observed in particle size after 60 days in all samples. The organoleptic characteristics (smell, taste and texture) remained unchanged in all of the preparations until the third month.

Conclusion and relevance A stable alcohol free diazepam suspension was achieved. The tablets produced a more stable formulation than the bulk source, especially when stored at a lower temperature. This formulation can solve the problem of shortages, allowing the appropriate administration of paediatric treatments, while allowing compliance with the recommended composition limits of ethanol, by excluding this excipient from its composition.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-029 PAEDIATRIC DRUG RESISTANT EPILEPSY: NITRAZEPAM 1 MG/ML SOLUTIONS TO AVOID CLINICAL THERAPEUTIC ERROR

[1]MA Berardi*, [2]GB Ortenzi, [2]V Moretti, [2]E Adresciani, [2]AMF Garzone, [3]S Cappanera, [1]C Polidori, [2]A Pompilio. *[1]Università Degli Studi Di Camerino 'Scuola Di Scienze Del Farmaco E Dei Prodotti Della Salute', Facoltà Di Farmacia, Camerino, Italy; [2]Ospedali Riuniti Di Ancona, Sod Farmacia Pediatrica Ospedale Pediatrico G Salesi, Ancona, Italy; [3]Ospedali Riuniti Ancona, Sod Neuropsichiatria Infantile, Ancona, Italy*

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Background and importance The management of paediatric patient with drug resistant epilepsy (EDR) is complicated and often requires therapy and dose adjustments. The clinical pharmacist and child neuropsychiatry unit cooperate to prevent clinical therapeutic errors, common in the prescription of drugs with reduced and personalised dosages.

Nitrazepam (NTR) in children is recommended in epileptic spasms, in Dravet, West and Lennox–Gastaut syndromes. There is a probable risk of administration error due to the low prescribed dosage (125 µg/kg)[1] and crushing of commercial tablets.

Aim and objectives To make a liquid formulation with a standard concentration, easily adaptable to paediatric needs as weight changes, that is palatability, suitable and simple to use during hospitalisation and at home.

Material and methods Multiphase study:

- Phase I: data collection.

Retrospective study examined the medical records of children born 2008–2019 with a certain diagnosis of EDR: patient number, sex, age, epilepsy classification according to the International League Against Epilepsy criteria,[2] antiepileptic therapy and dose of drug were collected.

- Phase II: subject study of nitrazepam, its dosage and the galenic compounding formulation it was possible to use.
- Phase III: chemical–physical–microbiological stability analysis of nitrazepam 1 mg/mL.

Samples were stored for 30 days at 2–8°C and/or ambient at 25°C. Chemical–physical stability was measured by quantitative determination of the molecular ions of nitrazepam C282.1/C236, using high pressure liquid chromatography (HPLC), equipped with a UV detector, interfaced with a triple quadrupole mass detector (mass spectrometer, MS/MS), column Luna C1850 mm, standard nitrazepam D5 100 µg/mL.[3] Microbiological stability was assessed according to the Italian Ufficial Farmacopea (FUI).[4]

Results A total of 101 children with EDR (54 males, 47 females) were studied, aged mainly 3–4 years (20%) and 9–10 years (33%). Classifications: focal onset in 34.86%, focal to bilateral tonic–clonic in 17.10%, generalised onset in 47.36% and unclassified in 0.65%. Thirty-one drugs are prescribed, the most used were: levetiracetam (27%), clobazam (25%), topiramate (21%) and NTR (12%). Required dosages of NTR difficult to administer: 0.625 mg, 0.83 mg, 1.25 mg, 1.66 mg and 2.5 mg. Three liquid galenic formulations were set up (NTR from Mogadon 5 mg tablets): NTR 1 mg/mL simple syrup methylcellulose 1%, NTR 1 mg/mL suspension tragacanth gum and NTR 1 mg/mL Syrspend SFAlkaDry.[5]

HPLC MS/MS analysis confirmed uniform and steady dosage, and 30 day stability for NTR 1 mg/mL suspension and NTR 1 mg/mL Syrspend SFAlkaDry.

Conclusion and relevance Good clinical practice and collaboration between departments allowed better management of epileptic seizures in children affected by severe EDR. Reproducible and safe therapy means improving patient's life and therapeutic compliance.

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No conflict of interest.

3PC-030 ANALYTICAL METHOD VALIDATION TO CARRY OUT PHYSICOCHEMICAL STABILITY STUDIES OF METHADONE ORAL SOLUTIONS

[1]EA Álvaro Alonso*, [2]MP Lorenzo García, [2]FJ Rupérez Pascualena, [2]A Aguilar Ros, [1]P Tejedor Prado, [1]A Lázaro Cebas, [1]I Cañamares Orbis, [1]S Esteban Casado, [1]A Such Díaz, [1]I Escobar Rodríguez. *[1]Hospital Universitario Infanta Leonor, Pharmacy, Madrid, Spain; [2]Universidad Ceu San Pablo, Pharmacy, Madrid, Spain*

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Background and importance On the basis of resolution 189/2018 published by our city health council, the hospital pharmacy service was entrusted with the centralisation of the procedure for the acquisition, compounding, distribution and dispensing of methadone to drug addicts in integral attention centres. In order to improve and increase the beyond use date (BUD) of methadone oral solutions, we carried out a physicochemical stability study.

Aim and objectives To develop an analytical method and validation to carry out a physicochemical stability study of two oral solutions of methadone to increase their BUD. Method development should be made in an effective and reproducible manner.

Material and methods The study was carried out on two formulations of methadone 10 mg/mL, which were prepared with and without parabens as preservatives. A high performance liquid chromatography (HPLC) Agilent 1100 was used, provided with a quaternary pump and an ultraviolet diode array detector to determine methadone. First we carried out the analytical method development to achieve the analytical performance characteristics. Then we performed validation of the analytical method obtaining linearity, instrumental intra-assay and inter-assay precision, and accuracy and recovery percentage.

Results Chromatographic conditions were: flow rate 1.6 mL/min, 55% acetonitrile and 45% phosphate buffer (adjusted to pH=10) as the mobile phase. Injection volume was 50 µL,

the temperature in the column compartment was 40°C. The column used was the Xterra C18 because methadone pKa is 8.3. Retention time for methadone was 4.5 min and for parabens 1.5 min.

The final methadone determination method was validated for a standard of 10 mg/mL and applied for the determination of methadone with two parabens. The most relevant results were: correlation coefficient r=0.9957 for methadone in the range tested (7.5–12.5 mg/mL); instrumental precision 0.33% for standards (n=10); intra-assay precision 0.53% (n=6) and inter-assay precision 1.95% (n=12). The relative standard deviation percentage for accuracy was 1.28%, and the percentage recovery was 101.5 ±1.5%.

Conclusion and relevance Analytical method development and validation procedures are vital in the discovery and development of drugs and pharmaceuticals to ensure performance of the method. The proposed HPLC conditions to determine methadone were proved to be valid and reproducible for carrying out physicochemical stability studies of different methadone oral solutions.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-031 CURRENT STATE OF THE ANTI-INFECTIVE OPHTHALMIC COMPOUNDING FORMULATION IN PHARMACY SERVICES: A NATIONAL SURVEY

A Castro Balado*, L Garcia-Quintanilla, C Mondelo-García, M González-Barcia, I Zarra-Ferro, A Fernández-Ferreiro. *Complejo Hospitalario Universitario De Santiago De Compostela, Hospital Pharmacist Service, Santiago De Compostela, Spain*

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Background and importance The ophthalmic formulation has for decades been postulated as the only alternative for the treatment of serious infective ocular diseases, since commercial presentations are not available. For this reason, most of these compounded formulas are made in hospital pharmacy services.

Aim and objectives To summarise the current state and processing variability of anti-infective ophthalmic compounded formulas through survey to pharmacists from different hospitals in the country.

Material and methods A survey was developed with questions related to anti-infective ophthalmic compounding formulations: facilities, stockage, use of freezing/preservatives, packaging, vehicles and validity periods. The questionnaire was developed through Google Forms and sent by email to hospital pharmacists nationwide in September 2019.

Results A total of 163 pharmacists from different hospital pharmacy departments answered the survey. Only 80% has installations that met the requirements of the Good Pharmacy Practice manual: 34% prepared anti-infective formulations on demand, while the rest had a stock. The median of the maximum eye drops/batch was 9.9 (IQR 3–10), and the median of the maximum intravitreal injections/batch was 10 (IQR 2–25). Related to eye drops, 49% used freezing on a regular basis, 26% under exceptional conditions and 25% never; while for intravitreal injections, the values were 47%, 13% and 40%, respectively. Eighty per cent never used ophthalmic preservatives while 20% used them under exceptional conditions. For the packaging of vancomycin eye drops, 82% used plastic, 15% glass and 3% both. As a vehicle for vancomycin eye drops, 36% used 0.9% NaCl, 25% DW 5%, 31% balanced salt solution, 7% artificial tears and 1% water for injection. Validity period was established according to: 53% bibliography, 40% risk matrix in the Good Pharmacy Practice manual, 6% both and 1% according to reference hospital standardised work procedures.

Conclusion and relevance Great variability was observed regarding the methodology used for the preparation of ophthalmic compounded formulas in hospitals throughout the country, highlighting the differences in the elaboration, packing and conservation of the same anti-infective ophthalmic compounding formulations.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Good Pharmacy Practice: https://www.mscbs.gob.es/profesionales/farmacia/documentacion.htm

Thanks to the pharmacists who completed the survey.

No conflict of interest.

3PC-032 AUTOLOGOUS TISSUE ADHESIVE IN OPHTHALMOLOGICAL SURGERY

[1]S Berisa*, [2]M Medina Persinal, [3]N Vazquez, [3]M Chacon, [3]J Merayo-Lloves, [3]A Meana, [4]L Fernandez-Vega Cueto-Felgueroso. *[1]Instituto Oftalmológico Fernández Vega, Farmacia, Oviedo, Spain; [2]Instituto Oftalmológico Fernández-Vega, Advanced Therapies and Regenerative Medicine, Oviedo, Spain; [3]Instituto Universitario Fernández Vega, Advanced Therapies and Regenerative Medicine, Oviedo, Spain; [4]Instituto Universitario Fernández Vega, Ophthalmology, Oviedo, Spain*

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Background and importance Sutures to replace tissue adhesives have enhanced importance. However, commercialised drugs are allogenic, synthetic and expensive, increasing surgery costs.

Aim and objectives

1. To produce an autologous tissue adhesive (ATA) easily compounded in ophthalmological surgery.
2. To show evidences of the safe and effectiveness of the ATA in preclinical studies.

Material and methods To produce 4 mL of ATA based on a fibrinogen (FC) and thrombin concentrate (TC) (proportion1:1), 20 mL of donor blood plasma were precipitated with protamine to prepare FC, and then 20 mL of plasma were precipitated with acetic acid to obtain a TC in a buffer ($CaCl_2$, $NaHCO_3$, NaCl). Drug was conditioned in two 2 mL syringes for topical ophthalmic administration by mixing with a needle.

The in vitro toxicity of the drug was studied in a human corneal epithelial model (described as QobuR), to evaluate the grade of irritation after 30 min of exposition time.[1]

Pterygium surgery was performed in four eyes of white New Zealand rabbits, using ATA to fix a frontal conjunctival autograft (4×5 mm) into the temporal bulbar conjunctive.

The grafted eyes were evaluated in vivo by clinical evaluation for 14–28 days and ex vivo by histology.

Results ATA produced from each donor showed a mean of 18.0 g/L of fibrinogen and 1500 UI/mL of thrombin. ATA instantly produced homogeneous clots when it was mixed with a needle.

Three in vitro studies of four ATA showed non-irritation due to high survival cell viabilities (>80%).

Good preclinical results were found:

- 20 mm^2 autograft could be fixed successfully.