4CPS-188 IMPLEMENTATION OF THIOPURINE PHARMACOGENETICS TO IMPROVE PAEDIATRIC SAFETY AT A TERTIARY HOSPITAL

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Background and Importance Thiopurines play a crucial role in the treatment of paediatric patients with acute lymphoid leukaemia (ALL). Although these drugs are administered almost continuously for over two years, their main drawback lies in the occurrence of adverse events (AEs), particularly hepatotoxicity and myelotoxicity, which can lead to treatment delays.

Research has established a link between these AEs and the genotypes of two enzymes involved in thiopurine metabolism: thiopurine methyltransferase (TPMT) and nudix 15 hydrolase (NUDT15). Currently, recommendations exist for adjusting the initial dosages based on genotype.

Aim and Objectives

- Determine the prevalence of alleles associated with the most common enzyme activity deficiencies for TPMT and NUDT15 in our region, comparing them with literature data.
- Implement an analysis and information circuit enabling individualised thiopurine dosing based on pharmacogenetics for paediatric ALL patients.

Material and Methods We conducted a literature review to identify alleles linked to intolerance to standard thiopurine doses. Considering the allelic prevalence in different populations, we selected three TPMT alleles and one NUDT15 allele according to ours. These alleles were classified as first-level by various agencies and consortiums. We designed primers for allele screening with Sanger sequencing technique.

Our centre's database contained 2,194 exomes with informed consent, which we analysed to estimate allele prevalence in our population. Techniques, test request procedures, and decision algorithms for initial dosages were protocolised based on current recommendations.

Results In a total of 2,194 exomes, we studied mutations rs1800462, rs1800460, and rs1142345 for TPMT, and rs116855232 for NUDT15. We identified 36, 113, 147, and 48 cases, respectively. Our population exhibited higher frequencies compared to non-Finnish Europeans (NFE) in the Genome Aggregation Database, with rates of 1.64% vs. 0.24%, 5.15% vs. 3.82%, 6.7% vs. 4.23%, and 2.18% vs. 0.29%, respectively.

Conclusion and Relevance Our results support the benefit of genetic testing in our population due to the prevalence of low-activity alleles.

We anticipate performing 10 to 15 genetic studies annually, aligning with the ALL cases we treat each year.

The implementation of an individualised dosing circuit based on pharmacogenetics represents a substantial advancement. This approach will enhance the safety and efficacy of thiopurine treatment.

This model can be replicated in hospitals with genetic determination capabilities through Sanger sequencing.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

4CPS-189 LOCAL EXPERIENCE ON THE USE OF CANNABIDIOL FOR THE TREATMENT OF REFRACTORY EPILEPSY: SAFETY AND EFFICACY ON A 10 PATIENT COHORT

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Background and Importance Cannabidiol is approved in Europe as adjunctive therapy for preventing seizures associated with Lennox-Gastaut Syndrome (LGS), Dravet Syndrome (DS), and Tuberous Sclerosis Complex (TSC) in patients with previous treatment refractory epilepsy.

Aim and Objectives This study aims to evaluate the efficacy and safety of cannabidiol in a cohort of patients from a medium-sized hospital.

Material and Methods An observational retrospective study was conducted. Patients diagnosed with LGS and DS who began treatment with cannabidiol from October 2019 to September 2023 were included. Data collected were demographics (gender, age), drug therapy (number of concomitant drugs) and clinical outcomes (Reduction > 50% on seizure rate and cannabidiol side effects).

Abstract 4CPS-189 Table 1

Pat	Age (years)	Sex	Indication	Treatment Duration (days)	Epidyolex dose (mg/Kg/day)	Drug AR	Concomitant ASD's	> 50% seizure rate reduction
1	48	M	DS	210	7,24	None	5	Yes
2	23	F	LGS	1432	22,85	None	3	Yes
3	21	M	LGS	1434	17,27	None	7	Yes
4	42	M	LGS	413	5,08	Digestive	7	Yes
5	21	F	LGS	668	13,33	Digestive	5	Yes
6	35	M	LGS	598	5,2	Digestive	4	Yes
7	53	M	LGS	852	16	None	5	Yes
8	23	M	LGS	1049	11,9	None	6	Not
9	38	M	LGS	1158	9,09	Digestive	5	Not
10	24	M	LGS	212	4,33	None	4	Not
	mean= 32,8	8 Male 2 Female	90% SLG 10% TSC	mean= 737,3 median= 633	mean= 11,23 median = 10,49	70% No AR 30% AR (digestive)	mean = 5,1 median = 5	70% responders rate