Incorporating epilepsy genetics into clinical practice: utility and cost saving

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Introduction

We established a regional epilepsy genetics service:
- southeast England
- serving a population of 3.5 million.

The service has two components:
- a specialist outpatient clinic
- a molecular diagnostic service.

We evaluated:
- the effectiveness and utility of NGS
- investigation costs
- the patient/referrer experience

Methods

- Prospective observational design over 18 months
- N=96 consecutive patients with primary Dx suspected genetic epilepsy
- Educational workshop for paediatricians

We used:
- Amplexa epilepsy NGS gene panels: 46 – 102 genes
- ACMG variant classification
- MDT clinical interpretation
- ILAE definition of AED resistance

We assessed:
- Diagnostic yield by age group
- Family and referrer satisfaction survey
- Investigational costs in neonatal epilepsy (n=16)
  - video EEG, MRI, metabolic, single genes

Results

Effectiveness and Utility

- 60% of patients had ≥ 1 variants
  - 19 benign
  - 16 VUS
  - 23 likely pathogenic
- SCN8a (n=4) and SCN2a (n=3) most common
- Turnaround Time: 21 DAYS
- Overall diagnostic yield 29% amongst AED resistant cases
- Treatment implications for 63% with pathogenic variants

Pathogenic variants:
- SCN8A, SCN2A, SCN1A, KCNQ2, HNRNPU, GRIN2A, SYNAP1, STXB1, STX1B, CDKL5, CHRNA4, PCDH19, PIGT

Conclusions

1. NGS panel has high utility and effectiveness if seizure onset <2 years
2. Earlier diagnostic use of gene panel could cut investigation costs by 70% or €7,000
3. Turnaround time is world leading 21 days vs. median diagnostic delay 3 years
4. Enthusiastic acceptance of genomic medicine by referrers and families

Cost

- Actual investigation costs neonatal epilepsy €10,171 (range: €5,534 – €16,972).
- Theoretical costs if gene panel first line: €3,083

Patient/Referrer Experience

- 100% families would recommend to friends and family
- 50% referrers think gene panel reduces investigations

Figure 1. Demographic breakdown of tested patients

Figure 2. Diagnostic yield by age of seizure onset

Figure 1.
Evelina London Children’s Hospital

Figure 2.

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Figure 1.

Figure 2.