

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

Results Ten patients were included on the analysed data set, with a mean age of 32.8 years, nine of them had LGS associated epilepsy, and one to DS. With a median treatment duration of 633 days and a cannabidiol median dose of 10,49 mg/Kg/day, 70% of patients reached a seizure reduction > 50%, being the majority of them out of drug related side effects.

Conclusion and Relevance As a real-life experience, our findings confirm that the safety and efficacy profiles of cannabidiol showed by the trials GWPCARE3 and GWPCARE4 (mean age=15 years)¹ are extended to our local adult population with a higher average age of 32.8 years.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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Conflict of Interest No conflict of interest.

4CPS-190 DEVELOPMENT OF TRANSMURAL PHARMACEUTICAL CARE IN A GENERAL HOSPITAL

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Background and Importance The transition between different care settings is vulnerable to medication errors. To avoid these errors, information about new medications must be shared between different care providers.

The PACT project, an integrated care project, proposes to carry out medication reconciliation according to a structured methodology using envelopes. At hospital admission, blue envelopes are used. They contain the patient's medication scheme previously produced by the reference pharmacist in a community pharmacy. At hospital discharge, the new medication scheme and the new prescriptions are placed in a green envelope. This envelope must be given to the reference pharmacist who must explain any changes to the patient.

Aim and objectives • To set up and evaluate the impact of pharmaceutical interventions aiming to implement the PACT medication reconciliation system at hospital discharge.

Material and Methods Two audits, each carried out over a period of 10 days in December 2022, were conducted in three care units on a pre-test group and a test group. The test group was constituted during the period of test which included pharmaceutical interventions (real-time interventions and outreach visits to practitioners).

- We evaluated the similarity between the two groups in terms of demographic and clinical characteristics and in terms of medication characteristics using Student's test and the Chi-Squared test (χ^2 test).
- The impact of the pharmaceutical interventions was then evaluated by comparing between the two groups the rate of green envelopes delivered to the patient. Data were analysed using χ^2 test.

Results

- The two groups were similar in terms of demographic and clinical characteristics. Regarding medication characteristics, the analysis confirmed the similarity between groups, except

for the number of newly prescribed medicines ($p = 0.04$) and the number of medicines to be stopped after hospitalisation ($p = 0.03$).

- The rate of green envelopes delivered to the patient at the end of hospitalisation was higher in the test group (78%) compared to the pre-test group (33%) ($p < 0.001$).

Conclusion and Relevance This work highlights the importance of developing the role of integrated care pharmacist coordinator to strengthen the communication on patient medications.

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Conflict of Interest No conflict of interest

4CPS-191 PRE-RADIOIODINE THERAPY SURGICAL MODALITIES: COMPARISON OF POST-OPERATIVE THYROGLOBULIN LEVELS IN PATIENTS UNDERGOING 1- OR 2-STEP THYROIDECTOMY FOR DIFFERENTIATED THYROID CANCER

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Background and Importance Surgical practices in thyroid oncology recently evolved towards de-escalation, with more frequent 2-step surgery (lobectomy then totalisation). Moreover, in non-metastatic thyroid cancers with low risks of recurrence, radioiodine therapy (RIT) to eliminate potential residual cancer cells has become optional, particularly in cases displaying low postoperative thyroglobulin (POTg) values. It is known that plasma thyroglobulin is correlated with the size of the post-thyroidectomy residue, excluding distant metastases. However, it is not known whether this residue is greater in the case of 1- or 2-step surgery. Indeed, the 2-stage approach may provide a more substantial residue, measurable by the POTg value. Clinicians should therefore take this notion into consideration when deciding on adjuvant RIT.

Aim and Objectives To compare POTg values in patients undergoing 1- or 2-step thyroidectomy for low-risk thyroid cancer, based on retrospective collection of biological data from operative and pathological reports in a cohort of RIT patients at our centre.

Material and Methods Inclusion criteria for this study were: non-metastatic patients with a low-risk pathology who had biological tests performed between surgery and RIT consultation, a non-detectable anti-thyroglobulin antibody assay, a period >28 days between surgery and biological tests, and TSH levels <5 μ IU/mL. Parameters useful for describing the patient population and comparing POTg values were compiled in a computerised spreadsheet and analysed.

Results Between 15 July 2016 and 24 February 2023, 70 patients from our centre met the inclusion criteria. Mean TSH value was 1.377 ± 1.336 μ IU/mL and mean POTg was 0.543 ± 1.067 ng/mL. Mean time between operations for patients treated in 2-steps was 82 ± 55 days and mean time between operation and biological test was 68 ± 54 days. Two groups