

Probability Of Bacteriological Contamination In Multidose Vial (MDVs) During Use: An Institutional Experience.

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ABSTRACT:

Many kinds of injectable drugs are used especially in operation theatres and emergency department e.g. thiopentone, ketamine, succinylcholine, mephentermine and Local anaesthetics multidose medications. But, during the successive use of multidose anaesthetic agents, microorganisms may contaminate these vials & enter the blood stream and may develop a variety of nosocomial infections resulting in prolonged hospitalization, increased morbidity & mortality of the patients. This study was done to know the probability of bacteriological contamination in MDVs during use. Samples were taken at various intervals e.g. at 0 hrs, at 24 hrs, at 72 hrs, 7th day and one sample within 30 days from the opening of vial & were sent to the microbiology laboratory for sterility checking. The exact reasons for MDVs contamination are said to be dependent on structural, economic and sociocultural factors. But, if aseptic technique is used consistently, an uncontaminated multidose vials may be used upto one month after puncture.

KEYWORDS: Multidose vials, injectable drugs, preservatives, sterility.

INTRODUCTION:

Multiple use containers of injectable medications commonly known as ‘multidose vials’. According to safe Injection Practices Coalition(2010) MDVs is defined as ‘A multidose vial is a bottle of liquid medication (injectable) that contains more than one dose of medication and is approved by the Food and Drug Administration(FDA) for use on multiple persons’¹. Many kinds of injectable drugs are used especially in operation theatres and emergency department as multidose medications e.g. thiopentone, ketamine, succinylcholine, midazolam, mephentermine, Xylocard 2%, LA s etc. These drugs are supplied as multidose to be used at different period of time for the same or different patients. But, during the successive use of multidose anaesthetic agents, microorganisms may contaminate these vial thus leading to variety of nosocomial infections like bacterial , viral and fungal resulting in prolonged hospitalization, increased morbidity & mortality of the patients. Multidose vials contain an antimicrobial preservative like benzyl alcohol , benzothonium chloride , methyl paraben , propyl paraben , metabisulphite , to help prevent the growth of bacteria. The preservative has no effect on viruses and does not protect against contamination when healthcare personnel fail to follow safe injection¹. In fact, even when the preservative is effective, contaminating bacterial organisms may remain viable in a multidose vial for upto 2 hours before the preservative becomes entirely effective².

Although MDVs are associated with a reduced costs, environmental waste and increased convenience , their infectious complications from MDVs can be life –threatening³. Most of the reported MDVs associated outbreaks have been related directly to poor aseptic technique, including the unacceptable practices of administering the same solution to more than one patient and entering a MDV with a used syringe and needle⁴ and leaving needle in the stopper[Table 1].

MDVs : For how long one can use them? Briefings on infection control, September, 2010⁵

US Pharmacopeia(USP2008), A General Chapter≤ 797≥ Pharmaceutical Compounding? Sterile Preparation, requires MDVs to be discarded 28 days after initial stopper penetration unless the manufacturer specifies otherwise. MDVs should be labelled to reflect penetration date/beyond –use date

CDC indicates that MDVs can be used until expiration date, unless there are concern with sterility⁶.

Summary of Recommendations from CDC and WHO for MDVs Use

Bulletin of WHO 2003;81:491-500⁷ :For MDVs safe use

Important to use single-dose vial rather than MDVs if possible. If MDVs must be used, it is essential that the person administering the injecton pierces the septum with a sterile needle and it is important not to leave any needle in place in the stopper.

Recommendations of Centers for Disease Control and Prevention(CDC)⁸: For MDVs safe use

Use single-dose vials for parenteral medications when possible. If MDVs are to be used

(a) Restrict its use to a single patient (b)Refrigerate MDVs after they are opened if recommended by the manufacturers.(c) Cleanse the access diaphragm of MDVs with 70% alcohol before inserting a device into the vial(d) Use a sterile device to access a MDVs and avoid touch contamination before penetrating the access diaphragm(e) Discard MDVs if sterility is compromised or when manufacturer’s stated expiration date is due.

MDVs use has always been a topic of debate for a long time. This study was designed to gather data regarding probability of bacterial contamination in multidose vials after first opening.

Materials & Methods:

It was prospective, case control, double blind study. Following institutional ethical committee approval, samples from multidose vials, commonly used in operation theatres were taken from different manufactures. They were noted for the presence of other preservatives and pharmacological agents. We took two vials of each drug with same batch number for all drugs under study. Just after penetration 2 ml-2 ml from each drug vial sent for bacteriological examination as control samples. Then, 2 ml-2 ml from each open drug vial of same drug was kept in room at 24⁰ C and in refrigerator at 8⁰C at various time interval as study samples. A secret marking was placed on drug coded for date of opening, not informing the person using drug. Other person took samples for culture and recording the data. Samples were taken at various interval.....

- (a) Zero hour-----first opening (b) After 24 hours
(c) After 72 hours (d) On 7th day (e) One sample on day 30.

Samples were sent to microbiology department for bacteriological testing. Samples were inoculated on Blood agar, Chocolate agar, Mac-conkey agar and Glucose broth. These media were incubated at 37 °C for 24 hours. Agar plates were inspected for bacterial growth, if no growth was observed on agar plates, then subculture from

Glucose broth was done on Blood agar, Chocolate agar, Mac-conkey agar and these plates were incubated at 37 °C for 24 hours.

RESULT:

In this study we have taken commonly used MDVs in operation theatres and emergency e.g. Thiopentone Sodium, Succinylcholine, Ketamine, Xylocard 2%, Mephenteramine Midazolam, Xylocaine with adrenaline, Bupivacaine. A total of 80 samples were collected [table2]. Except two samples(one of Ketamine and second of Xylocard 2%, showing growth of Gram negative Staphylococcus within 30 days of opening) all other samples were found sterile(2.5%).

DISCUSSION:

In some parts of world, especially in developing world, the use of MDVs intravenous injections is supposed to be a routine and economic practice. Most of practitioners are using them without being aware of serious inherent infections associated with their use and are bound to use them because of inadequate/ limited resources. Worthy of note are severe iatrogenic infections that from time to time have been cited in scientific literature as outbreaks but are in fact caused by the use of bacterially contaminated multiple-use vials⁹.

Studies of MDVs have revealed considerable variations in bacterial contamination rates ranging from 0% to 27%¹⁰. Some of these studies showed alarming contamination rates¹¹, whereas others mentioned only sterile vials. Thus favouring the multiple use of vials for reducing costs and general convenience¹² However, actual clinical infections resulting from contaminated MDVs have not been reported frequently in the medical literature¹³.

In a clinical study, solutions from multidose vials were cultured for the presence of microorganisms over a period of 6-48 days. No bacterial growth was observed in 59 separate samples¹⁴. Bacterial growth in 2 samples out of 80 samples within a period of one month favouring the statement that even when MDVs are bacteriostatic, the vials still support microbial growth¹⁵(table 2). There are several studies and reports addressing the possibility of contamination of MDVs during use and the ability of organism to survive in a variety of medications packed in MDVs¹³. Administration of a contaminated infusate is one of the commonly identified causes of nosocomial blood stream infection¹⁶. In the SCOPE database, the most common organisms causing nosocomial infections were coagulase –negative Staphylococci(31%), *S. aureus*(20%), Enterococci(9%) and *Candida spp*(9%)¹⁷. All of these are able to grow rapidly at room temperature in a variety of solutions.

Several factors affecting the stability and sterility of MDVs e.g. preservatives, storage temperature, chemical stability, container type, aseptic techniques etc. Available evidence suggests that MDVs can be stored safely at room temperature unless manufacturers' recommendations or drug stability dictate otherwise(Pearson 1996)¹⁸. In general, LAs are chemically stable for periods of weeks to months. In one study, the bactericidal activity of levobupivacaine was only 50% that of bupivacaine¹⁹. Ropivacaine has been shown to have either poor or no antimicrobial properties²⁰. The temperature of operation theatre was maintained at 24°C and operation theatre culture was found sterile during this study. Kirschke et al (2003) reported an outbreak of *S. aureus* from a MDVs of Xylocaine. In this case, the vial of lidocaine was refrigerated. However, the manufacturer recommends storing this product at room temperature²¹. CDC therefore has recommended that the manufacturer's instructions be consulted to determine the proper storage temperatures of MDVs, which are product specific²².

Highsmith and colleagues(1982) reported that when bacteria or yeasts were inoculated into some commonly used medications such as succinylcholine chloride and sodium thiopental for 96 hours at room temperature, rarely were micro-organisms recovered irrespective of whether they contained a preservative²³. Products could have been contaminated even in OT, if storage conditions are not satisfactory or exposed to oxygen, heat or humidity. Some medication types are more likely to cause outbreaks than others e.g. medications containing lipids, such as Propofol seem to be most dangerous, followed by preservative-free drugs⁹.

However, poor aseptic techniques employed during successive uses appear to be most likely route of contamination responsible for considerable morbidity and mortality. In most cases contamination of the infusate occurs extrinsically during manipulation of the fluid before the administration to the patient. Longfield and colleagues(1984) reported that though the overall risk of extrinsic contamination(introduced into the system during use) of MDVs appears to be small(estimated 0.5 per 1000 vials)¹⁰ which is similar to our study. But, the exact reasons are said to be complex and include structural, economic and sociocultural factors.

USP and APIC now recommend that opened or punctured MDVs be used for no more than 28 days unless the manufacturer specifies otherwise²⁴. In some cases, the discard time may be shorter or longer than 28 days-if the drug maker's expiration date specifies a longer time based on FDA approval research²⁵. Due to sporadic infections attributed to contaminated MDVs, some authorities have suggested discarding all MDVs within 24 hours²⁶. One of the proposed JCAHO National Patient Safety Goals for 2006 is the elimination of MDVs, whenever possible²⁷.

Bhat KG et al concluded from their study that even if accidental contamination of vials entered a number of times during use occurs, the self-sterilizing property of the vial contents would prevent bacterial infection from the source²⁸. So, use all MDVs according to your hospital policies once they are pierced and stored safely, according to the manufacturer's directions. Nevertheless, one can see opened, unlabelled MDVs vials stored in OTs improperly for future use.

Outbreaks related to unsafe injection practices indicate that some healthcare personnel are unaware of, do not understand, or do not adhere to basic principles of infection control and aseptic technique. Research shows that up to 25% of healthcare practitioners re-enter vials with needles just injected into patients²⁹. The sterile samples of this study at different periods of time give an impression of employees' proper aseptic technique (swabbing septum with spirit before puncture, not leaving needle in stopper, using new device for every prick) and good training, which is similar to Arrington ME et al reporting that merely an alteration in the drug aspiration technique causes a significant difference in the incidence of MDV contamination²⁹. Needles left in the septum of MDVs might encourage the use of the same syringe to repeatedly draw medications for one patient, a practice that may lead to vial contamination and infection among subsequent patients.

So, in one respect, MDVs are a great way to make it cost-effective with expensive medications especially in developing countries. On the other hand, they can cause multiple complications if staff members are not following very precise procedure.

CONCLUSION:

The intention of this study is not to promote the use of MDVs, but to encourage the healthcare providers to remain always adhere to safe injection Practice under Standard Precautions to prevent disease transmission from needles, syringes and MDVs. Various studies concluded that transmission risk from MDVs is very low and depends on the extent of the infection control measures taken by staff. But, if aseptic technique is used consistently, an uncontaminated multidose vial may be used up to a month.

Table 2: Microbiological examination of MDVs under study.

I.V. drug studied	At 0 Hr(Control group) just after first opening sent for lab		At 24 Hrs		At 72 Hrs		On 7 th Day		On 30 th day	
	Room(24□□° C)	Fridge(8□° C)	Room(24□□□°C)	Fridge(8 □C)	Room(24 °C)	Fridge(8□□° C)	Room(24□□° C)	Fridge(8° C)	Room(24 °C)	Fridge(8° C)
<i>Thiopentone(T)</i>	Tcrs	tcfs	T24rs	t24fs	T72rs	t72fs	T7rs	t7fs	T30rs	t30fs
<i>Ketamine(K)</i>	Kcrs	kcfs	K24rs	k24fs	K72rs	k72fs	K7rs	k7fs	K30rp*	k30fs
<i>Scoline(S)</i>	Scrs	scfs	S24rs	s24fs	S72rs	s72fs	S7rs	s7fs	S30rs	s30fs
<i>Mephenteramin(M)</i>	Mcrs	mcfs	M24rs	m24fs	M72rs	m72fs	M7rs	m7fs	M30rs	m30fs
<i>Midazolam(Mi)</i>	MIcrs	micfs	MI 24rs	mi24fs	MI72 rs	mi72fs	MI7rs	mi7fs	Mi30rs	mi30fs
<i>Xylocard2%(X)</i>	Xcrs	xcfs	X24rs	x24fs	X72 rs	x72fs	X7rs	x7fs	X30rp*	x30fs
<i>Bupivacaine(B)</i>	Bcrs	befs	B24rs	b24fs	B72 rs	b72fs	B7rs	b7fs	B30rs	b30fs
<i>Xylocaine +adrenaline(XA)</i>	XAcrs	xacfs	XA24rs	xa24fs	XA72rs	xa72fs	XA7rs	xa7fs	XA30rs	xa30fs

crs = control & sterile at room temperature; cfs = control & sterile in fridge; 24rs, 72rs, 7rs and 30rs = sterile at room temperature after 24, 72 hrs and on 7th and 30th day ; 24fs, 72fs,7fs and 30fs = sterile in fridge after 24, 72 hrs and on 7th and 30th day. 30rp= positive after 30th day

Table 1 Routes/modes of MDVs contamination

1) Through repeated access using improper aseptic techniques,
2) Contaminated septum and subsequent spread along the needle,
3) By direct entry through needle left in septum,
4) Contaminated MDVs(considered to be commonest mechanism)

Probability of bacterial contamination in MDVs vials..... (7)

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