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SCIENTIFIC ARTICLE

In vitro evaluation of antimicrobial features of vasopressors

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KEYWORDS
Antimicrobial activities;
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Abstract
Background: Drugs administered as intravenous infusion may be contaminated during several stages of production or preparation. However studies focusing on antibacterial effects of vasopressor drugs are very rare. This study investigates the *in vitro* antimicrobial activity of the clinically used forms of vasopressors.
Materials and methods: In vitro antimicrobial activities of vasopressor drugs of different concentrations were investigated by using the micro dilution technique. Microorganisms used in the test were *Escherichia coli* ATCC 25922, *Yersinia pseudotuberculosis* ATCC 911, *Pseudomonas aeruginosa* ATCC 10145, *Listeria monocytogenes* ATCC 43251, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* 702 Roma, *Mycobacterium smegmatis* ATCC607, *Candida albicans* ATCC 60193, and *Saccharomyces cerevisiae* RSKK 251. Antibacterial assays were performed in Mueller-Hinton broth at pH 7.3 and antifungal assays were performed in buffered Yeast Nitrogen Base at pH 7.0.
Results: Two different dopamine preparations showed antimicrobial activity. No other study drug showed any antimicrobial activity.
Conclusions: In our opinion, dopamine's antibacterial effects may be advantageous for inhibiting the spread of bacterial contamination during the preparation of the infusion solutions. However, it is important that strict guidelines regarding the need for sterile equipment and deliverables be adhered to during all procedures performed in the intensive care units.

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Introduction

Septic shock is the primary cause of death in critical care units. Shock states are primarily characterized by acute circulatory failure leading to tissue hypoperfusion, and potentially resulting in multi-organ failure. Observed hypotension can be the consequence of three major hemodynamic disorders: hypovolemia, vascular failure, and heart failure.[1] When appropriate fluid administration fails to restore adequate tissue perfusion and arterial pressure, vasopressors are usually necessary to increase mean systemic pressure, cardiac output, and oxygen delivery.[2]

In vitro studies focusing on catecholamine molecules demonstrated proliferation of bacteria.[3–5] A portion of catecholamines, which are used as vasopressor, are endogenously produced in the body. However, catecholamines used as vasopressor drugs are synthetically produced and infused for the treatment of cardiovascular failure which arises during septic shock. Dopamine, dobutamine, adrenaline and noradrenaline are most frequently used vasopressors prepared synthetically with supplemental chemicals having antioxidant and antimicrobial activity. Sodium metabisulfite, N-acetylcysteine and disodium edetate are the most frequently used antioxidant and antimicrobials for this purpose in drugs commonly found in medical markets (Table 1).

Considering several studies pointing catecholamine molecules' proliferating effect on bacteria, we investigated commercially prepared catecholamine products' *in vitro* effect on proliferation of several yeast and bacterial strains commonly encountered in septic shock.

Materials and methods

Microorganisms used in tests were obtained from the Refik Saydam Hifzissihha Institute (Ankara, Turkey) and were as follows: *Escherichia coli* ATCC 25922, *Yersinia pseudotuberculosis* ATCC 911, *Pseudomonas auroginosa* ATCC 10145, *Listeria monocytogenes* ATCC 43251, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* 709 ROMA, *Mycobacterium smegmatis* ATCC607, *Candida albicans* ATCC 60193 and *Saccharomyces cerevisiae* ATCC 60193.

Antimicrobial effects of the drugs were tested quantitatively in appropriate broth media using the double dilution method, and the minimum inhibitory concentration (MIC) values in μg/mL were determined.[6,7] Antibacterial assays were performed in Mueller-Hinton broth (MH) (Difco, Detroit, MI) at pH 7.3 and antifungal assays were performed in buffered Yeast Nitrogen Base (YNB) (Difco, Detroit, MI) at pH 7.0. Each tested drug was prepared in 0.1 mL volumes of sterile MH and YNB broths in concentrations ranging from 5 μg/mL to 5 mg/mL for microdilution. One drop (0.02 mL) of microorganism's suspension (approximately 10^6 microorganisms per mL) was added to the extract/broth dilutions. After incubation at 35 °C for 18–72 h, the media were examined for growth. MIC is defined as the lowest concentration of drug showing no growth of microorganism. The dilutions without visible growth were used to determine minimum bactericidal concentration (MBC) by spreading 100 μL of the sample across the surface of dried MH and YNB agar plates with sterile glass rods, and then incubating at 35 °C for 18 h. MBC of each extract is defined as the lowest concentration

Table 1 Study drugs and ingredients.

Catecholamine	Ingredients
Epinephrine	*In 1 mL Ampoule:* - Epinephrine 0.5 mg - Sodium chloride 8.5 mg - Metabisulfite 0.5 mg - Water for injection
Norepinephrine	*In 4 mL Ampoule:* - Norepinephrine bitartarate 8 mg (equivalent to 4 mg norepinephrine base) - Sodium metabisulfite 4 mg - Sodium chloride 34.35 mg - Water for injection
Dobutamine	*In 20 mL Ampoule:* - Dobutamine hydrochloride 280 mg (equivalent to 250 mg dobutamine base) - Sodium metabisulfite 4.8 mg - Water for injection
Dopamine	*In 5 mL Ampoule:* - Dopamine hydrochloride 200 mg - N-acetylcysteine 2 mg - Disodium edetate 2 mg - Water for injection
Dopamine	*In 5 mL Ampoule:* - Dopamine hydrochloride 200 mg - Sodium metabisulfite 50 mg