THE TRANSITION FROM THE USE OF BUPIVACAINE TO ROPIVACAINE IN THE DELIVERY ROOM, IN ORDER TO ACHIEVE A BETTER ANALGESIC EFFECT

3PC-031

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Background Ropivacaine is an amide local anaesthetic. It is not a new drug. This drug has the specificity to be less cardiotoxic, with reduced motor blockade, and can be used for regional anaesthesia such as epidural anaesthesia in the delivery room.

In July 2017, it was decided by the pharmaceutical services in Rambam Health Care Campus, together with the anaesthesiologist, to switch to the use of ropivacaine as an alternative to bupivacaine, which had been used for many years in the delivery room.

Purpose The transition from the use of bupivacaine to the use of ropivacaine for the purpose of regional anaesthesia in the delivery room, was carried out in order to achieve a better analgesic effect with minimal motor paralysis compared to bupivacaine.

Material and methods Ropivacaine is commercially available as a solution of 0.2% (200 mg/100 ml bag). In order to reduce the concentration to 0.1%, the hospital pharmacy added 85 ml of normal saline and 10 ml (0.5 mg) of fentanyl to each ropivacaine bag.

The preparation was done using the aseptic technique, labelled and stored in a refrigerator at 2°C–8°C, and given a shelf-life of 14 days.

Approximately 300 preparations were prepared each month, and supplied to the delivery room.

Results The administration of low-dose ropivacaine 0.1% over the same time as an alternative to the administration of bupivacaine at a concentration of 0.125% gave a very good analgesic effect. In addition, ropivacaine has a reduced motor block in comparison to bupivacaine, which has significant motor block.

Conclusion The administration of low-dose ropivacaine (0.1%) as a substitute for bupivacaine (0.125%) gave a very good analgesic effect. In addition, the anaesthesiologists observed a reduction in motor blockade using ropivacaine in comparison to that of bupivacaine.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

LOW-DOSE MORPHINE SOLUTION FOR SPINAL ANAESTHESIA – READY TO USE TO IMPROVE PATIENT SAFETY IN DRUG THERAPY

3PC-032

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Background Combination with a local anaesthetic agent, such as bupivacaine and a lipophilic opioid such as sufentanil, is frequently used in intrathecal anaesthesia for caesarean section. The combination with low-dose morphine solution 100 to 200 μg reduces wound pain after surgery.

No drug with low-dose morphine solution is licensed in Germany. Available products need dilution by factor 100. This two-step diluting procedure involves high risks of contamination and overdosing, the latter resulting in respiratory depression with delayed onset.

Purpose Therefore, anaesthesiologists requested the hospital pharmacy to supply a 100 μg/ml morphine solution for intrathecal administration.

Material and methods Literature research for published formulations, relevant stability criteria and published stability data.

Evaluation of compounding ready-to-administer (RTA) or ready-to-use (RTU) formulations and development of formulation and testing specifications.

Development of a stability indicating RP-HPLC method for determining morphine stability and occurrence of degradation products. Three test batches were examined directly after compounding, after sterilisation, on days 14, 30, 60, 150, 200 and 300.

Development of a product information and standard operating procedure for clinical use.

Results No published formulations could be found. The pH and oxygen in sterilised solution could be identified as published criteria limiting stability.

The shelf-life of prefilled syringes for intrathecal administration (RTA) is limited to 24 hour by the risk of microbial contamination and of extraction of syringe material components. Therefore, the decision was in favour of RTU formulation.

A formulation was developed by pharmaceutical principles. Low-dose morphine solution contains morphine hydrochloride trihydrate 100 μg/ml in isotonic sodium chloride solution at pH 2.8–3.3. After filtration, 2.2 ml of the solution is filled in 5 ml injection vials and autoclaved.

Stability testing proved the stability of the formulation over at least 300 days. No degradation products were detected.

An instruction leaflet, as well as standard operating procedure for safe clinical use of RTU low-dose morphine solution was developed in collaboration with anaesthesiologists and hospital pharmacists.

Conclusion Interdisciplinary collaboration of anaesthesiologists and hospital pharmacists enables the development of a simple and stable RTU low-dose morphine formulation for easy application. Patient safety in drug therapy with a high-risk procedure was improved comprehensively.

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No conflict of interest.

LABELLING WITHOUT STRENGTH FOR A PHARMACEUTICAL PREPARATION USED IN A BLINDED DOSAGE ADJUSTMENT OF CLOzapine

3PC-033

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Background Among other items, pharmaceutical preparations labelling must mention the strength of the active ingredient.

However, the clinical state of a 17-years-old patient on clozapine for schizophrenia required a blinded dosage adjustment to be successful.
**Purpose** Our aim was to prepare clozapine capsules, different strengths, macroscopically not discernible.

**Material and methods** The consent of the patient and his parents had been obtained.

In the absence of pure pharmaceutical raw material, the feasibility study (Good Preparation Practices) revealed crushability of the available tablets. They were micronised with a RETSCH RM 200 mortar apparatus for 4 min, particle size <3 mm.

The initial prescription (one capsule 165 mg in the morning, one capsule 260 mg in the evening, for 15 days) led us to prepare 15 capsules of size 00 (translucent) for the morning and 15 capsules size 000 (opaque red) for the evening. Excipient (lactose) was added if required.

The dose adjustment criterion was the clinical state of the patient.

**Results** The obligations for labelling had been fulfilled except for the strength, replaced by morning clozapine or evening clozapine. The clinical evaluation induced a first increase (+12%) of the morning dose after 5 weeks.

The correct dose was found after 9 weeks with +27% of the daily dose, targeted in the morning, without the patient’s fear of the changes. White blood cell counts every 4 weeks were normal. At the last dose increase, the volume of the powder necessitated to change the capsules from 00 to 000 and ivory colour (instead of translucent, not available). Nevertheless, these macroscopic changes did not have a nocebo effect.

Blinding required a double circuit of prescriptions: those given by the prescriber to the patient mentioning ‘morning capsule: 1, evening capsule: 1’ to be taken daily and those which were intended for us, specifying the strengths.

**Conclusion** All items required in the pharmaceutical preparations labelling must be fulfilled exhaustively to avoid any confusion. However, exceptionally and transiently, a labelling not mentioning the strength was relevant in helping the prescriber to manage a dosage adjustment and to achieve the desired clinical outcomes.

**REFERENCES AND/OR ACKNOWLEDGEMENTS**

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**IMIPENEM-FORTIFIED EYE DROPS FOR THE TREATMENT OF BACTERIAL KERATITIS: DEVELOPMENT AND CHARACTERISATION**

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**Background** Bacterial keratitis is an infectious ocular disease accompanied by inflammation that can cause severe visual impairment. Commercial eye drops are not effective in many cases, so it is necessary to develop fortified antibiotic eye drops with high drug concentrations in hospital pharmacy departments.

**Purpose** To develop and characterise imipenem eye drops through release and stability studies of three possible formulations for the treatment of resistant bacterial keratitis.

**Material and methods** Initially, three different vehicles were used for the development of 5 mg/ml imipenem eye drops: balanced salt solution (BSS); 0.4% hyaluronic acid (HA); and 0.84% ion-sensitive hydrogel composed of gellan gum and kappa carrageenan (ISH). Later, these three formulations were characterised. First, release assays were performed using vertical Franz cells (37°C, 100 rpm orbital shaker, 12–14 kD dialysis membrane) and artificial tears as receptor medium. The drug release was determined spectrophotometrically (298 nm). For the stability study, all formulations were stored at room temperature and at 4°C–8°C for 10 days protected from light. Each day, pH, transparency and concentration were determined.

**Results** Release studies showed that imipenem is delivered by a Higuchi diffusion in all formulations. However, ISH was more effective than BSS and HA in drug release control.

Stability studies showed that, at day 3, formulations stored at 4°C–8°C of BSS and HA maintain >90% of the initial concentration (IC), while in ISH it was 85%. At the same time, room temperature-stored samples preserved 60%–80% of the IC. At day 5, only BSS and HA formulations stored at 4°C–8°C maintain >85% of the IC. Finally, after 10 days of study, all samples stored at 4°C–8°C maintain around 70% of the IC, while those stored at room temperature only keep around 20%–30%. On the other hand, no significant pH and transparency variation were shown at both storing conditions.

**Conclusion** The ISH vehicle shows the best release characteristics. However, its poor physicochemical-stability would make its use difficult in clinical practice. For this reason, the optimal vehicles for the elaboration are BSS and HA.

It is recommended to store these eye drops at 4°C–8°C protected from light. Under these conditions, a validity period of 5 days can be established.

**REFERENCES AND/OR ACKNOWLEDGEMENTS**

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