International Journal of Obstetric Anesthesia (2008) **17**, 118–122

ELSEVIER

International Journal of Obstetric Anesthesia

ORIGINAL ARTICLE

Short term stability of pH-adjusted lidocaine-adrenaline epidural solution used for emergency caesarean section

C. Tuleu, J. Allam, H. Gill, S. M. Yentis

Department of Pharmaceutics, The School of Pharmacy, University of London, Magill Department of Anaesthesia, Intensive Care & Pain Management, Chelsea & Westminster Hospital, London, UK

Presented in part at the Obstetric Anaesthetists' Association Annual Meeting, Sheffield; May 2007

KEYWORDS
Analgesia, epidural; Drug stability; Adrenaline, lidocaine; Sodium bicarbonate

Accepted September 2007

ABSTRACT
Background: Lidocaine-bicarbonate-adrenaline mixtures are commonly used for epidural bolus doses for emergency caesarean section. Previous research has shown that adrenaline degrades completely 24 h after mixing. Anecdotal enquiries suggest that anaesthetists who use such mixtures commonly prepare the solution ahead of use, despite a lack of data about its stability between 0 and 24 h. The aim of this study was to monitor the degradation of adrenaline in the above mixture over 20 h.
Methods: 2 mL of sodium bicarbonate 8.4% was added to 20 mL of 2% lidocaine; 2 mL of this mixture was discarded and 0.1 mL of adrenaline 1:1000 added. The mixtures were stored in plastic syringes at 24 °C unprotected from light ($n = 3$) or in the dark ($n = 3$). Non-alkalinised controls were also prepared. Adrenaline and lidocaine were assayed by high performance liquid chromatography at 0, 2, 4, 6 and 20 h.
Results: In the bicarbonated mixture exposed to light, chemical degradation of adrenaline was fast at room temperature, only $73.0 \pm 3.6\%$ of adrenaline remaining after 6 h. In the dark, the stability of adrenaline improved and $95.8 \pm 3.6\%$ remained after 6 h. Negligible degradation occurred in the absence of bicarbonate in either condition. Lidocaine concentrations remained unchanged regardless of the storage conditions.
Conclusions: This study suggests that preparation of pH-adjusted lidocaine-adrenaline mixtures in advance and prolonged storage in the light is inadvisable.
© 2008 Elsevier Ltd. All rights reserved.

Introduction

Local anaesthetics are often mixed with other agents to improve the speed and quality of anaesthesia when converting epidural analgesia in labour to a block suitable for emergency caesarean section, although

C. Tuleu, **H. Gill**, Department of Pharmaceutics, The School of Pharmacy, University of London, **J. Allam**, **S.M. Yentis**, Magill Department of Anaesthesia, Intensive Care & Pain Management, Chelsea & Westminster Hospital, London, UK.
* Correspondence to: Dr Catherine Tuleu, Department of Pharmaceutics, The School of Pharmacy, University of London, 29-39 Brunswick Square, London, UK, Tel.: +442077535857; fax: +442077535942.
E-mail address: catherine.tuleu@pharmacy.ac.uk

0959-289X/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ijoa.2007.11.002

studies in this area are difficult and consequently relatively few. Bicarbonate has been shown to speed the onset of epidural lidocaine when used for emergency caesarean section.[1] Adrenaline is often added to this mixture to reduce local anaesthetic toxicity and prolong the block, and a recent UK survey of anaesthesia for emergency caesarean section found that adrenaline is added to epidural local anaesthetic by 24% of respondents, and bicarbonate by 12%.[2] Anecdotal enquiries both in the UK and around the world suggest that obstetric anaesthetists commonly prepare epidural mixtures in advance, sometimes several hours before use (personal communications). However, adrenaline has been shown to degrade completely 24 h after preparation of lidocaine-bicarbonate-adrenaline mixtures,[3] though no data for less than 24 h were presented. We therefore studied the degradation of adrenaline at shorter intervals after preparation of lidocaine-bicarbonate-adrenaline mixtures.

Material and methods

Two mL of 8.4% preservative-free sodium bicarbonate (BP Minijet®, International Medication Systems Ltd.) were added to 20 mL of 2% lidocaine hydrochloride (Martindale Pharmaceuticals) in a beaker. 2 mL were discarded to leave 20 mL of this alkalinised solution. Finally 0.1 mL of 1 mg/mL adrenaline acid tartrate (Hameln Pharmaceuticals Ltd.) was added with a 100-µl precision pipette. The whole solution was aspirated into a 20-mL disposable syringe and the resulting syringes containing 1 in 200000 (5 µg/mL) of adrenaline and 1.82% (18.2 mg/mL) of lidocaine were kept at room temperature (24 ± 1 °C) either unprotected from light, on the bench under an artificial daylight lamp or protected from light, in a cupboard. Non-alkalinised controls composed of 2% lidocaine hydrochloride 20 mL and 1 mg/mL adrenaline acid tartrate 0.1 mL were kept in the refrigerator at +4 °C wrapped in foil, and at room temperature unprotected from light. All the syringes were prepared in triplicate (n = 3) for each experiment.

Samples (2 mL) were withdrawn from each syringe at time 0 and after 2, 4, 6 and 20 h. The lidocaine and adrenaline concentrations were measured simultaneously by HPLC (Hewlett-Packard HP1050) and data acquired and analysed with PC Chrom+ version 4.0.9.0 software (H & A Scientific, Inc.). The method was as follows: injection volume 20 µl, column Supelco 15 cm × 4.6 mm, 5-µm Discovery®HSF5 reversed phase, gradient mobile phase of acetonitrile and formate buffer (ammonium formate 50 mmol/L adjusted to pH 3 with formic acid) as described in Table 1, UV detection at 266 nm.

Each sample was assayed immediately to avoid further degradation. The method for adrenaline was developed and validated to assay adrenaline with no interference from lidocaine or other excipients or degradation products present in the sample. Linearity, limit of detection, limit of quantification, accuracy, recovery and injection precision were assessed in accordance with the International Conference on Harmonisation of Technical Requirements for registration of Pharmaceuticals for Human use (www.ich.org), guideline Q2: validation of analytical methods.

The results for each set of three syringes are expressed as the mean ± SD (standard deviation) percentage of the content at time 0. Comparisons with baseline were made using repeated measures ANOVA, with $P < 0.05$ indicating statistical significance.

The pH of the various solutions were checked with pH test papers (Johnson universal test papers).

Results

Validation of the analytical method for adrenaline

The stability-indicating nature of the method was confirmed. The retention times of adrenaline and lidocaine were ~6 min and ~20 min respectively. Regression analysis showed linearity of the concentration of adrenaline with peak area under the curve (AUC) over the range of 0-50 µg/mL with a correlation coefficient (r^2) of 0.9986. The intra-day coefficients of variations for AUC and retention time were less than 1% demonstrating good repeatability. The minimal detection limits determined as three times the background noise was 0.17 µg/mL. The

Table 1 Chromatographic conditions for the adrenaline analysis

Time (min)	Mobile phase:		Flow rate (mL/min)	Remark
	Formate buffer pH 3	Acetonitrile		
0-6	100%	0%	1	Elution of adrenaline
6-20	Gradient down to 20%	Gradient up to 80%	1.5	Elution of lidocaine and any other excipients
20-30	100%	0%	1	Stabilisation of column

Download English Version:

https://daneshyari.com/en/article/2758122

Download Persian Version:

https://daneshyari.com/article/2758122

Daneshyari.com