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Morphine hydrochloride solution 0.5 mg/ml: A reconstitution kit for neonatal units

AKADEMISCHES
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Background

Children of opioid-dependent mothers often suffer from withdrawal symptoms after birth. The so-called neonatal abstinence syndrome (NAS) is characterized by irritability, tremor, hypertonicity, tachypnoea, vomiting and diarrhoea. The incidence of NAS has been reported with 50% - 95% of all babies who have been exposed to opioids in utero. Scoring systems help to assess whether a drug therapy should be initiated. [1, 2]

Any pharmaceutical solutions to treat newborns should contain suitable or no preservatives. The disadvantage of a preservative-free solution however is the short shelf-life of just a few days in most cases.

About two children in one year need to be treated for NAS in the neonatal unit of our hospital. In these cases opium tincture (Ph. Eur.) was diluted at the ratio of 1:25 on the ward.

Issues with the preparation led to the question how the treatment could be made safer.

Purpose

A safe and always available drug dosage form to treat NAS needed to be developed. The new formulation should also avoid frequent discards of narcotics in order to minimize efforts for preparation and documentation.

Methods

Current NAS treatment guidelines showed the predominant use of morphine solutions. In contrast to an opium tincture, the safety profile is more favourable. This is particularly due to the absence of alcohol and the use of a single active ingredient instead of an alkaloid mixture.

With *Morphinhydrochlorid-Lösung 0,5 mg/ml (NRF 29.3.)* there already exists a standardised, preservative-free formulation to treat NAS [2].

As it is a preservative-free solution with a limited shelf life of seven days at room temperature, it does not allow a previous production in the pharmacy. Furthermore, due to the low demand, a weekly production cycle would cause frequent discards of the narcotic substance including the need for extensive documentation in most cases. This problem was solved by separating the solvent from the ingredients.

Due to the small sample of 0.010 g morphine hydrochloride, which is at the minimum load of the analytical balance, a photometric analysis of three reconstituted batches was performed according to the commentary of the Ph. Eur. [3].

Regression analysis showed a linear relationship between morphine concentration and absorption at 297 nm. A calibration function could be calculated. For quantitative analysis, the powder was solved in 0.1 M sodium hydroxide, diluted and finally measured photometrically at 297 nm.

Conclusion

The kit for reconstitution of a morphine hydrochloride solution including a step-by-step instruction is simple and safe. It is economical by avoiding frequent discards of opioids and allows the treatment of neonatal abstinence syndrome even outside of hospital pharmacy working hours.

Results

A kit to reconstitute the standardised morphine hydrochloride solution 0.5 mg/ml on the neonatal unit was prepared.

In addition to the solid ingredients in a bottle, the kit contains illustrated instructions for reconstitution and all materials needed for the preparation and removal of the solution. (Figure 1 - 4)



Figure 1. Content of the reconstitution kit for the morphine hydrochloride solution 0.5 mg/ml (NRF 29.3.)

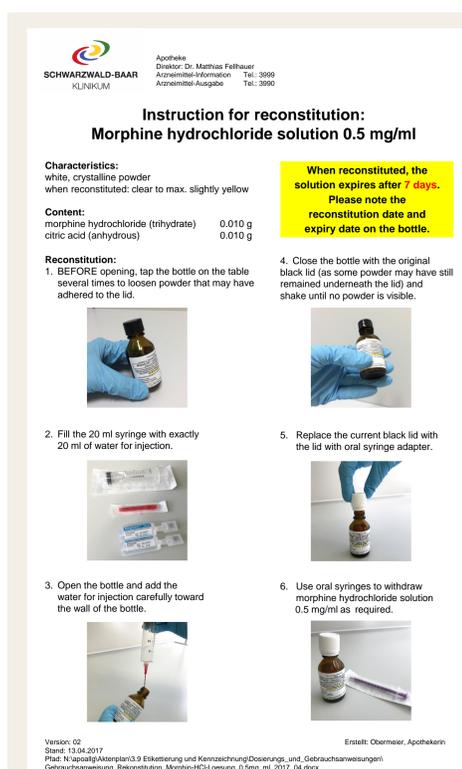


Figure 4. Instruction to reconstitute the morphine hydrochloride solution 0.5 mg/ml



Figure 2. Label of the kit to reconstitute a morphine hydrochloride solution 0.5 mg/ml



Figure 3. Label of the bottle

Photometric analysis of three reconstituted batches showed that the morphine hydrochloride concentrations (104 %, 102 %, 107 %) were in an acceptable range of ± 10 % [2].

References

- [1] Rohrmeister K et al. Neugeborene drogenabhängiger Mütter. Monatschr Kinderheilkd 2006. 154:79-89.
- [2] Morphinhydrochlorid-Lösung 0,5 mg/ml (NRF 29.3.). DAC/NRF 2015/1.
- [3] Bracher F et al. (Hrsg.). Monographie Morphinhydrochlorid. Arzneibuch-Kommentar. Wissenschaftliche Erläuterungen zum Europäischen und Deutschen Arzneibuch. 31. Lieferung 2009. WVG Stuttgart/Govi-Verlag Pharmazeutischer Verlag GmbH Eschborn.