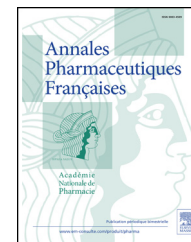




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ORIGINAL ARTICLE

Formulation and stability study of a pediatric 2% phenylephrine hydrochloride eye drop solution

Formulation et étude de stabilité d'un collyre pédiatrique de chlorhydrate de phényléphrine à 2%

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KEYWORDS

Phenylephrine hydrochloride;
Eye drop;
Premature infant;
Biocompatibility;
Stability study;
Mass spectrometry

Summary

Introduction. – We present formulation and stability evaluation of a 2% (w/v) phenylephrine hydrochloride biocompatible eye drop solution, routinely prepared in hospital pharmacy under aseptic conditions, for retinal examination of neonates and premature infants.

Materials and methods. – Eye drop solution was formulated by dissolution of phenylephrine hydrochloride and disodium hydrogen phosphate as buffering agent in sterile water for injection and sodium chloride for injection as isotonic agent. The previous solution was sterile filtered through under aseptic conditions, in an iso class 5 air quality clean room under horizontal laminar airflow hood. Physical stability (visual inspection, osmolality measurements), chemical stability (pH measurement, phenylephrine assay by liquid chromatography coupled with an

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ultra-high resolution and accurate mass) and sterility evaluation of phenylephrine eye drop solution stored at ambient temperature were studied during 60 days.

Results and discussion. – The formulated eye drop solution had a pH of 6.90 ± 0.05 and an osmolality of 285 ± 2 mOsm/kg. Throughout the 60 days study the solutions remained clear without any precipitation or color modification, sterility was maintained, pH and osmolality were not significantly modified and no significant loss of product was detected using liquid chromatography coupled with an ultra-high resolution and accurate mass instrument suggesting the lack of degradation.

Conclusion. – These results indicate that 2% phenylephrine hydrochloride eye drop solutions were physically, chemically and microbiologically stable for at least 60 days when stored in type I amber glass vials at room temperature, allowing the compounding of higher batch sizes. © 2014 Elsevier Masson SAS. All rights reserved.

MOTS CLÉS

Chlorhydrate de phényléphrine ;
Collyre ;
Enfant prématuré ;
Biocompatibilité ;
Étude de stabilité ;
Spectrométrie de masse

Résumé

Introduction. – Le but de l'étude est de mettre au point et d'évaluer la stabilité d'un collyre de chlorhydrate de phényléphrine à 2%, préparation hospitalière biocompatible pour l'examen de la rétine des enfants nouveau-nés et prématurés.

Matériels et méthodes. – Les collyres sont préparés par dissolution de chlorhydrate de phényléphrine et de phosphate disodique dans de l'eau pour préparation injectable et de chlorure de sodium isotonique comme agent isotonisant, suivi d'une filtration stérilisante et d'une répartition aseptique en zone à atmosphère contrôlée, sous hotte à flux laminaire horizontal. L'étude de stabilité sur 60 jours a été réalisée par inspection visuelle et mesure d'osmolalité (stabilité physique), mesure du pH et détermination des concentrations de phényléphrine par chromatographie liquide couplée à la spectrométrie de masse à haute résolution (stabilité chimique) et évaluation de la stérilité par ensemencement direct (stabilité microbiologique).

Résultats et discussion. – Le collyre retenu a un pH de $6,90 \pm 0,05$ et une osmolalité de 285 ± 2 mOsm/kg. Pendant les 60 jours de l'étude, les solutions restent limpides sans précipitation ni modification de couleur, la stérilité est maintenue, le pH et l'osmolalité ne sont pas significativement modifiés et aucune perte significative de produit n'est détectée par la méthode de dosage, suggérant l'absence de dégradation.

Conclusion. – Ces résultats montrent la stabilité physique, chimique et microbiologique du collyre de chlorhydrate de phényléphrine à 2% pendant au moins 60 jours lorsqu'il est conservé en flacon en verre ambré de type I, à température ambiante, ce qui nous a permis d'augmenter la taille des lots fabriqués.

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Phenylephrine hydrochloride (Fig. 1) is a sympathomimetic, alpha-adrenergic agonist drug. Following instillation in the eye, phenylephrine acts locally as a rapid and potent vasoconstrictor and mydriatic agent, by constricting ophthalmic blood vessels and radial muscle of the iris. Phenylephrine hydrochloride is commonly used in association with anticholinergic agents such as tropicamide or cyclopentolate to

produce maximal dilation of the pupil for examination of the peripheral retina [1,2].

In Rennes University Hospital Department of Pediatrics, 10 to 15 dilations are performed weekly, for retinal examination of neonates and premature infants. Several systemic side effects of topical phenylephrine have been reported in neonates and children undergoing retinopathy of prematurity screening, such as increased blood pressure [3], pulmonary edema [4] and grand mal seizure [5].

Other side effects such as paralytic ileus, necrotizing enterocolitis and feeding intolerance were significantly increased when anti-cholinergic drug tropicamide or cyclopentolate was associated to phenylephrine [6].

As systemic side effects in children may be significantly underreported, it is strongly recommended to adopt strategies for reducing systemic absorption and toxicity of ocular phenylephrine, for example to use the lowest available concentration of topical drug, to occlude the nasolacrimal passage after topical instillation by gently but firmly pressing the tear duct against the nose immediately after instillation

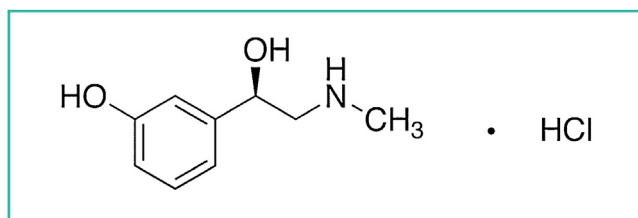


Figure 1. Chemical structure of phenylephrine hydrochloride.
Structure chimique du chlorhydrate de phényléphrine.

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