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Sterility of Anesthetic Multiple-dose Vials after Opening

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Despite the widespread use of multiple dose vials (MDV) for anesthetic medications, there is a paucity of data concerning the sterility of in-use MDV. The purpose of this study was to analyze the frequency of bacterial contamination of MDV used in current anesthesia practice. The authors collected weekly samples from 351 in-use MDV for seven consecutive weeks and cultured them using appropriate bacterial growth media. The vials contained drugs including neuromuscular blockers, anticholinergics, and an induction agent. They were sampled from locations designated for elective as well as emergency surgery. Six vial subgroups were studied with multiple samplings for 6–48 days. One-half of all opened vials remained in use after 4–9 days, while less than 5% remained after 6 weeks. No vial yielded bacteria. The authors conclude that the incidence of MDV contamination with live bacteria is low for the anesthetic medications studied. This appeared to be true even for vials with increasing duration of use and for vials from locations where emergency surgery commonly was performed. (Key words: Anesthetics, intravenous: contamination. Bacteria: drug contamination.)

MULTIPLE-DOSE VIALS (MDV) commonly are used to store and dispense anesthetic medications. While some services discard all opened MDV at the end of every case, many others keep them on anesthesia carts for periods ranging from a few hours to many months.[1] Concern has been raised over the potential for bacterial inoculation from contaminated MDV.[2] In surgical patients, the risks of sepsis from nosocomial bacteremia are enhanced because immune defenses may be impaired by the stress of the operation, effects of anesthesia,[3] and preexisting medical conditions.

Previously reported MDV contamination rates range from 0 to 27%.[4–10] There are only a few reports on the sterility of MDV used in anesthesia.[1,11,12] The number of MDV sampled in these studies has been small, and their composition has not been representative of the variety of medications currently found on anesthesia carts. Other studies have examined larger MDV populations in the hospital ward setting.[7,9,10] The results from these studies may not apply to MDV used in contemporary anesthesia practice. Since the vials studied in these reports contained medications commonly dispensed as intramuscular or subcutaneous injections on hospital wards, one might expect a higher contamination rate than for MDV containing medications dispensed intravenously in the operating room. On the other hand, strict adherence to aseptic technique is not always maintained in the immediate management of critical intraoperative incidents. These often unavoidable lapses in technique could lead to higher contamination rates of vials used in the operating room. To clarify the extent of live bacterial contamination of MDV used in anesthetic practice, we examined a large number of in-use MDV containing predominately intravenous medications that are kept on anesthesia carts in our operating rooms.

Materials and Methods

At our institution, MDV are stored on anesthesia carts at all anesthetizing locations. Opened MDV are reused until empty or until the manufacturer's expiration date. Vials are otherwise undated. Although there is some variation in technique, the rubber septum of each vial generally is wiped with 70% isopropyl alcohol prior to puncture with a sterile needle. A vial entered by a needle that is known to have been contaminated is not reused for subsequent patients.

Anesthesia personnel were not informed of the nature and purpose of the study. All opened MDV remaining on anesthesia carts at the end of the working day were sampled weekly during seven consecutive weeks. The vial septa were cleaned with 70% isopropyl alcohol, and 1-ml samples were withdrawn using sterile syringes and needles. Once sampled, MDV were numbered inconspicuously and returned to the cart. All samples were held at room temperature and cultured within 2 h from the time they were obtained. One-tenth milliliter of the sample was placed on chocolate agar plates, while the remainder was cultured in 10 ml brain heart infusion broth (Scott Laboratories, Fiskeville, Rhode Island), to

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TABLE 1. Composition of Multiple-dose Vials Sampled

Medication	Concentration	Preservative	pH	No. of Samples	Per Cent of Total
Tubocurarine chloride inj. USP (Squibb)*	3 mg/ml	Chlorobutanol 0.5%	2.5–5.0	89	18
Atropine sulfate inj. (Elkins-Sinn)†	0.4 mg/ml	Benzyl alcohol 1.5%	3.0–6.5	80	17
Pavulon® (pancuronium bromide) (Organon)*	1 mg/ml	Benzyl alcohol 1%, Sodium acetate 0.2%	4.0	62	13
Robinul® (glycoprolate inj.) (Robins)‡	0.2 mg/ml	Benzyl alcohol 0.9%	2.0–3.0	59	12
Sucostrin® (succinylcholine chloride) (Squibb)*	20 mg/ml	Methylparaben 0.1%, Propylparaben 0.01%	3.0–4.5	59	12
Prostigmin® (neostigmine methylsulfate) (Roche)‡	1 mg/ml	Phenol 0.45%, Sodium acetate 0.02%	5.9	47	10
Metubine® (metocurine iodide) (Lilly)*	2 mg/ml	Phenol 0.5%	4.0–4.3	41	9
Xylocaine® 1% (lidocaine HCl) (Astra)†	10 mg/ml	Methylparaben 0.1%	5.0–7.0	30	6
Ketalar® (ketamine HCl Inj.) (Parke-Davis)*	10 mg/ml	Benzethonium chloride 0.01%	3.5–5.5	9	2
Tensilon® (edrophonium chloride) (Roche)*	10 mg/ml	Phenol 0.45%, Sodium sulfate 0.2%	5.4	6	1

* Isotonic.
† Slightly hypertonic.
‡ Hypotonic.

facilitate isolation of fastidious bacteria. Incubation was carried out at 37° C for 48 h (plates) and 10 days (broth). Test inoculations of plates and broth with known bacterial cultures were performed routinely throughout the study.

Statistical evaluation: Expected contamination frequencies were estimated using the Poisson distribution.

Results

A total of 482 samples were collected from 351 MDV on carts in 11 general operating rooms, three obstetric operating rooms, and two locations used for administering regional anesthesia. The mean time between sampling dates was 8 days (range 5–15 days). The composition of the sample population by type of drug and preservative is shown in table 1. Of the vials sampled more than once, 98 were sampled twice, 24 three times, 8 four times, and one vial was sampled five times.

None of the samples yielded bacterial growth either on agar plates or in broth. Random plates and broth tubes supported the growth of a variety of common bacteria. Figure 1 shows the fate of opened MDV. We continued contamination surveillance testing on six cross-sectional vial subgroups for 6–48 days. Each subgroup is composed of all opened vials found stored in anesthesia carts on a particular sampling date, with the exception of previously sampled vials. Fifty per cent of opened MDV disappeared from our carts within 4–9 days. By 2 weeks, 9–32% of the sampled open vials remained on carts, while less than 5% remained at 6 weeks.

At an estimated hypothetic contamination frequency of 0.62%, there was a 95% probability of detecting at least one positive culture out of a total of 482 specimens.

Discussion

Differences in technique of vial entry, quality of preservatives, and types of drugs studied might have contributed to the wide spread (0–27%) of contamination rates previously observed. Sampling techniques and study design also may have played a role. In the past the approach has been to sample a collection of vials at one time. We believe that the results of any study of MDV contamination are more meaningful when the in-use

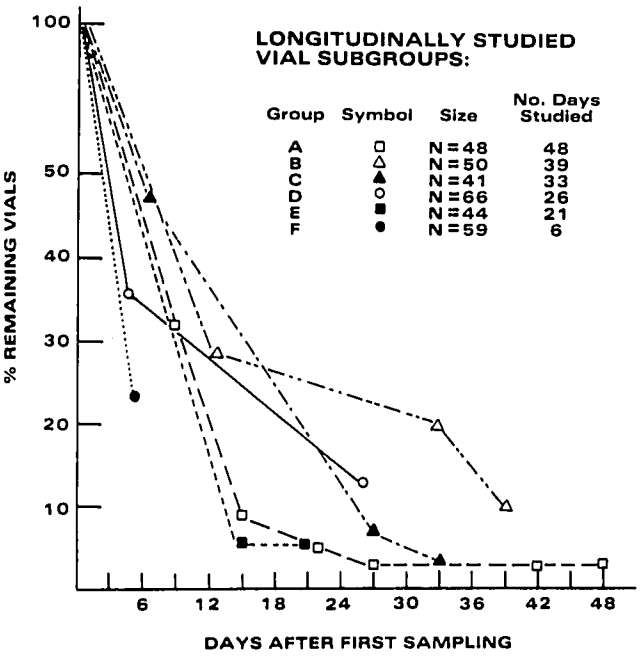

FIG. 1. Utilization of MDV over time after first sampling: each curve represents a vial subgroup and its pattern of disappearance from anesthesia carts over time.

characteristics of the vials are defined and contamination assessed in a longitudinal fashion. We have confined our investigation to vials for intravenous injection by anesthesia personnel in an operating room environment. By checking for vial sterility several times during the useful life of the vials, we believe the likelihood of detecting significant contamination was increased. Furthermore, unlike previous investigators, we were able to quantitate vial utilization half-life (fig. 1).

Although the exact incidence of MDV contamination cannot be determined from our data, it appears to be low. Our inability to isolate bacteria from any of the MDV studied is noteworthy, particularly in light of previous work suggesting a less stringent approach to asepsis taken by anesthesia personnel[2,3,13] and despite the longitudinal character of the study, which was designed to increase the yield of contaminated vials. Furthermore, vials from anesthetizing locations designated for emergency cases, where breaks in aseptic technique during MDV entry may be likely to occur,[7] were uniformly sterile. This is consistent with results from previous work on deliberate contamination of MDV, which demonstrated that heavy bacterial contamination of the rubber septum or of the needle was required in order to produce consistently positive MDV cultures. Minor breaks in technique, such as failure to use an alcohol swab or skin contamination of the rubber septum, only infrequently led to culture positive vials.[8] It might be argued that some of our MDV contained viable bacteria at one point during their useful life. When deliberately inoculated MDV are cultured, the highest bacterial counts occur during the first 24 h following contamination; by 48–96 h most are sterile again.[8,11,14] This has been attributed to the effect of preservatives, to the bacteriocidal or bacteriostatic activity of the drug itself, or to low *p*H of MDV solutions. Our samples were taken 30 min to several hours after the end of the last case of the day for each particular location. Yet, no period of transient contamination was evident from our results.

In summary, we conclude that bacterial contamination of MDV used in current anesthesia practice, is very low. Although we did not specifically study this, we observed that MDV from operating areas handling emergency procedures likewise were not associated with demonstrable contamination. The use of MDV in anesthesia appears relatively safe with respect to the iatrogenic transmission of bacteria. Grossly contaminated MDV or those that have been entered without proper technique, as may happen during emergency resuscitation, of course should be discarded. Unfortunately, contamination also may involve viral particles[1,15] and pyrogens such as endotoxin,[15] either of which may represent a significant threat to the surgical patient. Further investigation in this area is needed.

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