Multidose Vials Versus Single-Dose Vials: a Study in Sterility and Cost-Effectiveness

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A total of 197 multidose injectable vials were collected from 10 different nursing stations and evaluated for sterility. Experimental contamination studies were undertaken, and the cost-effectiveness of multidose vials was compared with that of single-dose vials. Our results showed that bacterial contamination of multidose injectable vials was not a significant hazard; in addition, contrary to common belief, the use of multidose vials was not always successful as a cost-containment measure.

The use of multidose injectable vials in hospitals continues to be promoted as a cost-containment measure for hospitals and taxpayers. While the medication is on the ward, the vial is entered into several times and presumed to remain sterile. As part of a study for the infection control program at the Veterans Administration Medical Center, Wood, Wis., we compared the sterility and cost-effectiveness of these vials with that of single-dose vials for the same medication (5; J. A. Jacobson, J. C. Bawden, J. C. Jackson, R. K. Anderson, and J. P. Burke, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 21st, Chicago, Ill., abstr. no. 853). Experimentally contaminated vials were also evaluated (6).

We collected 197 open injectable vials, containing 50 different medications scheduled for removal from the wards at the end of a 1-month period, from 10 different nursing stations at the Veterans Administration Medical Center. We sent them to the microbiology laboratory. The volume of medication used per vial was obtained by subtracting the remaining volume from the original volume. Using a sterile technique, we removed 1-ml aliquots from 190 vials and inoculated each into 5 ml of thioglycolate broth without indicator-135C (BBL Microbiology Systems, Cockeysville, Md.). The broths were incubated at 36°C and examined visually each day for growth for up to 7 days. A total of 28 random broths which showed no turbidity upon visual examination after 48 h of incubation were subcultured to quadrants of blood agar plates as blind subcultures and held for 48 h at 36°C before being discarded. Because only a small amount of medication was available in the remaining seven vials, measured portions (0.1 to 0.5 ml) were cultured in proportionate volumes of thioglycolate broth and examined visually. The thioglycolate broth was selected for use as an all-supportive medium for aerobic and anaerobic bacteria and yeasts. The medications on the wards were either refrigerated or stored at room temperature according to specifications on the vials. We chose to test the growth potential of contaminating bacteria, if any; hence, we carried out incubations at 36°C.

To simulate contamination of vials which may occur with breaks in technique (1, 4, 19), we deliberately implanted six of the most commonly used medications with bacteria, arbitrarily designated low-level and high-level contamination. The bacterial solution consisted of 107 CFU of approximately equal numbers of Bacillus sp. (NRLL B4418), coagulase-negative staphylococci (ATCC 12228), Escherichia coli (ATCC 25923), Pseudomonas sp. (not P. aeruginosa), and diphtheroids per ml. Pseudomonas sp. was obtained from cold tap water; diphtheroids were obtained from a skin sample. The attempts at low-level contamination consisted of entering the vial without alcohol swabbing, contaminating the rubber septum of the vial by touching to skin, and wiping the septum with alcohol gauze dipped into the bacterial solution. The attempts at high-level contamination consisted of leaving the bacteria-contaminated swab on the septum for 20 min and then withdrawing medication, immersing the needle in the bacterial solution and entering the vial, and placing the bacterial solution (0.1 ml) in the vial and then withdrawing medication immediately and at 24, 48, 72, and 96 h. All specimens withdrawn in this manner were plated directly onto blood agar plates for semiquantitative bacterial counts and incubated at 36°C for up to 4 days. Also, in two separate experiments four vials were touched on blood
agar plates, and the number of bacteria per square centimeter was counted. For the skin contamination study, four thumb surface samples from hospital employees were plated and area measured, and the number of bacteria per square centimeter was counted.

Of the 50 different medications represented in the total of 197 vials collected, 28 are currently only available in multidose vials. These were therefore eliminated from further cost accounting studies. The remaining 22 medications, constituting 92 vials, were used for cost analysis. The cost of each multidose vial was compared with the cost of the corresponding single-dose vial multiplied by the number of doses routinely used from multidose vials.

Our results showed that, while multidose vials were at the nursing stations, 25% or less of the original volume of medication per vial was used in 177 of 197 vials (90%). The number of times each vial was entered ranged from 1 to 10 (average, 4.5). All 197 vials tested for sterility revealed no bacterial or fungal growth at 7 days. As shown in Table 1, attempts at low-level contamination of the six most commonly used medications essentially resulted in no growth. In attempts at high-level contamination, all the vials tested (with two exceptions) showed heavy bacterial growth. After inoculation with bacterial solution F (Table 1), all vials appeared to contain clear solutions upon visual examination. However, subculturing at 24-h intervals showed moderate to heavy growth initially (0 and 24 h), with a 10- to 100-fold decrease in the number of bacteria at 96 h. *Pseudomonas* sp., *Bacillus* sp., and diphtheroids were the predominant flora surviving. The number of bacteria present on the unswabbed vials and thumb surface samples varied greatly; the average was 30 and 21 colonies per square centimeter, respectively. The colonies consisted of coagulase-negative staphylococci, diphtheroids, and a saprophytic mold.

On the basis of limited data available for this cost accounting study, the total cost of the medications purchased in 92 multidose vials was $223.77. The unit dose cost of these drugs was multiplied by the number of times the medication was used on the ward; the total cost was $120.00. Thus, a missed potential savings of 46% was obvious, with part of the problem being the low usage of multidose vials.

This study was undertaken primarily to assess the safety of using multidose vials in a hospital setting from the sterility standpoint. Several previous studies (1, 2, 4, 7–9) showed a 1 to 2.8% contamination rate of multidose vials, with two experimental studies (7, 9) showing total sterility. The results of a recent simulated contamination study in storage conditions (3) suggested that the risk of significant microbial contamination for at least some medications is low but varies with the medication. Our results showed that all 197 vials collected from the wards were sterile; the one-sided 95% confidence limit for the actual contamination was 0 to 1.51%.

As part of the infection control policy for nursing at the Veterans Administration Medical Center, reconstituted vials are given a 2-week outdate. They are removed by the pharmacy service at the end of a 1-month period. Thus, multidose vials can potentially be used for a maximum of 29 days. In a setting where usage of multidose vials is low, the common generalization that use of multidose vials is a cost-containment measure is not necessarily true. We feel that hospitals should evaluate individual wards for multidose vial usage, patient turnover, and number of patients on ward on the same medication and review policies on removal of medications from the wards. Our studies indicated that there was adequate bacteriostasis in the multidose vials for patient care and, vials subjected to attempts at more importantly, experimental low-level contamination retained adequate sterility. However, wastage of medication in multidose vials is a continuing factor; their use is not necessarily a cost-containment measure.

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<th>Method of contamination</th>
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- A, Entering vial without alcohol swabbing; B, skin contamination of the rubber septum; C, wiping the septum with contaminated gauze; D, contaminating the septum for 20 min; E, contaminating the needle; and F, placing bacteria into the vial and immediately withdrawing medication.
- +, No growth; +/−, less than five colonies per plate (no growth in 48 h, growth in 72 to 96 h); +, 5 to 9 colonies per plate; ++, 10 to 49 colonies per plate; ++++, 50 to 200 colonies per plate.

LITERATURE CITED