3PC-021 AMPHOTERICIN AND COLISTIN GELS FOR NECROTISING WOUNDS: GALENIC AND MICROBIOLOGICAL VALIDATION

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Background and Importance In the intensive care unit, wound infections are complications with highly associated morbimortality, especially in immunocompromised patients. In some circumstances, a combination of endovenous and topical therapies may be required. Due to the lack of adequate commercial presentations, a compounded topical treatment could be a solution to manage a specific infection.

Aim and Objectives Developing a sterile topical gel of Amphotericin B-deoxycholate (Amfob-dc) and colistin to treat severe necrotic wound caused by *Aspergillus fumigatu*, *Acinetobacter baumanii* and *Rhizopus arizus refractory* to surgical debridement in a critical patient. Galenic and microbiological validation.

Material and Methods Bibliographic research was done first and based on the information compiled, it was decided to use sterile water-soluble gel(Varihesive Hydrogel®) as an excipient base. Varihesive Hydrogel is used on the debridement of necrotic wounds. When used with AmfoB-dc 0,15% and colisitin 0,5% in sterile conditions, both refrigerated, remained 7-days stable based on the risk matrix (low risk) of Good Pharmacy Practices. For galenic and microbiological validation, 3 samples of both gels were stored in refrigerator and in room temperature protected from light. Organoleptic characteristics (colour and fluidity), pH and weight were controlled and validated at days 0,7,14,21 and 28 of preparation. Microbiological validation was performed at day 28. Efficacy of treatment was studied with wound reduction and granulation one month after the initiation of the treatment, which was applied 3 tid.

Results Particle-free, homogeneous and viscous gels were obtained. The AmfoB-dc gel exhibited yellow colour and the colistin-based gel gray-translucent. No microbial growth was observed between days 0 to 28. Organoleptic characteristics remained constant throughout the period, however, once stored at cold tempatures they exhibited more viscosity.There were no differences in pH levels or weight variation of >10% (table 1).

Clinical Outcomes were excellent one month after the initiation resulting in an 80% reduction and granulation of the wounds and negative microbiological cultures.

Abstract 3PC-021 Table 1

AmfoB-dc					
pH (Day)	**0**	**7**	**14**	**21**	**28**
RT	7	7	7	7	7
Refrigerator	7	6.5	7	7	7
Weight (Day)	**0**	**7**	**14**	**21**	**28**
RT	7.5	7.6	7.1	7.0	7.0
Refrigerator	8.9	8.9	9.0	8.9	8.8
Colistin					
pH (Day)	**0**	**7**	**14**	**21**	**28**
RT	7	7	6	6	7
Refrigerator	7	7	6	6	6
Weight (Day)	**0**	**7**	**14**	**21**	**28**
RT	9.1	9.1	9.0	8.7	9.1
Refrigerator	9.2	9.2	9.2	9.2	9.2

Conclusion and Relevance These formulations are simple and give accurate results as a targeted therapy for necrotising infected wounds. The individualised topical preparations allow to solve problems of unavailability of adequate commercial forms. According to our validation, the galenic stability of the product seemed to be extended. However, further stability and quantitative studies should be conducted.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

3PC-027 STABILITY OF TACROLIMUS ORAL SUSPENSION IN DISPOSABLE POLYPROPYLENE SYRINGE

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Background and Importance Within the post-operative period following a solid organ transplantation, multidisciplinary teams prioritise tacrolimus administration *per os* to minimise the neurotoxicity associated with its use via continuous intravenous infusion. Despite being classified as a hazardous drug, there is no tacrolimus liquid dosage form commercially available ready for direct administration by oral route.

Aim and Objectives To validate physical, chemical and microbiological stability of an affordable extemporaneous tacrolimus oral solution/suspension in single-dose disposable polypropylene syringe.

Material and Methods A search on chemical compatibility between tacrolimus and polypropylene was accomplished. The formulation developed for study case was split in three samples stored at 20–25°C and three others at 2–8°C, ensuring every assay was performed in triplicate.

Stability parameters were tested every 7 days for a 28-day period. The analysis included organoleptic properties, sedimentation time, homogeneity, pH, redispersibility, crystal growth and weight variation. In order to identify and quantify any potential colony-forming unit (CFU), cultures with blood agar were read after 24 and 48 hours from incubation at 37°C, whereas Sabouraud agar cultures were read after 24, 48, 72 and 96 h.

Results Chemical stability of tacrolimus 1 mg/mL suspension formulated with 1:1 Ora Plus® and Ora Sweet® in polypropylene syringe was reported.

For the present study, tacrolimus 1 mg/mL suspension based on a 2:1 blend of simple syrup and carboxymethylcellulose 1.5% aqueous gel was developed since its composition is simpler and saves € 8,51/100 mL.

Physical and chemical parameters remained constant during all the study period regardless of storage temperature: The formulation was homogeneous, sheer with yellowish hue and sweet. No crystal growth or sediment were observed. Median weight variation was 0.96% for the fraction stored at 20–25°C (0.38%–1.65%) and 0.75% for the stored at 2–8°C (0.58%–1.08%). Average pH values were 5.70 (5.60–5.76) and 5.72 (5.70–5.76) respectively.

One *Staphylococcus hominis*CFU was detected on day 14 in one sample stored at 2–8°C. No subsequent microbial growth was found, therefore it was considered contamination

Conclusion and Relevance Tacrolimus 1 mg/mL oral suspension in simple syrup and carboxymethylcellulose 1.5% in a 2:1 ratio is stable when conditioned in polyproplylene syringe for 28 days and stored at room or refrigerator temperature.

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3PC-030 EVALUATION OF EXCIPIENTS USED IN PAEDIATRIC COMPOUNDED FORMULATIONS PRESCRIBED IN A NEONATAL INTENSIVE CARE UNIT

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Background and Importance The absence of marketed medicines adjusted to the pathophysiological profile of the neonate often implies the preparation of personalised compounded medicines. To meet therapeutic needs and improve medicines' stability, several vehicles have been developed and studied for different drugs. The choice of excipients is a critical point in paediatric compounded formulations (PCF), as there are limits inherent to the target population.

Aim and Objectives Evaluation of exposure to PCF excipients, according to individualised medical prescriptions to patients admitted to a Neonatal Intensive Care Unit (NICU) between September 2019 and August 2020, considering the recommended limits. Search for related adverse events (AEs) when limits are exceeded. Propose solutions for the non-conformities detected.

Material and Methods Definition of excipients to be evaluated, search of the respective recommended limits and AE reported.

Ranking PCF containing at least one of the selected excipients and calculation of its concentration in the formulation.

Analysis of prescriptions, calculation of excipient/patient daily intake and evaluation according to age recommendations.

In cases where the limits were exceeded, search the patient's medical record for AE that may be related to exposure to the excipient.

Results Evaluated excipients: benzyl alcohol, benzoic acid/sodium benzoate, ethanol, propylene glycol (PG), propylparaben (PP), polysorbate 80 and sorbitol.

Considering the 10 selected PCF, present in 86 prescriptions corresponding to 172 exposures, only 2 of the evaluated excipients were found: PP and PG. In 52 exposures there was ingestion above recommended limits, 50 of which were of PG in neonates with less than 28 days of age. 5 records of AE described in bibliography with a causal link were found in the medical files.

Conclusion and Relevance In cases of formulations where exceeded excipient limits were detected, an alternative with a different composition or concentration should be investigated. As 50 out of 52 non-compliances were with PG, used as a solvent in the paraben concentrate, this formulation will be tested using water instead of PG. It was not possible to retrospectively confirm a causal assessment related to the AE found as these are common clinical conditions in these patients. Individualisation of medication through compounding is the right direction as it best suits the patient's profile. However, the choice of excipients is crucial for patient safety.

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3PC-032 USE OF ORAL KETAMINE FORMULATION IN PATIENTS WITH CHRONIC REFRACTORY PAIN

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Background and Importance Chronic pain lasts more than three months and includes primary and neuropathic pain. Ketamine provides analgesia and amnesia at a subanaesthetic dose, therefore proposing its use as chronic pain treatment when it is refractory to the standard based on tricyclic antidepressants (TCAs), gabapentinoids, and opioids.

Aim and Objectives To analyse the use of an oral formulation of ketamine prepared and dispensed by hospital pharmacy at a third-level hospital in chronic refractory pain (CRP) treatment.

Material and Methods Observational retrospective study including a cohort of patients with CRP treated with an oral 10 mg/ml ketamine solution at a third-level hospital between January 2021 to December 2021. All of them signed informed consent. A tolerance test with intravenous ketamine was performed on every patient before initiating treatment. Data were collected from clinical history and pharmacy programs. For statistical analysis, continuous variables were categorised according to median (range) or percentage values.

Results 30 patients were included (67% men, median age 48.5 years (18–73)). Chronic pain type was neuropathic in all cases, cancer-associated (37%), trauma-caused neuronal damage (33%), demyelinating (17%), and 14% to other causes. Patients received oral ketamine during a median of 20 months (1–58) and daily dosage varied from 40 mg to 150 mg, the most frequent being 60 mg/d (40%), 90 mg/d (27%) and 120 mg/d (23%). 80% were in adjuvant treatment with opioids; of them, 88% took major opioids. 40% had reached the therapeutic limit by being treated with opioids, TCAs and gabapentinoids without any differences in pain origin. 43% had not included TCAs in treatment.

Treatment was discontinued in 5 patients (17%); 4 due to adverse effects (dizziness, cognitive alterations, tachycardia, hypertension), and 1 due to death unrelated to treatment.

Conclusion and Relevance This study shows oral ketamine analgesic use in neuropathic CRP treatment at 40–150 mg/d; the most frequent 60 mg/d and 90 mg/d. Inferior to those referred to in the literature (up to 400 mg/d). Good tolerance and an acceptable safety profile were observed (17% discontinued) without serious adverse events. As to adjuvant treatment, 80% received opioids and 40% the combination of opioids, gabapentinoid, and TCAs. More studies are needed to evaluate the long-term effectiveness and safety of oral ketamine treatment and to position it in CRP management.