Annales Pharmaceutiques Françaises (2016) xxx, xxx—xxx

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

ORIGINAL ARTICLE

Long-term stability of ketamine hydrochloride 50 mg/ml injection in 3 ml syringes

Stabilité à long terme de chlorhydrate de ketamine à 50 mg/mL dans des seringues de 3 mL

S. Huvelle[a], M. Godet[a,d], J.-D. Hecq[b,d,*], P. Gillet[b], B. Bihin[c], J. Jamart[c], L. Galanti[a,d]

[a] *Medical Laboratory, CHU Dinant Godinne, UCL Namur, 1, avenue Therasse, 5530 Yvoir, Belgium*
[b] *Department of Pharmacy, CHU Dinant Godinne, UCL Namur, 1, avenue Therasse, 5530 Yvoir, Belgium*
[c] *Scientific Support Unit, CHU Dinant Godinne, UCL Namur, 1, avenue Therasse, 5530 Yvoir, Belgium*
[d] *Drug Stability Research Group, CHU Dinant Godinne, UCL Namur, 1, avenue Therasse, 5530 Yvoir, Belgium*

Received 29 January 2016; accepted 16 March 2016

KEYWORDS
Ketamine;
Ultraperformance liquid chromatography;
Centralized intravenous admixtures services

Summary
Introduction. — Ketamine hydrochloride (Ketalar®) injection is often used as a general anesthetic agent. It is particularly suited to short-term interventions. It can also be used as an inducer of anesthesia before the administration of other anesthetic agents. The aim of this study was to evaluate the stability of ketamine hydrochloride in 3 ml polypropylene syringes after storage for up to 180 days at room temperature.
Method. — Syringes containing ketamine hydrochloride (50 mg/ml) were prepared and stored at room temperature (25 °C) for 180 days. The concentrations were measured by validated ultra-performance liquid chromatography-diode array detection at 0, 7, 14, 28, 60, 84, 112, 140 and 180 days. A degradation test was performed to evaluate the specificity of the analysis. At each time point, the pH, color and visible particles of each solution were also assessed.

* Corresponding author. Department of Pharmacy, CHU Dinant Godinne, UCL Namur, 1, avenue Therasse, 5530 Yvoir, Belgium.
E-mail address: jean-daniel.hecq@uclouvain.be (J.-D. Hecq).

http://dx.doi.org/10.1016/j.pharma.2016.03.003

Please cite this article in press as: Huvelle S, et al. Long-term stability of ketamine hydrochloride 50 mg/ml injection in 3 ml syringes. Ann Pharm Fr (2016), http://dx.doi.org/10.1016/j.pharma.2016.03.003

Results. — Degradation tests proved no interfering peaks with ketamine. All solutions were physically stable during the storage. The lower confidence limit of the concentration for these solutions remains superior to 90% of the initial concentration at this date as recommended by the Food and Drug Administration (FDA) until 180 days (100% ± 2%).
Conclusion. — Solutions of ketamine (50 mg/ml) were chemically stable for 180 days in polypropylene syringes with storage at room temperature and could be prepared in advance by a centralized intravenous admixture service.

MOTS CLÉS
Kétamine ;
Chromatographie liquide à ultra performance ;
Unité centrale de reconstitution d'injectables

Résumé
Introduction. — Le chlorhydrate de kétamine (Ketalar®) injection est souvent utilisé comme un agent anesthésique général. Il est particulièrement adapté pour les interventions à court terme. Il peut également être utilisé comme un inducteur de l'anesthésie avant l'administration d'autres agents anesthésiques. Le but de cette étude était d'évaluer la stabilité du chlorhydrate de kétamine dans des seringues en polypropylène de 3 mL après un stockage de 180 j à température ambiante.
Méthode. — Des seringues contenant du chlorhydrate de kétamine à 50 mg/mL ont été préparées et conservées à la température ambiante (25 °C) pendant 180 j. Les concentrations ont été mesurées par chromatographie liquide à ultra performance avec détection à barrettes de diodes aux jours 0, 7, 14, 28, 60, 84, 112, 140 et 180. Un essai de dégradation a été effectué afin d'évaluer la spécificité de l'analyse. À chaque point dans le temps, le pH, la couleur et des particules visibles de chaque solution ont également été évalués.
Résultats. — Les essais de dégradation n'ont prouvé aucun pic d'interférence avec la kétamine. Toutes les solutions ont été physiquement stables durant le stockage. La limite inférieure de confiance de la concentration pour ces solutions reste supérieure à 90 % de la concentration initiale à cette date comme recommandé par la Food and Drug Administration (FDA) jusqu'à 180 j (100 % ± 2 %).
Conclusion. — Les solutions de kétamine (50 mg/mL) sont chimiquement stables pendant 180 j dans des seringues en polypropylène après stockage à température ambiante et pourraient être préparées à l'avance par une unité centrale de reconstitution d'injectables.

Introduction

Ketamine hydrochloride (Ketalar®, Pfizer, Brussels, Belgium) injection is often used as a general anesthetic agent. It is particularly suited to short-term interventions. It can also be used as an inducer of anesthesia before the administration of other anesthetic agents [1].

The chemical stability of solutions of ketamine was studied at different concentrations, from 0.10 to 25 mg/ml and in glass vials or polypropylene syringes with good results [2—5].

Drug shortage became a national, European and global problem [6—9].

The preparation of intravenous treatments by a Centralized Intravenous Admixtures Service (CIVAS) contributes to the global management of treatment by providing ready-to-use injectable drugs with acceptable physicochemical and bacteriological quality and by relieving nursing staff from the tasks of infusion preparation [10—12].

To avoid an out-of-stock situation for this drug and to reduce the elimination of partially used vials, the packaging of ketamine in his original concentration (50 mg/ml) in ready-to-use syringes was investigated. This presentation meets the daily practice of the anesthetists in the operating room. The utilization of 3 ml-syringes is required by the IV compounding robot, which cannot use smaller volume syringes [13].

The aim of this study was to evaluate the stability of ketamine hydrochloride in 3 ml polypropylene syringes after storage for up to 180 days at room temperature with a novel UPLC method which allows a rapid quantification and can be used for the quality control of production of such infusions.

Materials and methods

Solution preparation

Under aseptic conditions, 45 3 ml-syringes (Terumo, Haasrode, Belgium, Lot 61318404) were prepared, containing 1 ml of non-diluted solution of Ketalar® (Pfizer, Brussels,

Please cite this article in press as: Huvelle S, et al. Long-term stability of ketamine hydrochloride 50 mg/ml injection in 3 ml syringes. Ann Pharm Fr (2016), http://dx.doi.org/10.1016/j.pharma.2016.03.003