Lidocaine and Bupivacaine Syringe Stability Study

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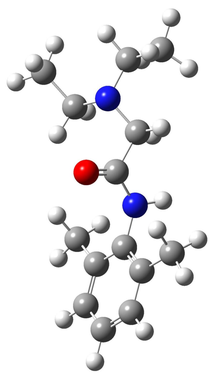
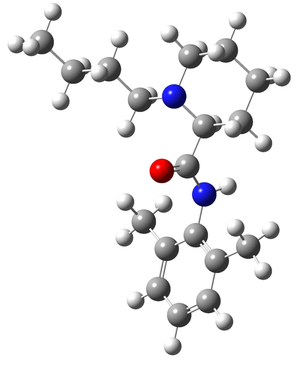
Introduction

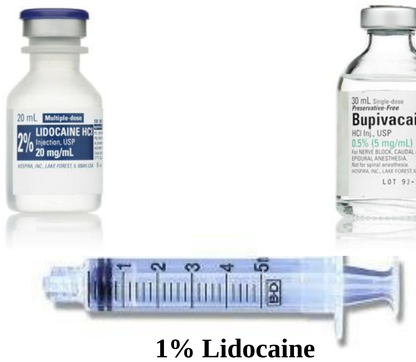
Mixtures of lidocaine with bupivacaine are commonly used for sensory blockade to control pain at the time of a procedure and to decrease discomfort immediately afterwards. Combining the two anesthetic agents in one syringe offers an advantage of the rapid onset of lidocaine and the prolonged duration of bupivacaine. The purpose of this study was to test the stability of a mixture yielding 1% lidocaine and 0.25% bupivacaine in a 5 mL BD syringe at room temperature without protection from light over the course of nine days.



2% Lidocaine

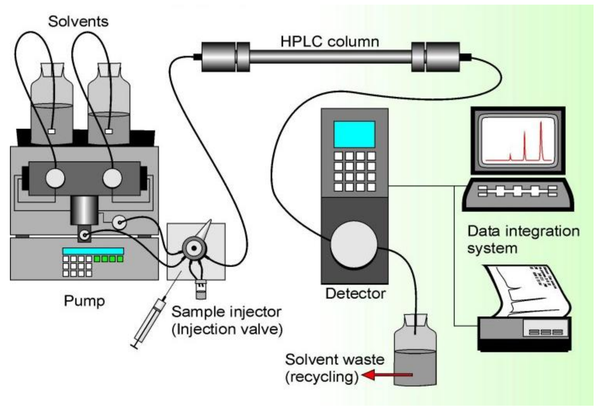


0.5% Bupivacaine



1% Lidocaine
0.25% Bupivacaine

Methods

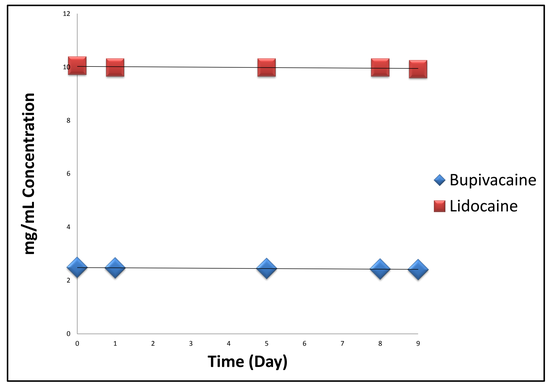


Scheme of a HPLC System

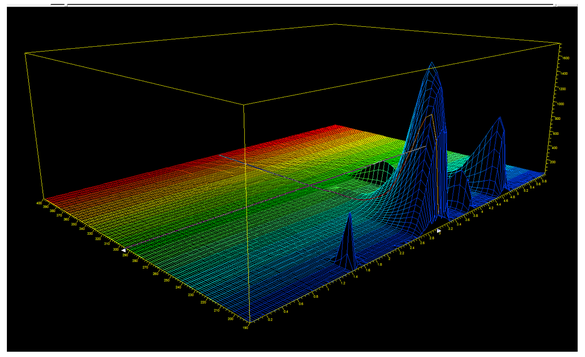
A solution of equal volumes of 2% lidocaine for injection with methylparaben and 0.5% preservative-free bupivacaine for injection was prepared and used to fill three 5 mL BD syringes with a final concentration of lidocaine 1% and bupivacaine 0.25%. We used the previously established HPLC method using an Agilent SB-C18 3.5 µm 4.6x250 mm column with a mobile phase of 30 mM potassium dihydrogen phosphate buffer (0.16% triethylamine, pH adjusted to 4.85) and acetonitrile in a ratio of 63:37 (v/v) with UV detection at 220 nm. The stability-indicating aspect of this study was verified with the following degradation analysis: acid (HCl), base (NaOH), oxidation (3% H_2O_2), heat (added H_2O and autoclaved), and control (added H_2O) in order to provide an insight into degradation pathways and degradation products. Linear regression analysis was done on the methylparaben-free reference standards of lidocaine and bupivacaine. In order to identify methylparaben on the resulting chromatogram, a separate run of methylparaben was completed. The samples were kept at room temperature and were not protected from light.

Results

Calibration curves were constructed for each analyte over the concentration range of 5-15 mg/mL of lidocaine and 1.5-3.5 mg/mL of bupivacaine. A regression analysis for each standard yielded an $R^2 \geq 0.995$. By comparing the retention factors and responses of the peaks in the chromatogram of the standard solution, peaks were assigned within the chromatogram of samples. The retention times for lidocaine and bupivacaine were 4.6 and 7.2 minutes, respectively. Peak areas were used to determine the concentration of a compound in the sample. The graph of concentration of each analyte as a function of time showed no degradation over the period of nine days.



Graph of Concentration as a Function of Time



3D Spectrum Plot of
Lidocaine-Bupivacaine Sample from BD Syringe

Discussion

In an effort to determine whether it is feasible to prepare batch unit doses of lidocaine and bupivacaine mixture in syringes, we performed stability study using HPLC analysis. We found no degradation of compounds and no significant changes in the concentrations over the course of nine days. We used 5 mL BD syringes in our analysis. Recently, Institute for Safe Medication Practices, based on reports from some hospitals, issued a warning about a time-dependent loss of potency with certain medications prepared in advance in 3 mL and 5 mL BD syringes. One of such medications is fentanyl, which showed a decline in potency to 67% on average at 48 hours. The issue might be related to black plunger rod stoppers from a secondary supplier that affects pH sensitive medications. The investigation is ongoing, but until further information is available from BD and the problem is resolved, hospitals using BD 3 mL and 5 mL syringes should prepare medication syringes as close to the time of administration as possible.

Conclusions

This study showed that lidocaine 2% and bupivacaine 0.5% will be stable when mixed in equal volumes and stored in a BD syringe at room temperature without protection from light for nine days.

References

1. Qin WW, Jiao Z, Zhong MK, et al. Simultaneous determination of procaine, lidocaine, ropivacaine, tetracaine and bupivacaine in human plasma by high-performance liquid chromatography. J Chromatogr B Analyt Technol Biomed Life Sci. 2010;878(15-16):1185-9.
2. Special ALERT: Loss of drug potency. ISMP Medication Safety Alert! Acute Care. July 30, 2015. Available at: www.ismp.org