Atropine and ephedrine adsorption to syringe plastic

BILL LEWIS, CRNA, PharmD
ERIC JARVI, PhD
PAUL CADY, PhD
Pocatello, Idaho

The purpose of this study was to compare daily changes in the concentration of atropine or ephedrine sulfate solutions that had been stored up to 4 days in plastic or glass syringes. Sets of three plastic and one glass syringe were used for each drug; the glass syringes acted as controls. Each set of syringes was labeled as day 0, 1, 2, 3, or 4. Syringes with medication were laid horizontally, had needles attached, and were stored in the dark at an ambient temperature. Each day, the assigned set of syringes was analyzed by high-performance liquid chromatography. Results showed that the change in the ephedrine sulfate concentration in the plastic syringes from day 0 to day 4 was less than 1.4%. Atropine sulfate decreased 52% over 4 days, with the largest single drop occurring during the first 24 hours.

It can be concluded that the two brands of ephedrine sulfate stored up to 4 days at ambient temperature in the brand of syringe used do not significantly decrease in concentration. However, this was not the case with the brand of atropine sulfate studied. The practice of storing atropine sulfate in plastic syringes should be discouraged, because of the possibility of loss of potency due to medication adsorption to syringe plastic.

Key words: Adsorption, atropine, ephedrine, plastic, syringe.

Introduction

Anesthesia providers must use medications of known concentrations to provide efficient and safe anesthesia. It has been the anesthetist-author's experience that medications are sometimes left ready for use in plastic syringes on anesthesia carts or in drawers. Depending upon a hospital's caseload these syringes may be at the ready for minutes, hours, or days. The practice of storing medication in plastic syringes for days should be discouraged.

The possibilities of microbial contamination, narcotics control problems, medication tampering by others, medication breakdown, and adsorption of medication to plastic must be considered. Because of these variables, questions may arise concerning the safety and efficacy of medication that has been stored for days in plastic syringes.

This study attempted to determine whether ephedrine sulfate or atropine sulfate, when stored in a plastic syringe for up to 4 days, adsorbs to plastic and results in a lower concentration of medication over time.

Reliable expiration dating and potency can only be assured in the original packaging. Little has been published about anesthesia-related medication that is stored in plastic (Table I).

Although atropine was used in a previous stability study, neither ephedrine sulfate nor atropine sulfate stability alone has been reported. The manufacturers of these medications also have not conducted research because syringes are considered transfer devices not storage devices; therefore, they are not required to conduct such research.

Methods and materials

Two brands of preservative-free ephedrine sulfate and one brand of preservative-free atropine sulfate were chosen. The following medications were purchased from a local supplier:

1. Atropine sulfate injection, USP Elkins-Sinn, Inc.; 0.4 mg/mL; 1-mL vials; NDC 0641-0320-25; lot 040300; expiration, October 1992.
2. Ephedrine sulfate injection, USP Abbott Laboratories; 50 mg/mL; 1-mL ampules; NDC 0074-3073-03; lot 49-0310DK; expiration, August 1, 1993.
3. Ephedrine sulfate, USP Eli Lilly and Co., 50 mg/mL; 1-mL ampules; NDC 0002-1603-16; lot 5AJ11B; expiration, March 1, 1994, and lot...
Time frame

Table I

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Conditions</th>
<th>Concentration change</th>
<th>Time frame</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>Polyvinyl IV bags</td>
<td>Decrease</td>
<td>24 hours</td>
</tr>
<tr>
<td>Aminophylline and dopamine</td>
<td>Polypropylene syringes</td>
<td>Stable</td>
<td>18 hours</td>
</tr>
<tr>
<td>Droperidol</td>
<td>Polyvinyl IV bags</td>
<td>Decrease</td>
<td>168 hours</td>
</tr>
<tr>
<td>Meperidine, promethazine and atropine (same syringe)</td>
<td>Polypropylene syringe</td>
<td>Stable</td>
<td>24 hours</td>
</tr>
<tr>
<td>Morphine</td>
<td>Polypropylene syringe</td>
<td>Stable</td>
<td>36 hours</td>
</tr>
<tr>
<td>Thiopental</td>
<td>Polypropylene syringe</td>
<td>93% retention of potency</td>
<td>5 days at 25°C</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Polyvinyl chloride bag</td>
<td>Stable</td>
<td>30 hours</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Polyvinyl chloride bag</td>
<td>Loss</td>
<td>3 hours</td>
</tr>
</tbody>
</table>

4NX09B; expiration, November 1, 1993.

High-performance liquid chromatography (HPLC) techniques were used to analyze samples.

The drug-specific HPLC analysis technique for ephedrine, as described by Kountourellis and associates, was used. The instruments and mobile phase were as follows: Model M-6000A pump (Waters Associates); a C18 precolumn cartridge; a Model 481 spectrophotometer (Waters Associates); an SP4270 integrator (Spectra-Physics); and a Nova-Pak C18 (15-cm × 3.9-mm) column. The mobile phase consisted of acetonitrile: methanol:0.015 mol/L ammonium acetate (85:10:5). The aqueous portion was adjusted to a pH of 5.7 with acetic acid. The entire mobile phase was filtered through a 0.45-μm filter and degassed prior to use. The flow rate was 1.0 mL/min. The column effluent was monitored at 257 nm.

Atropine sulfate was analyzed using a method reported by Li. The instruments used were as described above, with the addition of a column heater (Timberline Instruments, Inc.) to maintain the column temperature at 40°C. The mobile phase was prepared by adding sufficient 0.01 mol/L ammonium phosphate dibasic (26 mL) to bring the pH of two liters of 0.01 mol/L ammonium phosphate monobasic to 5.0. Acetonitrile was added to this solution for a final composition of (33:67) acetonitrile:buffer solution. This mobile phase was filtered through a 0.45-μm filter and degassed before use. The flow rate was 1.0 mL/min, and the column effluent was monitored at 257 nm.

Medications were drawn into sterile 3-mL Becton Dickinson Slip Tip® syringes, composed of polypropylene plastic with a rubber-tipped plunger, and 2-mL Micro-Mate® sterile glass syringes by Popper and Sons, Inc., which were purchased unsterile. The syringes were washed in de-ionized water, wrapped in sterilizing bags, and steam-sterilized the same as any central supply.

Sterile Becton Dickinson Precision Glide® 20-gauge, 1-inch polypropylene plastic needles were used to draw up medication and cap syringes. Medications were drawn into the needle and syringe to the 1-mL line for medications whose ampules contained more than 1 mL. For medication in ampules that contained exactly 1 mL, the entire medication volume was drawn into the syringe barrel, leaving the needle volume empty. All air was expelled from syringes. These supplies were purchased through a local supplier as would any anesthesia department.

For each medication, five sets of 3-5 plastic and one glass syringe with 1 mL of medication were prepared. Each set of plastic and glass syringes was labeled as day 0, day 1, day 2, day 3, or day 4. Glass syringes acted as controls. Syringes with medication were positioned as they would be in an operating room department. For each medication, five sets of 3-5 plastic and one glass syringe with 1 mL of medication were prepared. Each set of plastic and glass syringes was labeled as day 0, day 1, day 2, day 3, or day 4. Glass syringes acted as controls. Syringes with medication were positioned as they would be in an operating room department, ready for immediate use—needles attached and laid horizontally. However, over the 4-day study period, they were covered with a towel in a closed drawer except during analysis to eliminate light degradation, as recommended by the manufacturer of one of the medications. The temperatures of the stored syringes and the study environment were recorded daily and maintained at 24-27°C, which is slightly higher than recommended for an operating room temperature.

Each day, all syringes were inspected for precipitate or color change. The assigned day's medication in syringes was analyzed for medication concentration. Three analyses were run on each plastic and glass syringe, and averages of the three analyses were used for statistical analysis. If the average syringe concentration showed a significant decrease (or increase) over day 0, the HPLC chro-
matographs were evaluated for other peaks that represented possible breakdown products. If no extra peaks were found, a decrease was assumed to have resulted from plastic adsorption.

Statistical analysis was by ANOVA, with an alpha of $P < 0.05$ considered to be significant.

**Results**

No color change or precipitate was noted in any syringe. Data for levels of medication, expressed as a percentage of controls, are given in Table II. Table III shows the average percentage change in medication concentration from day 0, which was used as a baseline.

For both brands of ephedrine sulfate, there were no statistically or clinically significant decreases in drug concentration between day 0 and day 4. After the first day, the loss of medication remained essentially the same. In Abbott's brand of ephedrine sulfate, the largest decrease for plastic syringes was 1.4% and for glass, 3.3% (Table III). Eli Lilly’s decreases were 1.1% and 1.5%, respectively.

Plastic syringes with atropine sulfate had decreases ranging from 43-52%, with the largest decrease (44%) after the first 24 hours, beyond which the decrease was fairly consistent (Table III). Glass syringe decreases ranged from 11-35%. There were no extra peaks in the HPLC chromatographs for atropine.

**Discussion**

The practice of leaving medications in syringes on or in anesthesia carts for periods of time exceeding a single patient’s use continues. The authors acknowledge that this is not an acceptable practice, nor do they condone it; however, unused medication in syringes has been seen by the anesthetist-author. Whether the stored syringes are used by anesthesia personnel is unknown; however, the anesthetist-author does not use them.

Infection control policies should direct that syringes containing unused medication be discarded after each patient use. In the real world, an individual’s practice may not always follow a facility’s policies. Individual anesthesia personnel, and

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**Table II**

<table>
<thead>
<tr>
<th>Drug stability expressed as a percentage of control (SE)</th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ephedrine sulfate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbott</td>
<td>98 (0.91)</td>
<td>101 (0.53)</td>
<td>99 (0.03)</td>
<td>99 (0.45)</td>
<td>101 (0.2)</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>99 (0.12)</td>
<td>99 (0.33)</td>
<td>102 (0.27)</td>
<td>100 (0.6)</td>
<td>99 (0.59)</td>
</tr>
<tr>
<td>Atropine sulfate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elkins-Sinn</td>
<td>81 (6.1)</td>
<td>63 (4.7)</td>
<td>53 (2.2)</td>
<td>60 (3.4)</td>
<td>46 (2.5)</td>
</tr>
</tbody>
</table>

Concentration of glass syringe medication controls × 100
Concentration of medication in plastic syringes

**Table III**

<table>
<thead>
<tr>
<th>Medication concentration percentage change from day 0 (SE)</th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ephedrine sulfate—Abbott</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plastic</td>
<td>NA</td>
<td>-1 (0.53)</td>
<td>-1.4 (0.03)</td>
<td>-1.2 (0.45)</td>
<td>-0.9 (0.2)</td>
</tr>
<tr>
<td>Glass</td>
<td>NA</td>
<td>-3.3 (0.21)</td>
<td>-2.2 (0.16)</td>
<td>-1.7 (0.11)</td>
<td>-3.2 (0.63)</td>
</tr>
<tr>
<td>Ephedrine sulfate—Eli Lilly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plastic</td>
<td>NA</td>
<td>-1.1 (0.33)</td>
<td>+0.6 (0.27)</td>
<td>-0.9 (0.56)</td>
<td>-0.7 (0.59)</td>
</tr>
<tr>
<td>Glass</td>
<td>NA</td>
<td>-1 (0.38)</td>
<td>-1.5 (0.28)</td>
<td>-1.5 (0.32)</td>
<td>-0.8 (0.23)</td>
</tr>
<tr>
<td>Atropine sulfate—Elkins-Sinn</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plastic</td>
<td>NA</td>
<td>-44 (4.1)</td>
<td>-43 (2.4)</td>
<td>-52 (2.7)</td>
<td>-50 (2.8)</td>
</tr>
<tr>
<td>Glass</td>
<td>NA</td>
<td>-28 (1.53)</td>
<td>-13 (0.64)</td>
<td>-35 (0.31)</td>
<td>-11 (0.39)</td>
</tr>
</tbody>
</table>

**Percentages change in medication concentration on days 1-4, using day 0 as the control day**
not whole departments, may be inadvertently breaking policy. Hopefully, those who still follow this practice will be discouraged, if not by infection control policies then by this study.

There are other possible explanations for a decrease in atropine concentration in addition to its adsorption by plastic. Benzyl alcohol, which is used as a solvent for Elkins-Sinn’s atropine, absorbs into some types of rubber. Atropine sulfate may become less soluble because benzyl alcohol absorbed into the rubber and was not available for the solubilization of atropine. Atropine sulfate may be converted to atropine base and become more lipid-soluble, which would tend to allow it to adsorb to plastic and absorb into the rubber plunger tip. Medications themselves can absorb into certain rubber, which may be another explanation for the decrease in atropine sulfate concentration.

The loss of atropine from the glass syringes is worthy of comment. New plastic syringes were used for each sample. Because of cost, the glass syringes were reused for the ephedrine and atropine studies. The ephedrine portion was completed before the atropine portion. Before they were first used, the glass syringes were rinsed with deionized water, wrapped in sterilizing bags, and steam-sterilized. After each use, they were rinsed a number of times with deionized water, wrapped, and again steam-sterilized. Atropine binding sites on the glass may have been exposed during multiple processings, allowing atropine to attach to these binding sites. Another possible explanation is that decomposition products may have been present that eluded after the chromatographs’ run times of 7 minutes. It is possible that waiting longer than 7 minutes would have revealed extra peaks that might have represented breakdown products.

**Conclusion**

The practice of storing Elkins-Sinn’s brand of atropine sulfate in Becton Dickinson polypropylene syringes should be discouraged, because of, but not exclusively because of, the decrease in medication concentration, apparently due to drug adsorption to the syringe plastic. This could hold true for other brands of atropine and syringes as well.

Within 24 hours, there was a 44% decrease in the atropine sulfate concentration in plastic syringes. Based on this study, it appears that drawing up 0.4 mg of atropine on Monday and administering it on Tuesday could possibly result in the administration of 0.2 mg of atropine and, perhaps, bradycardia when tachycardia is the desired effect. The point within the first 24 hours at which the 44% drop occurred could not be determined because of the study’s design, which called for the first analysis to be done at 24 hours. This would be an interesting question for another investigation.

Although the study shows stability when ephedrine is stored in plastic syringes, there are other problems with storing it in such syringes, including possible microbial contamination, medication tampering by others, and medication breakdown. The practice of storing medication in plastic syringes for days should be discouraged.

**REFERENCES**


**AUTHORS**

Bill Lewis, CRNA, PharmD, earned his bachelor of science degree in Nursing from the University of Northern Colorado in 1979; graduated from St. Joseph Hospital School of Nurse Anesthesia, Lancaster, Pennsylvania, in 1981; and earned a doctor of pharmacy (PharmD) degree from Idaho State University in 1992. At the time of this research, he was a locum tenens anesthetist and a geriatric pharmacy resident in Pocatello, Idaho. He is presently a locum tenens anesthetist in many western states and a staff anesthetist in Pocatello.

Eric Jarvi, PhD, earned his bachelor of science degree in Health Care Sciences from Southern Illinois University in 1979, his master’s degree in Toxicology from George Washington University in 1981, and his PhD in Pharmacology/Toxicology from Oregon State University in 1985. He has been affiliated with the Idaho State University College of Pharmacy since 1980.

Paul Cady, PhD, earned his bachelor of science degree in Pharmacy (RPPh) in 1980, his master’s degree in Hospital Pharmacy Administration in 1985, and his PhD in Pharmacy Administration in 1988 from the University of Arizona. He has been affiliated with Idaho State University since 1990.