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Original Article / Özgün Araştırma

Bacterial Contamination of Anaesthetic and Vasopressor Drugs in the Operating Theatres

Ameliyathanelerde Anestetik ve Vazopressör İlaçların Bakteriyel Kontaminasyonu

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Abstract / Öz

Objective: The aim of this study was to determine the incidence of bacterial and fungal contamination in anaesthetic and vasopressor drugs before and after use in operating theatres.

Methods: A cross-sectional study was conducted in the operating theatres of a university hospital. We collected 945 samples of three different drugs, namely, propofol, vecuronium and ephedrine, from 20 operating rooms and refrigerators where the unused drugs were stored. Each drug was divided into two groups, the pre-use group and the post-use group. The pre-use drugs were cultured before the patient received the drug. The post-use drugs were cultured after the patient had received the drug or after the drugs had been transferred to other syringes. The culture results were reported as either positive or negative.

Results: Out of the 945 drug samples, 26 (2.8%, 95% confidence interval=1.8%–4.0%) gave a positive culture. Of the 317 propofol samples, 20 (6.3%) were found to have bacterial contamination, 11 in the pre-use group and 9 in the post-use group. Of the 318 ephedrine samples, 6 (1.9%) were found to be positive on culture, one in the pre-use group and five in the post-use group. Vecuronium gave no positive cultures. All organisms were non-pathogenic, and no fungal contamination was found.

Conclusion: The incidence of bacterial contamination in anaesthetic and vasopressor drugs was 2.8%. Anaesthetic teams must be aware of contamination issues in anaesthetic drugs that have been prepared for later use and, in order to reduce the risk of contamination, they must improve the methods of administering drugs to patients.

Keywords: Anaesthetic drug, contamination, operating room, sterility

Amaç: Bu çalışmanın amacı, ameliyathanelerde kullanım öncesi ve sonrası anestetik ve vazopressör ilaçlarda meydana gelen bakteriyel ve fungal kontaminasyon insidansını belirlemekti.

Yöntemler: Bu kesitsel çalışma bir üniversite hastanesinin ameliyathanelerinde gerçekleştirilmiştir. Propofol, veküronyum ve efedrin olmak üzere üç farklı ilaçtan 945 numune, 20 ameliyathane ve kalan ilaçların depolandığı buzdolaplarından alındı. Her bir ilaç kullanım öncesi ve kullanım sonrası olmak üzere iki gruba ayrıldı. Hasta ilacı almadan önce, kullanım öncesi ilaçların kültürü yapıldı. Kullanım sonrası ilaçların kültürleri, hasta ilacı aldıktan sonra veya ilaçlar diğer şırıngalara transfer edildikten sonra yapıldı. Kültür sonuçları pozitif ya da negatif olarak raporlandı.

Bulgular: Dokuz yüz kırk beş ilaç numunesinden 26'sında (%2,8, %95 güven aralığı=%1,8–%4,0) pozitif kültür elde edildi. Üç yüz on yedi propofol numunesinden 20'sinde (%6,3) bakteriyel kontaminasyon tespit edildi. Bunlardan 11'i kullanım öncesi gruptayken 9'u kullanım sonrası gruptaydı. Üç yüz on sekiz efedrin numunesinden 6'sında (1'i kullanım öncesi grupta ve 5'i kullanım sonrası grupta) kültür pozitif bulundu. Veküronyum numunelerinden pozitif kültür elde edilmedi. Tüm organizmalar nonpatojenikti ve fungal kontaminasyon gözlenmedi.

Sonuç: Anestetik ve vazopressör ilaçlarda bakteriyel kontaminasyon insidansı %2,8 olarak bulundu. Anestezi grupları sonraki kullanım için hazırlanan anestetik ilaçlarda oluşabilecek kontaminasyon probleminin farkında olmalıdırlar. Kontaminasyon riskini azaltmak için, hastalara ilaç uygulama yöntemlerini geliştirmelidirler.

Anahtar kelimeler: Anestetik ilaç, kontaminasyon, ameliyathane, sterilite

Introduction

One responsibility of an anaesthetic team is to prepare anaesthetic drugs, including induction drugs, muscle relaxants and resuscitation drugs, so they are ready to be used in both emergency and non-emergency situations. To reduce costs, multidose vials are often used in routine practice, allowing unused drugs to be stored for later use in other patients (1, 2). However, the sterility of prepared drugs, stored in vials and syringes, has been questioned.

Many studies have investigated the sterility of stored drugs (2-5). Most of these studies were conducted in laboratory settings (6-8), and not in real operating room conditions (2, 4, 9), i.e. analysing drugs stored in syringes (2, 4, 5, 10) or in multidose vials (3, 11). Thus, in this study, we collected drug samples such as ready-to-use drug vials, pre-mixed drugs and single vs multidose vials from various operating rooms. The drug samples had been stored for different durations and prepared by different methods.

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The primary objective of this study was to determine the incidence of bacterial and fungal contamination of two common anaesthetic drugs and one vasopressor drug before and after using them in the operating theatres. The secondary objectives were to evaluate the sterility of routine practices in terms of drug preparation and storage, and to determine the factors associated with a positive culture result.

Methods

The study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand (Chairperson: Associate Professor Verapol Chandeyin) on 11th July 2011 with the protocol number: EC 54-261-08-7-3. Written informed consent was waived because the study was not conducted on patients.

Study setting

The cross-sectional study was conducted between October 2011 and February 2012 in the operating theatres of the Songklanagarind Hospital, a 853-bed tertiary-care university hospital situated in southern Thailand. There were 20 operating rooms pertaining to the following departments: ear, nose and throat (ENT); ophthalmology; obstetrics and gynaecology (OB-GYN); orthopaedics; surgery (general, cardiovascular and thoracic, neurology, urology, plastic, trauma, vascular, paediatric). There was also a cardiac catheterization laboratory and a radiology suite.

Drug samples

Drug samples were obtained from the 20 operating rooms, a post-anaesthetic care unit (PACU) and refrigerators where the drugs were stored. Two anaesthetic drugs, propofol (Fresofol®, Fresenius Kabi Austria GmbH, Graz, Austria), and vecuronium (Norcuron®, N.V. Organon, Oss, The Netherlands) and one vasopressor drug, ephedrine hydrochloride (The Government Pharmaceutical Organization, Bangkok, Thailand), were selected for culture because they have different methods of preparation and shelf lives.

Propofol is a lipid containing an emulsion without antimicrobial preservatives, and is stored in glass ampoules, ready for use. Vecuronium, an intermediate acting non-depolarizing muscle relaxant, is stored as a powder in glass vials, diluted in normal saline before use and then stored in multidose vials. Ephedrine is a vasopressor which contains no preservatives, is stored in glass ampoules and is diluted in normal saline before use.

Anaesthetic drugs are diluted in 100 mL of normal saline solution, and the same solution is used for many patients until it is finished. The recommended duration of drug storage after opening the container is different for all three drugs. Propofol should be used within 12 hours after opening the ampoule. Vecuronium should be used within 1 week after preparation, and ephedrine should be used within 3 days after preparation. All unused drugs are kept on the anaesthesia cart during working hours, and stored in a refrigerator after working hours.

In routine practice, drugs are prepared using a sterile plastic syringe and sterile needle. For glass ampoules containing propofol and ephedrine, the ampoule neck is not wiped with an alcohol cotton swab before being opened. For multidose vials containing vecuronium, the rubber membrane is wiped with a 70% alcohol cotton swab before preparation and drawing. The personnel preparing the drugs do not normally wear gloves, although some disinfect their hands with alcohol gel. The date and time of drug preparation is recorded. For propofol, any unused drug left in the ampoule is pooled together to use in the next patient. After transferring the drug to another sterile plastic syringe, drugs are used on many patients. A new sterile needle is replaced on the syringe after drug transfer.

Samples of the three drugs were collected for culture. Each drug was divided into two groups, pre-use and post-use. The pre-use group contained drugs that were cultured before the patient had received the drug. The post-use group contained drugs that were cultured after the patient had received the drug or the drugs had been transferred to other syringes. Drugs in the post-use group were not collected from the same vials or syringes of the pre-use group.

The principal investigator collected the drug samples from the operating rooms and refrigerators where the drugs were stored during and outside working hours. No prior notice was given to anaesthetic personnel of the sample drug collection. One millilitre of sample was randomly taken from the prepared drug syringes or drawn from the multidose vials, then placed in a sterile bottle before being sent to the Micro-organism Culture Laboratory Centre. The date and time of sample storage was recorded. The culture results were reported as either positive or negative. In the samples that gave positive cultures, the organisms present were also identified.

Statistical analysis

For sample size calculation, the prevalence of positive drug cultures needed to be known, so a pilot study was conducted, and it was found that the prevalence of positive cultures was 10.5% (two out of 19 samples were positive). Thus, in order to estimate the prevalence of positive cultures with a precision of 5%, 139 samples per group were required. Allowance was made for a 10% of unusable data, thereby requiring 153 samples per group.

The prevalence of positive cultures for different storage durations and operating rooms are presented descriptively with 95% confidence intervals (CI).

The chi-squared (Fisher's exact test) was used to compare the culture results between different types of drugs, personnel preparing the drugs and day of storage. Drug storage dura-

tion was grouped into four categories and compared by the chi-square test. The independent association of each factor with a positive culture result was assessed by logistic regression. A p-value<0.05 was considered to indicate statistical significance. The R version 3.0.1 was used to analyse the data.

Results

A total of 945 drug samples, collected from 20 operating rooms and storage refrigerators, were cultured. Figure 1 shows the flow diagram of the study.

Of the 945 (2.8%) drug samples, 26 were positive on culture (95% CI=1.8%–4.0%). From those, 12 samples belonged to the pre-use group and 14 samples, to the post-use group. Of the 317 propofol samples, 20 (76.9%) were culture-positive, while only 6 of 318 ephedrine samples were culture-positive. Vecuronium gave no positive culture in either the pre-use or the post-use groups. The proportion of positive cultures from all drugs before use (12 samples) was not different from that after use (14 samples) (p=0.84). The number of positive cultures for propofol in the pre-use group was higher than in the post-use group (Table 1). By contrast, the number of positive cultures for ephedrine in the pre-use group was lower than in the post-use group.

The operating rooms that were found to have culture-positive samples were ophthalmology (five samples), OB-GYN

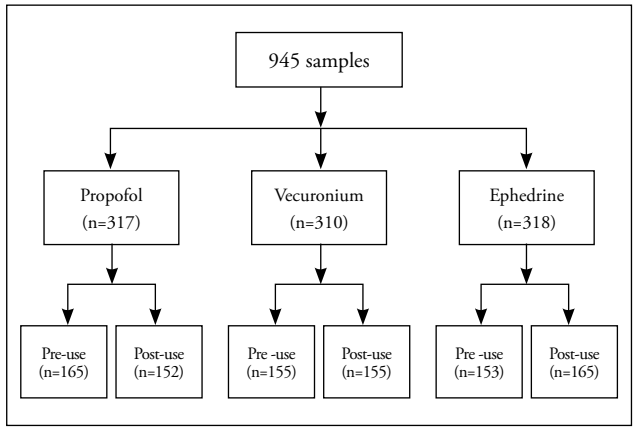

Figure 1. Flow diagram of the drug sample

Table 1. Summary of culture results for propofol and ephedrine among the different operating rooms

	Propofol				Ephedrine			
	Pre-use		Post-use		Pre-use		Post-use	
Location	Positive culture/ Total	% (95% CI)	Positive culture/ Total	% (95% CI)	Positive culture/ Total	% (95% CI)	Positive culture/ Total	% (95% CI)
Ophthalmology	2/14	14% (1.8%-43%)	2/16	13% (1.6%-38%)	0/4	0% (0% - 60%)	1/4	25% (0.6%-81%)
ENT	1/28	3.6% (0.1%-18%)	1/15	6.7% (0.2%-32%)	0/10	0% (0%-31%)	0/9	0% (0%-34%)
OB-GYN	3/49	6.1% (1.3%-17%)	2/21	9.5% (1.2%-30%)	0/25	0% (0% -14%)	0/13	0% (0%-25%)
Neurology	1/7	14% (0.4%-58%)	1/16	6.3% (0.2%-30%)	0/8	0% (0%-37%)	1/10	10% (0.3%-45%)
General	2/45	4.4% (0.5%-15%)	1/30	3.3% (0.1%-17%)	1/39	2.6% (0.1%-13%)	0/20	0% (0%-17%)
CVT	0/3	0% (0%-71%)	0/6	0% (0%-46%)	0/7	0% (0%-41%)	0/2	0% (0%-85%)
Orthopaedic	1/7	14% (0.4%-58%)	0/11	0% (0%-29%)	0/16	0% (0%-21%)	0/7	0% (0%-41%)
Emergency	1/12	8.3% (0.2%-38%)	1/11	9.1% (0.2%-42%)	0/14	0% (0%-23%)	0/10	0% (0%-31%)
Remote	0/0	0%	1/4	25% (0.6%-81%)	0/7	0% (0%-41%)	0/1	0% (0%-98%)
PACU	0/0	0%	0/0	0%	0/22	0% (0%-15%)	0/3	0% (0%-71%)
Refrigerator	0/0	0%	0/22	0% (0%-15%)	0/1	0% (0%-98%)	3/86	3.5% (0.7%-9.9%)

Values are numbers. CI: confidence interval; ENT: ear-nose-throat; OB-GYN: obstetric-gynaecologic; CVT: cardiovascular thoracic; PACU: post-anaesthetic care unit

Table 2. Summary of culture results for propofol and ephedrine for the different storage durations

	Propofol		Ephedrine	
Duration of storage	**Positive culture/ Total**	**Percentage (95% CI)**	**Positive culture/ Total**	**Percentage (95% CI)**
Immediate (pre-use)	11/165	6.7% (3.4%-12%)	1/153	0.7% (0.02%-3.6%)
<3 hours	1/23	4.3% (0.1%-22%)	0/2	0% (0%-85%)
3-6 hours	6/75	8.0% (3.0%-17%)	0/6	0% (0%-46%)
6-12 hours	2/38	5.3% (0.6%-18%)	0/12	0% (0%-27%)
12-24 hours	0/14	0% (0%-23%)	1/39	2.6% (0.06%-13%)
>24 hours	0/2	0% (0%-85%)	4/106	3.8% (1.0%-9.4%)
Total	20/317	6.3% (3.9%-9.6%)	6/318	1.9% (0.7%-4.1%)

Values are numbers. CI: confidence interval

Table 3. Comparison of the positive culture results between the pre-use and post-use groups for different drugs

	Propofol (n=317)		Ephedrine (n=318)	
Bacteria	**Pre-use**	**Post-use**	**Pre-use**	**Post-use**
Staphylococcus epidermidis	6	5	0	2
Staphylococcus coagulase negative	2	1	0	0
Staphylococcus saprophyticus	0	0	0	1
Corynebacterium spp.	2	2	1	1
Micrococcus spp.	1	1	0	1

(five samples), general surgery (four samples), neurology (three samples), ENT (one sample), emergency operating rooms (one sample), orthopaedic (one sample) and remote operating rooms (one sample). Three samples from drugs stored in the refrigerators were also positive. The positive culture results among the different operating rooms are shown in Table 1.

Propofol had been contaminated 3.0–8.3 hours after preparation, while ephedrine had been contaminated 19.9–71.4 hours after preparation (Table 2).

Staphylococcus epidermidis was the most common organism found among the samples that were positive on culture (Table 3). Fungal contamination was not found in any of the culture results. The patients who had received contaminated drugs were discharged without any signs or symptoms of infection.

Type of drug was the only significant factor associated with culture results (Table 4). From the logistic regression model, propofol was 3.2 times (95% CI=1.1–9.0) more likely to be contaminated compared to ephedrine, after adjusting for other factors. No other factors could significantly predict a positive culture result.

Table 4. Summary of factors associated with culture results

	Culture result		
Variable	**Negative (n=919)**	**Positive (n=26)**	**p**
Drug			<0.001
Propofol	297 (32.3%)	20 (76.9%)	
Ephedrine	312 (33.9%)	6 (23.1%)	
Vecuronium	310 (33.7%)	0 (0%)	
Personnel preparing the drugs			0.64
Anaesthetist resident	56 (6.09%)	0 (0%)	
Anaesthetist nurse	805 (87.6%)	25 (96.2%)	
Anaesthetist nurse trainee	58 (6.31%)	1 (3.85%)	
Day of culture			0.52
Monday –Friday	908 (98.8%)	26 (100%)	
Saturday –Sunday	11 (1.19%)	0 (0%)	
Time period of culture			0.87
8 a.m.–4 p.m.	821 (89.3%)	24 (92.3%)	
4 p.m.–8 a.m.	98 (10.7%)	2 (7.69%)	
Duration of drug storage (hours)			0.87
Immediate (Pre-use)	460 (50.1%)	12 (46.2%)	
<3	26 (2.83%)	1 (3.85%)	
3–6	96 (10.4%)	6 (23.1%)	
>6	337 (36.7%)	7 (26.9%)	

Values are numbers (percentages).

Discussion

In this study, the incidence of drug contamination was 2.8%, which was within the range of other reported studies (5, 6, 9, 12-14). However, Driver et al. (2) and Wagner et al. (4)

studied the sterility of the anaesthetic and resuscitative drug syringes used in obstetric operating rooms and found no organisms in any syringe. The positive organisms found in this study, such as *Staphylococcus epidermidis*, *Staphylococcus coagulase negative*, *Staphylococcus saprophyticus*, *Corynebacterium* spp. and *Micrococcus* spp., are mostly found in air, human skin and the environment. These organisms are non-pathogenic in a normal host, but they can cause infections in a compromised host.

Propofol was contaminated before use probably because the necks of the glass ampoules were not wiped with alcohol before being opened. Contamination in post-use propofol could be due to the drug preparation process and storage: non-sterile hands, non-sterile ambient air or environment and lack of an antimicrobial agent (disodium edetate, EDTA) in the propofol used in our hospital. Contamination of propofol was found in only one of the 20 positive samples within 3 hours after preparation (5%), which is earlier than the manufacturer's recommendation (12 hours). Thus, propofol should probably be used within 3 hours after opening the ampoules.

Ephedrine was also contaminated in both the pre-use and post-use groups. The pre-use group may have been contaminated during the preparation process, since the necks of the glass ampoules were not wiped with alcohol before being opened, and piggyback normal saline was used for multiple drug dilutions. The post-use group may have been contaminated during the storage and transfer process, since drugs are stored in the anaesthetic cart or refrigerators, and the anaesthetic personnel do not wear gloves during drug preparation and transfer.

Vecuronium samples were not found to be contaminated at all, probably because the aseptic technique is applied using 70% isopropyl alcohol on the rubber vial stoppers, and the sterile needles are changed every time before use. However, transmission of blood-borne pathogens can occur with multidose vials, as found in other studies (3, 15, 16).

As for multidose vials, the recommendation of the Centers for Disease Control and Prevention (CDC) was to use them on a single patient whenever possible. If multidose vials must be used for more than one patient, they should only be kept and accessed in a medication preparation area such as a nurse station. In operating rooms, multidose vials (normally kept in anaesthesia carts) should only be administered to a single patient, so as to prevent inadvertent contamination of the vial through direct or indirect contact with potentially contaminated surfaces or equipment that could lead to infections in other patients (3, 17, 18).

The strengths of this study were that only one researcher collected the samples and anaesthetic personnel were not given prior notice of the sample drug collection. The limitations of the study were that we could not identify the exact cause of contamination after drug use. For example, contamination could have occurred during the preparation, transfer or storage process.

Conclusion

Anaesthetic teams must be aware of contamination issues in the anaesthetic drugs that are prepared for later use, and improve methods of transferring drugs from vial to vial for later use to prevent contamination. Single-dose vials, and using one needle and one syringe on a single patient are recommended. The use of multidose vials should be discouraged.

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