Journal of Clinical Anesthesia (2016) **34**, xxx–xxx

ELSEVIER

Journal of Clinical Anesthesia

Original contribution

In vitro antimicrobial activity of commonly used vasoactive drugs

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Received 27 March 2015; revised 1 May 2016; accepted 2 May 2016

Keywords:
Antimicrobial activities;
Catecholamine;
Drug contamination;
Infusion

Abstract

Study Objective: Microbial contamination during preparation of the infusion drugs is an important issue in intensive care units. Objective of this study was to investigate in vitro antimicrobial properties of commonly used vasoactive drugs.

Design: Prospective study.

Setting: Clinical microbiology laboratory of a university hospital.

Measurements: Growth of the microorganisms *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* in saline dilutions of adrenaline at 1, 10, and 100 μg/mL; noradrenaline at 1, 10, and 100 μg/mL; and dopamine at 0.1, 1, and 10 mg/mL concentrations was investigated. Each drug solution and saline were analyzed with a digital pH meter.

Main Results: Saline dilutions of adrenaline, noradrenaline, and dopamine at clinically used concentrations decreased microbial growth. The highest concentration doses of adrenaline, noradrenaline, and dopamine used in the study had significant antimicrobial effect when compared to the low and moderate doses. This effect was shown with the all microorganisms. *S aureus*, *S epidermidis*, and *C albicans* were more sensitive; on the other hand, *E coli* and *P aeruginosa* were more resistant against the effect of the drug dilutions.

Conclusions: To limit microbial growth in case of contamination of the drug solution, it is advisable to use more concentrated dilutions of adrenaline, noradrenaline, and dopamine used in clinical practice.

1. Introduction

Hospital-acquired infections are one of the major problems that increase mortality and morbidity. Microbial contamination may occur with various source and invasive interventions. Patients in the intensive care units (ICUs) especially require invasive procedures and frequently have multiple predisposing factors to the infection.

Microbial contamination during preparation of drug solutions is another cause of infusion-related microbial contact

Conflict of interest statement: The authors declare no conflict of interest. In this study, resources of the Clinical Microbiology Laboratory of the Kirikkale University were used.

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http://dx.doi.org/10.1016/j.jclinane.2016.05.008
0952-8180/

which is also higher in ICUs [1]. Particulate or organic material contamination might be observed on infusion despite microfilter use and strict adherence to the infusion regimen [2]. Moreover, 1-way valves are not able to prevent bacterial contamination of intravenous infusions [3].

Vasoactive drugs are usually necessary to restore tissue perfusion in patients in ICU. Syringe pumps are used to infuse high-concentration solutions. More dilute preparations may be infused from a bag of fluid, but this should be via an infusion.

In case of accidental microbial contamination of these drugs during preparation or infusion, there are no available data about the effects of clinically used concentrations of adrenaline, noradrenaline, and dopamine on microorganismal growth. In this study, we aimed to investigate in vitro antimicrobial properties of these commonly used vasoactive drugs.

2. Materials and methods

Drug dilutions were prepared using strict aseptic technique under laminar airflow. Alcohol swabs for ampoules were also used to prevent external contaminations. Drugs were diluted with saline to perform 1, 10, and 100 μg/mL concentrations for adrenaline, the same concentrations for noradrenaline bitartrate, and 0.1, 1, and 10 mg/mL for dopamine. Contents of the study drugs were indicated as following: adrenaline 1 mL ampoule: adrenaline 0.5 mg, metabisulphite 0.5 mg, sodium chloride 8.5 mg, and water for injection; noradrenaline 4 mL ampoule: noradrenaline bitartrate 8 mg (equivalent to 4 mg noradrenaline base), sodium metabisulphite 4 mg, sodium chloride 34.35 mg, and water for injection; dopamine 5 mL ampoule: dopamine hydrochloride 200 mg and sodium metabisulphite 50 mg. Each drug solution and saline were analyzed with a digital pH meter (H2211pH/orp meter; Hanna Instruments).

Standard strains of common hospital acquired pathogens *Staphylococcus aureus* (American Type Culture Collection [ATCC] 25923), *Staphylococcus epidermidis* (methicillin-resistant strain ATCC 12228), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), and *Candida albicans* (ATCC 90028) were evaluated. Several bacterial colonies were obtained from test solutions and inoculated to the blood agar at 35°C for 24 hours. Three to 4 colonies were obtained from each isolate and inoculated in 3 mL of Mueller-Hinton broth, then diluted with saline to perform McFarland standard concentration of 0.5.

A hundred microliters inoculum of each microorganism was suspended into 2 mL of each drug dilution and gently mixed, immediately after the drug dilutions have been prepared. A hundred microliters of suspension was obtained and subplated to the 5% sheep blood medium and incubated at 37°C for 24 hours. The same volume of samples from each culture media was subplated to the blood agar, saline, and brain-heart infusion (BHI) broth for bacteria, to the Sabouraud agar and saline for *C. albicans* at 37°C. Saline and BHI broth were used as controls for bacteria; saline and Sabouraud agar were also used as controls for *C albicans*. Samples from drug solutions were directly inoculated to blood agar to detect contamination. Three sampling were performed for each measurement and mean values of the number of colony-forming units per milliliter (cfu/mL) were calculated by the same investigator at 0, 2, 12, 24, and 48 hours.

Data analysis was performed by using SPSS for Windows, version 15 (SPSS, Inc, Chicago, IL). Data are presented as mean ± SD. Comparisons were made with using repeated-measures analysis of variance. In the case of significance, Mann-Whitney *U* test or Wilcoxon test for paired samples was used. $P < .05$ indicated significance.

3. Results

Changes in growth of *S aureus* were indicated in Figure 1. Saline dilutions of adrenaline at 100 μg/mL; noradrenaline at 1, 10, and 100 μg/mL; and dopamine at 1 and 10 mg/mL concentrations significantly decreased the cfu of *S aureus*. The inhibitions of microbial growth of *S epidermidis* and *C albicans* were observed in saline dilutions of adrenaline at 1, 10, and 100 μg/mL; noradrenaline at 1, 10, and 100 μg/mL; and dopamine at 0.1, 1, and 10 mg/mL concentrations, as shown in Figures 2 and 3. Changes in the cfu of *C albicans* occurred at later periods. Saline dilutions of adrenaline at 100 μg/mL, noradrenaline at 100 μg/mL, and dopamine at 1 and 10 mg/mL concentrations also significantly decreased the cfu of *E coli* and *P aeruginosa*, as indicated in Figures 4 and 5. The highest concentration doses of adrenaline, noradrenaline, and dopamine used in the study had significant antimicrobial effect when compared to the low and moderate doses ($P < .05$). This effect was shown with the all microorganisms. *P aeruginosa* was the only microorganism that has an increase in the cfu in saline, in a time-dependent manner. On the other hand, saline dilutions of dopamine at 10 mg/mL concentration inhibited growth of *P aeruginosa* at 12 hours. BHI broth increased the cfu of *S aureus*, *S epidermidis*, *E coli*, and *P aeruginosa*. Sabouraud agar also increased the cfu of *C albicans.* There was no growth on control samples obtained from the drug solutions.

The pH values of the drug solutions were 5.00 for saline; 5.05, 4.84, and 4.33 for adrenaline at 1, 10, and 100 μg/mL concentrations; 4.85, 4.35, and 3.70 for noradrenaline at 1, 10, and 100 μg/mL concentrations; and 4.88, 4.40, and 3.70 for dopamine at 0.1, 1, and 10 mg/mL concentrations, respectively.

4. Discussion

This study showed that saline dilutions of adrenaline, noradrenaline, and dopamine at clinically used concentrations decreased microorganismal growth, and this effect was more prominent at higher concentrations. Dopamine exhibited powerful antimicrobial effect on all the microorganisms, especially