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# Bacterial contamination of propofol vials: The second report from Turkey

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## ABSTRACT

**Objective:** In this study, we look at the case report of an outbreak of sepsis in patients who underwent upper gastrointestinal endoscopy or colonoscopy during three consecutive days. Twelve patients had diagnostic procedures in the endoscopy unit between 05 May 2018 and 07 May 2018. Of the 12 patients, three had upper gastrointestinal endoscopy, six had a colonoscopy, and three had a combination of two procedures. Within two days of discharge, five patients diagnosed with SIRS and referred with fever as the major sign were hospitalized to the infectious diseases clinic. In our Endoscopy Unit, media, drug, and material cultures were taken for microbiological analysis, and microbial agents were searched. Growth was detected only in the propofol drawn into the syringe that was used on the patient. This study highlights the importance of strict compliance with aseptic injection guidance and constant analysis of microbiological data

**Keywords:** Propofol vial, Contamination

## INTRODUCTION

There are many benefits to using propofol over other intravenous anesthetics, benefits such as early onset and rapid elimination, fewer side effects, and short duration of action (1). Propofol lipid emulsion can be associated with microbiological contamination, which has two sources: intrinsic, which comes from the manufacturing environment, or extrinsic, which happens after opening the vial, and extrinsic contamination is usually more common (2). Although microbiological contamination has sometimes led to the outbreak of sepsis and postoperative infections in the United States and developed countries (3), it has not received much attention in developing countries and Turkey. As far as we know, in Turkey, only one study has been conducted on propel contamination and its clinical significance. Problems and deficiencies in aseptic techniques can lead to viral or bacterial infections. Suppose a contaminated solution is injected into a patient. In that case, the symptoms of sepsis can appear in less than a few hours and can even be fatal to the patient (4). One of the opportunistic bacterium seen in cases of bacterial and wound infection outbreak is Serratia marcescens (5). Due to the high crude mortality rate of bacteremias (about 35% to 60%), these infections should be taken seriously (6, 7). In this study, we look at the case report of an outbreak of sepsis in patients who underwent upper gastrointestinal endoscopy or colonoscopy during three consecutive days.

## MATERIAL and METHODS

This study has been conducted using the Helsinki Declaration's principles and approved by the local Institutional Review Board.

Twelve patients had diagnostic procedures in the endoscopy unit between 05 May 2018 and 07 May 2018. Of the 12 patients, three had upper gastrointestinal endoscopy, six had a colonoscopy, and three had a combination of two procedures. All patients were discharged on the same day after successful, uncomplicated procedures.

Sepsis diagnosis was based for the patients who were isolated S. marcescens from blood culture and met two or more from the following four parameters over three hours: 1) fever (>38°C); 2) leucocytosis(>12 x 109/L) or leucopenia (<4 x 109/L) or >10% immature (band) forms; 3) tachycardia (> 90 beats per minute); 4) tachypnoea (> 20 breaths per minute) or hyperventilation (pCO2< 4.3 kPa) .8

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**Statistics**

Statistical analyzes were performed with SPSS Version 22.0 (SPSS Inc, Chicago, IL, USA). Chi-brothers to design what each could be. Very convenient logistic regression analyzes were performed for predictors of culture positives. Statistical influences are included in the regression analysis. Statistically, P <0.05 was considered significant.

# RESULTS

Within two days of discharge, five patients diagnosed with SIRS and referred with fever as the major sign were hospitalized to the infectious diseases clinic. The patient was hospitalized, and their vitals were checked. Antibiotic treatments were started. The fever subsided within 48-72 hours. Meropenem-Levofloxacin was used for their treatments. During admission, mean values (range) for white blood cell, C-reactive protein, aspartate aminotransferase, alanine aminotransferase, urea, and creatinine of SIRS patients were respectively 22900 mg/L (range, 3600 to 39000), 7.8 mg/L (range, 0.27 to 13), 77.3 U/L (range, 13 to 172), 65.4 U/L (range, 14 to 212), 30 mg/dl (range, 15 to 41), 1.14 µmol/L (range, 0.66 to 1.92). Demographic and laboratory characteristics of patients are shown in **Table 1**.

Four of these five SIRS patients had positive blood cultures with S. marcescens, and all strains were uniformly susceptible to meropenem (MICs<0.25 mg/l) and levofloxacin (MICs<0.25 mg/l).

Cultures were obtained from the environment, water, and surfaces in the endoscopic intervention room and shown in **Table 2**.

In propofol, S. marcescens was identified. Endoscopic procedures were not performed on the same day but on different days and times. Propofol serial number 17382033 used in all cases with culture was removed. Closed propofol vials of the same batches were correspondingly cultured and found sterile. Incident notification to the "Ministry of Health" and "Turkey Pharmaceuticals and Medical Devices Agency" was performed.

Following obtaining samples from possible infection sources, further use of the endoscopy unit was suspended for three days. After consulting and receiving the opinions of the anesthesiologist and other personnel in the unit, the mentioned problems were noted. A written protocol for daily cleaning included three cleaning stages at the beginning of the day, between operations, and at the end of the day. New instructions for storing, preparing, and using medications were also introduced. Determining which materials should be stored in the endoscopy unit was the responsibility of the hospital infection control team, and infection control procedures were instructed for the theatre personnel.

The endoscopy unit was suspended for three days after obtaining samples from possible infection sources. Opinions and suggestions of the anesthesiologist, technician, and other healthcare professionals working in the endoscopy unit were taken, and the problems they emphasized regarding their daily work routines were noted. A new guide has been created to prepare, store, and use drugs handled in the clinic. A new protocol has also been developed for cleaning measures to be performed before, between, and after endoscopic procedures. The in-hospital infection control committee determined the materials and drugs to be kept and excluded in the endoscopy unit. The staff of the endoscopy unit was informed about infection control procedures.

**Table 1.** Demographic and laboratory characteristics of patients

| Operations | Patient 1 Endoscopy/Colonoscopy/Endoscopy Biopsy | Patient 2 Endoscopy/Colonoscopy/Endoscopy Biopsy | Patient 3 Colonoscopy/ Biopsy | Patient 4 Flexible Sigmoidoscopy | Patient 5 Colonoscopy |
|---|---|---|---|---|---|
| **First-day WBC** | 38.000 | 39.000 | 13.000 | 3.600 | 21.000 |
| **Third-day WBC** | 26.000 | 40.000 | 6.000 | 24.000 | 9.00 |
| **Fifth-day WBC** | 9.000 | 16.000 | 2.96 | Discharged | Discharged |
| **First-day CRP** | 13 | 5.97 | 8.8 | 0.27 | 11 |
| **Third-day CRP** | 7 | 13.85 | 15.3 | 11.87 | 10 |
| **Fifth-day CRP** | 1.13 | 6.72 | 2.96 | Discharged | Discharged |
| **First-day AST/ALT** | 19/14 | 105/61 | 13/14 | 23/26 | 172/212 |
| **Third-day AST/ALT** | 22/16 | 45/50 | 26/18 | 86/80 | 65/122 |
| **Fifth-day AST/ALT** | 20/16 | 17/27 | 52/46 | Discharged | Discharged |
| **First-day urea/creatinine** | 39/0.84 | 41/1.26 | 21/10.2 | 34/1.92 | 15/0.66 |
| **Third-day urea/creatinine** | 26/0.71 | 64/108 | 13/0.86 | 68/4.46 | 11/0.63 |
| **Fifth-day urea/creatinine** | 28/0.72 | 41/0.75 | 11/0.65 | Discharged | Discharged |

**Table 2.** Cultured sources in the endoscopic intervention room

| Source | Organism |
|---|---|
| Vial of propofol in use | Serratia marcescens |
| Unopened vials of propofol | Negative |
| Disinfectant in use | Negative |
| Unopened disinfectant | Negative |
| Water from the suction system | Negative |
| Endoscopic channel | Negative |
| Colonoscopic channel | Negative |

# DISCUSSION

To our knowledge, this is the second report of its kind in Turkey. In 2019, Cilli et al. reported an outbreak of sepsis caused by propofol contaminated with S. marcescens in three patients (4).. Although propofol has been used in Turkey since 1990, no sepsis outbreaks of sepsis have been reported since then. However, generally accepting sepsis as a surgical complication can cause an outbreak to be undiagnosed.

In our Endoscopy Unit, media, drug, and material cultures were taken for microbiological analysis, and microbial agents were searched. Growth was detected only in the propofol drawn into the syringe that was used on the patient. Patients were hospitalized in the Infectious Diseases Clinic by making their first interventions in the Emergency Service. Infection Control Committee meeting was held, and the clinical status of the patients and the precautions to be taken were discussed. The high-level disinfectant effectiveness check was repeated, and positive results were obtained.

The first outbreak reported due to contaminated propofol was published in 1992 and was a surgical field infection caused by S. aureus in the USA (3). In the literature, twenty propofol-related outbreaks have been reported to date. In these outbreaks, 144 cases were infected, and 10 patients died. Four outbreaks involving S. marcescens have found their place in the literature, and the 5th reported outbreak is this study (9). In 2014, Ersoz et al. reported a meningitis outbreak because of S.marcescens after spinal anesthesia (10). In 2017, Us et al. reported an outbreak of soft tissue and wound infection of S. marcescens in subjects undergoing wound care (11)

Medications and parenteral solutions contamination by S. marcescens have been the source of prior hospital-acquired infection outbreaks (12). Prefilled syringes, prepared solutions, and Multi-dose vials are essential infection tools (13, 14). S. marcescens can cause bacteremia, respiratory infections in ICU, and surgical site infections after invasive procedures (14, 15). In the present study, a previously prepared anesthetic drug is contaminated with S. marcescens. The main problem in this outbreak was re-using vials and standard syringes that may have caused contamination during the outbreak. In the post-outbreak evaluation, it was observed that some drugs were used a few days after they were prepared, in violation of hospital policies. In a performance-based payment system in Turkey, it is expected from the surgeons to make more surgery. Anesthesiologists have a short time to provide medicines between surgeries, which can sometimes fail to comply with basic infection control measures. Also, it was not practical to use disposable propofol bottles as “single-use.”

One of the limitations of this study is that all the data in this study came from one institution, and some related details of the influencing factors and event histories may not be adequately documented, which may affect the outcome. Therefore, interpretations of the results of this study should be made with caution.

# CONCLUSION

Outbreaks caused by contaminated propofol continue to find a place in the literature. In the outbreak presented in this study, S. marcescens was separated from an opened propofol bottle and salt solution in the garbage and various syringes filled with propofol. Cultures made in unopened propofol ampoules were found sterile. This study highlights the importance of strict compliance with aseptic injection guidance and constant analysis of microbiological data.

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