

THE STABILITY OF READY-TO-USE (RTU) EPHEDRINE HYDROCHLORIDE IN POLYPROPYLENE SYRINGES FOR USE IN MATERNAL HYPOTENSION

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Background and Objective

Lumbar epidural analgesia or spinal analgesia are now very frequently prescribed during labour. Maternal hypotension is perhaps the most common complication of regional analgesia and anaesthesia in obstetric patients and should be rapidly treated to avoid foetal distress. Ephedrine is the vasopressor of choice and must be administered immediately. In the HUG, syringes were prepared extemporaneously either by anaesthesiologists or nursing staff by transferring the contents of 2ml ampoules containing 20mg of ephedrine into syringes that were placed at the bedside of each parturient. Its preparation in obstetrics in such an emergency situation is time consuming and can increase the risk of errors and/or infection. Furthermore, these solutions prepared in advance can increase costs due to wastage (unused syringes are discarded at the end of the day). The objective of the study was 1) to develop a RTU ephedrine syringe, prepared under aseptic conditions supplied by the pharmacy, that can be put back in stock for another patient if not used and 2) to determine its chemical stability over a period of 12 months.



Method

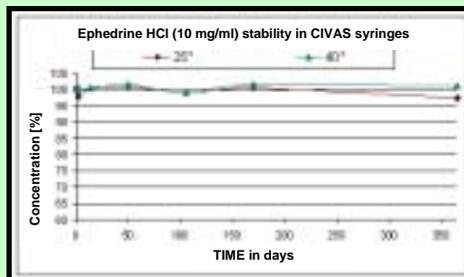
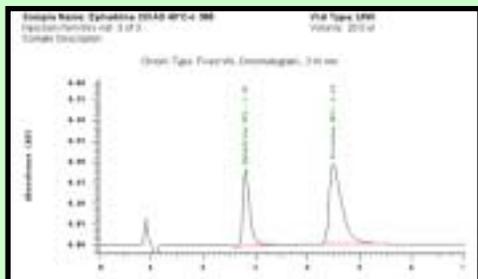
A solution containing ephedrine hydrochloride (20mg/2ml) was prepared by the pharmacy and filled aseptically under clean room conditions into polypropylene syringes (Plastipak[®] Becton Dickinson) individually packed in sterile plastic sachets and stored at 25±2°C and 40±2°C. The samples were analysed according to ICH guidelines¹ at 0, 2 and 14 days, 2, 3, 6 and 12 months using a validated HPLC assay². The analysis of the 40 °C samples was also performed for 12 months. Sterility testing was performed throughout the study in order to determine the integrity of the syringes. The pH was routinely controlled. Visual inspection for the eventual presence of particulate matter was also carried out

HPLC Parameters

Merck Hitachi System with high pressure pump L-600 and D6000 interface.
 Column: Lichrospher RP100
 C8 (5microns)
 125/4/8mm.
 Mobile Phase: Potassium dihydrogenphosphate buffer 0.01M pH 3.0
 Acetonitrile R
 Diethylamine
 900:100:1
 Final pH adjusted to 5.0 +/- 0.1 with Phosphoric acid 0.1 N
 Flow rate: 2.0 ml/min.
 Injection Volume: 20 µl
 Detection: UV 214 nm
 Internal standard: Procain HCl 10 mg/ml
 Ephedrin standard: Ephedrine HCl SR 5 mg/ml

Results

The HPLC method was stability indicating as no degradation peaks were detected. The injections were judged to be stable if the drug levels remained above 90% of the original concentration at the time of preparation. The results obtained were above 95% after 12 months at room temperature. (see table or graphic) The pH did not change appreciably throughout the study and the results of the sterility tests were found to be negative in all cases.



Conclusions

RTU syringes supplied by the pharmacy and stored in obstetrics were stable for at least 12 months at room temperature with no significant loss in potency. Unused syringes in their original unopened sachets can be put back in stock and subsequently made available for other patients. Results have shown time saving for hospital personnel and drastic reduction in costs due to wastage. Furthermore, the availability of prefilled syringes decreases the delay in drawing up the drug in emergency situations. Ongoing studies with phenylephrine are being carried out in the HUG which is used similarly for the reduction of spinal anaesthesia-induced hypotension during caesarean section³.

References

- 1 ICH guidelines Q1A (R2); www.ich.org
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- 3 A.G. Gihan, A.E. Sherif Eg J Anaesth 2003;19:45-50