profound intellectual disability at the age of 24 months

In 2019, Prof Jóźwiak published the results of a follow up study of these infants when they reached 7-9 years of age. At this age, researchers also observed the preventative group had:

- A higher IQ score
- Lower rates of intellectual disability
- Lower rates of epilepsy

In 2013, the EPISTOP trial started. Studies took place at 16 sites across Europe, the USA and Australia. EPISTOP had two aims:

1. To prove that early treatment of subclinical seizures significantly reduces drug-resistancy and neurodevelopmental delay in children with TSC
2. To provide a prospective analysis of clinical and molecular biomarkers (measures) in the course of epileptogenesis (the development of epilepsy)

The study came to an end in April 2019. The results showed that preventative treatment delays the onset and lowers the frequency of epilepsy, compared to conventional treatment. The group treated preventatively had less drug resistant epilepsy, and lower rates of infantile spams. Infants without seizures did not go on to develop autism or any neurodevelopmental delay.

It is also important to mention that both groups (preventive treatment and conventional treatment) had very frequent visits with video EEG. None of the infants therefore had severe disability at age 2 years, as any and every abnormality was picked up by the doctors during these visits. This may explain why there were no statistically significant differences in the intellectual disability between both groups. This means that doctors were able to diagnose epilepsy much earlier than usual.

All infants without epilepsy had normal intellectual function, which supports the concept that epilepsy is the main contributor to intellectual disability in TSC.

A few take home messages:

- Recent EEG studies prove that video EEG is a good biomarker (measure) of epilepsy development.
- Early appearance of slow background activity on an EEG is a predictor of epilepsy onset.
- EEG surveillance significantly reduces the risk of severe intellectual disability in individuals with TSC.
- Preventative treatment may decrease the risk of clinical seizures, drug resistant epilepsy and infantile spams.
- The EPISTOP study has demonstrated that preventative treatment of epilepsy decreases the risk of intellectual disability. However, preventative treatment was not shown to influence the risk of ASD.