detecting the symptoms and signs of toxicity for avoid unwanted effects, it is possible by frequent visits to the hospital pharmacy.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

4CPS-241 FINAL VALIDITY OF A TOOL FOR RATING SIGNIFICANCE OF PHARMACISTS' CLINICAL CONTRIBUTIONS IN HOSPITAL

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Background and Importance To date there is no gold standard for rating clinical significance of pharmacy contributions to care.

IMPACCTS (InstruMent for PhArmacy Clinical Contributions To care Significance) is based on the Hatoum scale[1] and consists of five ordered categories or levels, each underpinned by descriptive statements (total of 45 statements).

A robust process to ensure simplicity and clarity of the instrument has been previously reported.[2]

Aim and Objectives Aim: To complete the validation of IMPACCTS.

Objectives were to:

- demonstrate comprehensiveness of IMPACCTS
- quantify interrater reliability of IMPACCTS

Material and Methods This study was completed February 2022. The study did not require ethics approval.

To assess comprehensiveness, 20 senior pharmacists with prior experience of using IMPACCTS were paired to review 45 scenarios (450 different scenarios in total) and asked to find a corresponding statement, or failing that, a suitable significance level.

For interrater reliability, all 20 pharmacists were given the same 15 detailed scenarios to rate clinical significance. Intraclass correlation statistics (two-way, random effects, absolute agreement, individual) were calculated using Stata v14.

All data were collected via a web survey platform.

Results Comprehensiveness – for all scenarios, at least one person found a statement. For 441/450 (98%) scenarios, both respondents in a pair found a corresponding statement. Out of the nine scenarios where one person from the pair did not find a statement, a level could be assigned for eight of these. Therefore, a statement and/or level could be assigned for 449/450 (99.8%) of the scenarios by all respondent pairs.

Intraclass correlation was 0.71 (95% CI = 0.55, 0.86) which demonstrates moderate to good pharmacist interrater agreement.

Conclusion and Relevance This study demonstrates excellent comprehensiveness and moderate to good interrater reliability of IMPACCTS. These data support readiness of the tool for use in research and practice to assess clinical severity of pharmacy contributions in hospital.

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Conflict of Interest No conflict of interest.

4CPS-242 ISAVUCONAZOLE TREATMENT IN TWO PAEDIATRIC PATIENTS DURING EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT: THE ROLE OF THERAPEUTIC DRUG MONITORING

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Background and Importance Extracorporeal membrane oxygenation (ECMO) may lead to pharmacokinetic alterations of antimicrobials. Isavuconazole is not approved in paediatric patients (PedP) (off-label use) and data on paediatric ECMO are non-existent.

Aim and Objectives To describe two case reports using therapeutic drug monitoring (TDM) to optimise isavuconazole dosage in PedP during ECMO.

Material and Methods Prospective study in critically ill PedP treated with intravenous isavuconazole receiving ECMO (January 2021to August 2022). Biodemographic, clinical and pharmacokinetic data were collected. Initial proposed dose of isavuconazole base was 5.4 mg/kg (first 48h q8h, followed by q24h; maximum 200 mg/dose). Isavuconazole trough serum concentration (IsaCmin) of 2.5-5 µg/mL was considered as therapeutic range (internal protocol). Continuous variables were expressed as median (range).

Results 1) A 2-year-old boy (11.5kg, 90cm) lung transplant recipient (pulmonary capillary hemangiomatosis) diagnosed with tracheobronchitis caused by *Aspergillus flavus* (9 months after transplant). Isavuconazole was started at a proposed dose and IsaCmin remained in therapeutic range: 5.1(2.5-5.5) µg/mL. Secondary prophylaxis with isavuconazole was maintained (same dose), requiring ECMO due to severe acute respiratory failure (multifactorial). During ECMO (165 days), it was necessary to increase the dose to 16.5 (8.7-19.1) mg/kg/24h to achieve target concentration of median IsaCmin 2.82 (1.3-6.5) µg/mL (24 blood samples). No new fungal infections were observed but sadly the patient died due to intracranial haemorrhage.

2) A 11-year-old girl (70kg, 158cm) admitted for influenza A infection and necrotising pneumonia (*Staphylococcus aureus*), requiring ECMO. Invasive fungal infection was probable (EORTC criteria; positive galactomannan and tracheal aspirate for *Aspergillus niger*) and isavuconazole was started: loading dose of 300mg/6h (suspected interaction with pentobarbital during first 48h) and TDM-guided maintenance therapy. During ECMO (30 days) median maintenance dose was 900mg (12.9mg/kg)/24h (varied widely ranging from 200mg/12h to 250mg/4h) and median IsaCmin remained in the therapeutic range: 4.0 (1.1-8.4) µg/mL (9 blood samples). After ECMO decannulation, isavuconazole dose was reduced to 200mg/12-24h and median IsaCmin remained in range: 3.9 (2.8-11.4)

µg/mL. She continues isavuconazole maintenance treatment with a partial response.

Conclusion and Relevance

- PedP on ECMO may require higher doses of isavuconazole to achieve therapeutic concentrations, suggesting that TDM may be clinically useful.
- Further studies in critically ill PedP, especially those on ECMO, are necessary to confirm the optimal isavuconazole dosage.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

4CPS-243 DELAYED HIV TREATMENT AND FACTORS ASSOCIATED

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Background and Importance Clinical practice guidelines (EACS, DHHS, Gesida) recommend starting antiretroviral therapy (ART) as soon as possible after HIV diagnosis, irrespective of CD4 cell count (CD4c). Postponing ART start until complementary assessments depends on the setting, medical indications and risk of loss from care.

Aim and Objectives To analyse delay in treatment initiation over the past ten years and to understand factors associated with delayed ART initiation.

Material and Methods Retrospective observational study in patients diagnosed with HIV infection in an integrated health area from January-2012 to June-2022. Variables collected: age, sex, route of infection, healthcare setting of diagnosis, time from diagnosis to ART initiation (delay time), ART, AIDS stage, baseline VL and CD4c.

Data were collected from electronic medical records and outpatient dispensation program. Statistical analysis was performed using Student´s t-test and linear regression method (dependent variable: delay time) by SPSS® v.15.0.

Results 108 patients were included, median age was 34 years (IQR 29.2-42.7) and 76.9% were men. 41.7% were diagnosed in primary care and 58.4% in the hospital setting. 38.9% were in AIDS stage at diagnosis. The predominant route of infection was men who have sex with men (MSM) 50.9%.

ART was initiated with nucleoside reverse-transcriptase inhibitors (NRTI) combined with integrase-strand-transfer inhibitors (INSTI) 66.7%, non-nucleoside reverse-transcriptase inhibitors (NNRTI) 13% and boosted protease inhibitors (PI/b) 20.4%.

The median baseline logVL was 4.63 (4.13-5.14) and CD4c was 325 (95-500).

The median delay was 21 days (IQR 9-55). Factors associated with delay: baseline CD4c (for every 100 CD4 increase the delay time was extended by 2.29 days (95% CI 0.56 to 4.02; p=0.01); baseline logVL (-3.25 days 95% CI 1.57-8.08; p=0.18); AIDS at diagnosis (-5.40 days; 95% CI 3.30-14.10; p=0.2); use of INSTI or PI/b compared to NNRTI (-31.28 days; 95% CI 7.85-54.71; p= 0.016). For each year of evolution, the time to ART initiation was reduced by 3.05 days (95% CI1.59-4.50; p<0.001). Comparing 2012-2018 vs 2019-2022, the delay was reduced by 20 days (95% CI13.66 to 27.26; p<0,001).

Conclusion and Relevance The delay to ART initiation has been significantly reduced in recent years. Factors related to the decrease in delay are lower CD4c, starting treatment with INSTI or PI/b vs NNRTI and being within 2019-2022 vs 2012-2018.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

4CPS-246 TREATMENT AND NURSING CARE OF MUCORMYCOSIS IN PAEDIATRICS: A CASE REPORT

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Background and Importance Mucormycosis is a serious fungal infection that causes fast invasion, especially in immunocompromised people.

Rhino-orbital cerebral involvement manifests with oedema, sinusitis, periorbital cellulitis and others.

Treatment often requires combined endovenous and topical therapy, and depending on the involvement, surgery.

Aim and Objectives Explaining the therapeutic approach and evolution of a very severe lesion with deep necrosis in the right nostril, with rapid progression and infected by Acinetobacter Baumanii extremely multidrug-resistant (ABXDR), Aspergillus niger and Rhizopus arizus.

Material and Methods A 13-year-old patient (45kg) with Atypical Haemolytic Uremic Syndrome, admitted in another centre where she started treatment with eculizumab and receive corticotherapy, was transferred to our centre due to clinical worsening.

Presented a rapidly progression lesion with deep necrosis in the right nostril.

Wound culture isolated Acinetobacter Baumanii extremely multidrug-resistant (ABXDR) and Aspergillus Niger. Subsequently, Rhizopus arizus was isolated in the biopsy and a diagnosis of rhino-orbital mucormycosis was made. Furthermore, ABXDR is isolated in conjunctival swab and tracheal aspirate.

Systemic treatment was started with isavuconazole (loading dose: 200mg/8h for 2 days and maintenance with 200mg/24h, plasmatic levels 3.85µg/mL), liposomal amphotericin-B (225 mg/24h), meropenem 2g/8h given as a 4-hour extended infusion and nebulised colistin 2MUI every 8 h.

Locally, the wound was first surgically debrided in two steps and targeted therapy was initiated. Due to the lack of commercially available formulations, sterile gels of amphotericin B deoxycholate 0.15% and colistin 0.5% were prepared by the pharmacy service; both were prepared on a water-soluble basis. They were applied every 4 hours alternately.

During admission, topical dressings with sodium hypochlorite fomentation (MicrodacynR) plus bacteriostatic gel-based mesh (Cutimed SorbactR) were performed every 24h.

A pharmacy-prepared colistin 0.2%/6h ophthalmic gel was applied to the eyes.

Throughout the hospitalisation, the wound was closely monitored performing smears to detect the microbial growth.

Results Clinical Outcomes were a rapid wound reduction with 80% granulation and negative microbial cultures after 28 days