Spiking of intravenous bags does not cause time-dependent microbial contamination: a preliminary report

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As the result of an apparent misinterpretation of the United States Pharmacopeia (USP) Chapter 797 Standards for Pharmaceutical Compounding[1] by the Association for Professionals in Infection Control and Epidemiology (APIC),[2] the Joint Commission, without scientific evidence, is requiring that intravenous (IV) solution bags must be spiked no sooner than 1 hour before being connected to a patient to avoid contamination.

Recent studies have shown no growth in normal saline (NS) over a 4-hour period[3] and in lactated Ringer's (LR) over an 8-hour period[4] after spiking. Unfortunately, these short time intervals could not be used to support our longstanding hospital policy, which had permitted 24 hours of storage before discard or use. In addition, we wanted to extend the observation period to 9 days to maximize the probability of detecting even low-level microbial contamination. Finally, we wanted to verify that our protocol was sufficiently sensitive to detect a low level of contamination (0.1 CFU/mL) because previous studies have demonstrated that low levels of contamination can be difficult to detect.[5]

Methods

Our anesthesia technologists spiked IV bags in the anesthesia workroom using our standard protocol. The technician removed each IV administration set (Codan US, Santa Ana, CA) from its sterile packaging using clean gloves, without masks or gowns. The plastic outer covering of the IV bags (Hospira, Lake Forest, IL) was removed, and the bags were hung on IV poles. Each IV bag administration port cover was removed, and the administration set spike was inserted into the IV bag in the usual manner. The end cap of the IV administration set was removed, and the roller clamp was opened. When fluid was seen emerging from the distal tip of the IV set, after all air bubbles had been removed, the fluid was stopped with the roller clamp and the end cap of the IV tubing was replaced. To avoid affecting standard procedure, the technologists were not informed about the study prior to bag spiking.

In the first part of the study, 25 one-liter bags of normal saline (NS) were spiked and placed in storage at room temperature in the anesthesia workroom. At 1 hour, 24 hours, 48 hours, 5 days, and 9 days, 5 bags were randomly selected and sampled for microbial contamination. At each time interval, 20-mL samples were collected after thorough mixing by repeatedly squeezing each bag immediately before sampling. All samples were taken from the rubber stopper on the IV bag after it was cleaned with alcohol. The stopper was allowed to dry completely before a sample was taken. Each 20-mL sample was divided equally and placed into 2 BACTEC Plus Aerobic/F blood culture vials (Becton Dickinson, Sparks, MD). The sample vials were transported to the clinical microbiology laboratory and incubated in the BACTEC FX blood culture system (Becton Dickinson). The vials were monitored for 5 days for growth of bacteria and fungi. Each culture vial contained a fluorescent chemical sensor to detect increases in carbon dioxide produced by the growth of microorganisms, including bacteria and fungi. Each vial was monitored every 10 minutes for an increase in fluorescence. A positive reading would indicate the presence of microorganisms. To confirm microbial growth in positive vials detected by the BACTEC system, smears were obtained and Gram stained. A subculture on media for isolation (ie, blood agar and chocolate agar) was used to identify any microbes detected by the BACTEC system. In the second part of the study, we added an additional 3 groups. Group 2 consisted of 5 bags of 5% dextrose in lactated Ringer's (D5LR), a chemically complex solution more vulnerable to microbial contamination and sustained growth, for comparison to NS group 1. We also wanted to have positive controls to verify that both NS and D5LR solutions could support readily detectable bacterial growth following low-level contamination (0.1 CFU/mL). Group 3 consisted of 5 bags of NS contaminated with *E. coli*, and group 4 consisted of 5 bags of D5LR contaminated with *E. coli*. Both groups 3 and 4 were inoculated with *E. coli* at time zero. *Escherichia coli* was selected as the positive control based on microbiology recommendation. Sampling protocol for part 2 was identical to the one used in part 1 described above. The contaminated bags were stored at room temperature in a private locked office in the hospital to eliminate any chance of cross-contamination.

Results

At 1 hour and after 1, 2, 3, and 9 days in storage, no growth of bacteria or fungi was observed in any sample of group 1 (NS) or group 2 (D5LR) following 5 days of incubation under standard blood-culture conditions (Table 1). The positive control groups of NS (group 3) and D5LR (group 4) that were inoculated with *E. coli* all grew confirmed *E. coli* colonies at all sample times (Table 1). No other microorganisms were detected in either group. Unfortunately, the samples from group 3 (NS with *E. coli*) from day 9 were lost.

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Table 1. Results of Microbial Growth for Each Study Group

Study Group	Day 0	Day 1	Day 2	Day 5	Day 9
Group 1 (NS)	No growth	No growth	No growth	No growth	No growth
Group 2 (D5LR)	No growth	No growth	No growth	No growth	No growth
Group 3 (NS with 100 CFU/L *E. coli*)	+ Growth	+ Growth	+ Growth	+ Growth	Lost data
Group 4 (D5LR with 100 CFU/L *E. coli*)	+ Growth	+ Growth	+ Growth	+ Growth	+ Growth

NOTE. NS, normal saline; D5LR, 5% dextrose in lactated Ringer's; CFU, colony-forming units; *E. coli, Escherichia coli.*

Discussion

The widespread misinterpretation of USP 797 regarding contamination of IV bags 1 hour after spiking would mean that any sterile solution (and its administration set) would have to be disposed of every 60 minutes, a clearly untenable situation. In operating rooms and many other areas of the hospital, IV bags are spiked and readily available for prompt patient care and hospital efficiency. Indeed, requiring that a sterile solution be connected to a patient within one hour after spiking and then allowing that solution to be administered over many hours seems illogical unless connection to a patient somehow prevents contamination.

The USP chapter 797 is not vague regarding the context under which its standards apply. In the introduction to USP 797 it clearly states, "The standards in this chapter do not pertain to the *clinical administration* of compounded sterile preparations to patients …" Because clinical administration of a commercially prepared IV or arterial line flush solution requires spiking, USP 797 standards do not pertain in that circumstance (confirmed by personal communication from the USP Liaison Officer for Chapter 797).

Although our study was not powered to detect a truly rare event, it does demonstrate that under the standard nonsterile anesthesia workroom conditions in which our 40 NS and D5LR bags were spiked and stored, no unanticipated growth of bacteria or fungi could be detected at any time up to 9 days after spiking and nonsterile storage. A subsequent study of 400 spiked containers has been proposed that will provide sufficient power $(1-\beta=0.8)$ to detect a 0.5% contamination rate. More than 16,000 samples would be required to detect a 1 in 10,000 contamination rate, emphasizing the difficulty of proving no effect.

This study emphasizes the need for evidence-based decisions in all aspects of hospital management to ensure that the efficient delivery of high-quality healthcare is the highest priority. Arbitrary and unfounded time limitations on spiked intravascular fluids are an unnecessary compromise of efficiency without any evidence of improved patient safety. Although these non–evidence-based measures are well intentioned, in acute-care settings when timely intravascular access is crucial, these policies may not only be inefficient but, in fact, may also be detrimental to patient care.

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