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MICROBIOLOGICAL CONTAMINATION OF PROPOFOL

CONTAMINAREA MICROBIOLOGICĂ A PROPOFOLULUI

C. PEȘTEAN[1)*], N. DAFERMOS[2)], G. NADĂȘ[1)]

ABSTRACT | REZUMAT

Propofol is one of the most used anesthetics administered intravenously in both humans and animals.

In order to assess the propofol contamination level depending on the storage conditions and period of time from exposure to the environment, propofol samples were stored at room temperature or refrigerated. From these speciments, samples were harvested at 0, 4, 8, 12 and 24 hours and cultivated on the following culture media Mueller-Hinton agar, MacConkey selective agar and Blood agar medium. Gram stain was used for bacteriological examination.

Keywords: contamination, microbiological, propofol

Propofolul este unul dintre cele mai utilizate anestezice administrate intravenos atât la oameni cât și la animale. Pentru a evalua nivelul de contaminare al propofolului, în funcție de condițiile de depozitare și de perioada de timp de la expunerea la mediu, probele de propofol au fost depozitate la temperatura camerei sau au fost păstrate la frigider. Din aceste probe, eșantioane au fost recoltate la 0, 4, 8, 12 și 24 de ore și cultivate pe următorele medii de cultură: Mueller-Hinton, agar selectiv MacConkey și agar cu sânge. Pentru examinarea bacteriologică s-a folosit colorația Gram.

Cuvinte cheie: contaminare, microbiologic, propofol

Propofol (2,6-diisopropylphenol) is one of the most common intravenous anesthetic agents for sedation, induction and maintenance of anesthesia in small animal patients being approved in the United States since 1996 (2, 6). The popularity of this anesthetic can be explained by its low incidence of anesthesia-related side effects, the short half-life of the drug, rapid onset and elimination times, predictability and ease of titration (12, 7). Administration of propofol has been associated with several iatrogenic infections even if it is considered to be relatively safe (15).

Formulation as a lipid emulsion with soya bean oil, glycerol and egg lecithin promotes growth of bacteria and yeasts following contamination, some studies have also suggested that exposure to propofol can negatively impact patient immune defenses (5, 7).

There are studies that demonstrate that exposure to propofol contributes to increased mortality in a rat model of sepsis as well as increased mortality and morbidity following systemic bacterial infections (14, 10). Propofol has also been associated with a higher incidence in wound infections in dogs and cats after surgery.Unanimous current recommendations for propofol use in veterinary practice are to discard within 6 hours any drug remaining after withdrawal of the required dose, as the product contains no antimicrobial preservative (11, 3). The purpose of this study is to evaluate successively the microbiological contamination for a period of 24 hours of propofol samples exposed to the environment and stored at room temperature or refrigerated.

1) University of Agricultural Sciences and Veterinary Medicine, Faculty of Veterinary Medicine of Cluj-Napoca, Romania
2) Practitioner in Heraklion, Greece
*) *Corresponding author: cosmin.pestean@usamvcluj.ro*

MATERIALS AND METHODS

The study was performed within the Laboratory of Microbiology, Faculty of Veterinary Medicine of Cluj-Napoca, during April 2017. A 20 ml vial of Propofol Fresenius was opened and 3 ml were spread in each of 6 different sterile tubes.

Three samples were incubated in room temperature (RT) and the other 3 were refrigerated (RF).

In order to follow the contamination of propofol, the tubes were kept open and from both RT and RF tubes, Mueller-Hinton, blood agar and MacConkey agar samples were inoculated at time 0 and at 4, 8, 12 and 24 hours. The experiment was duplicated for accuracy. The plates were then incubated at 37ºC for 24 h and evaluated regarding the feature of the colonies and their microscopic characters. Gram staining smears were performed from isolated colonies and the identification of bacteria was based on the morphological characters.

RESULTS AND DISCUSSIONS

Of the thirty samples of propofol taken on study on the first day of experiment and inoculated on the Mueller-Hinton agar, 27 were negative and only 3 positive: 1.1RF12' (Fig. 1), 1.1RF24' and 1.2RF24'.

These results suggest that only some of the samples kept in the refrigerator for at least 12 hours were contaminated and surprisingly no sample left at room temperature.

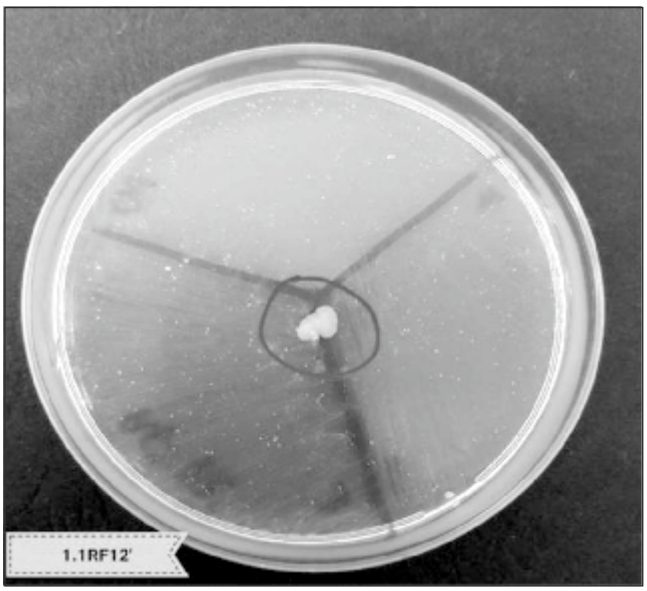

Fig. 1. Bacterial colonies from sample 1.1RF12' on Mueller-Hinton agar

Fig. 2. Gram-Positive aspect of smear from sample 1.2RF24'

When repeating the experiment, from the samples of propofol evaluated and inoculated on the Mueller-Hinton agar, only one was positive: 2.1RT0'. This result is totally different from the previous results; unexpectedly the contaminated sample was from time 0', moment when the material to be researched was divided into containers. Gram staining smears were performed from isolated colonies on Mueller-Hinton agar (Fig. 2).

The four positive samples were transferred on another culture medium; MacConkey agar for additional differentiation. MacConkey selective agar is used for the isolation of gram-negative enteric bacteria and the differentiation of lactose fermenting from lactose non-fermenting gram-negative bacteria.

After 24 hours of incubation, on this MacConkey selective medium only one sample was positive: 1.1 RF12' (Fig. 3).

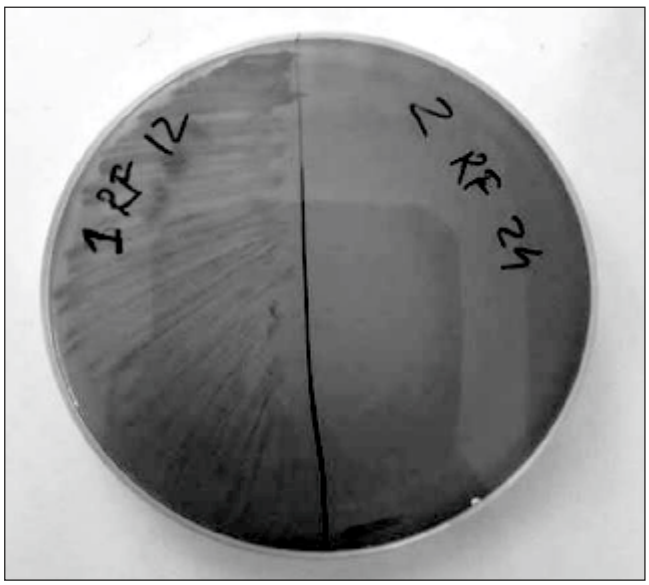

Fig. 3. Bacterial colonies from sample 1.1RF12' on MacConkey selective medium

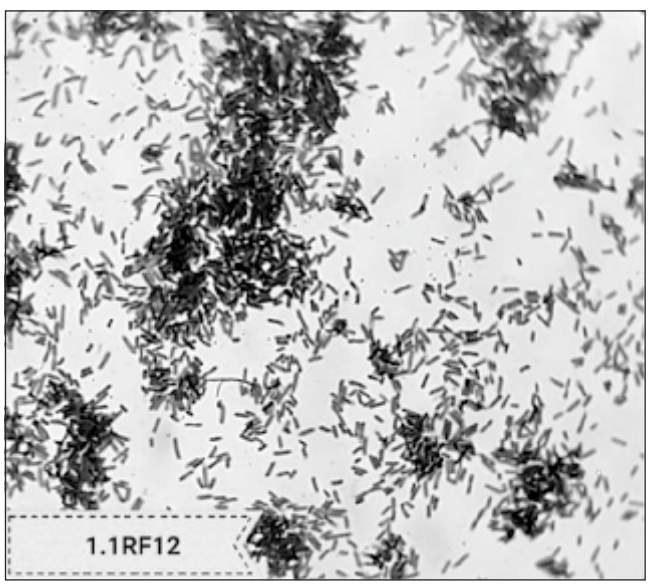

Fig. 4. *Escherichia Coli* (lactose positive) in sample 1.1RF12'

All three negative samples on the MacConkey agar environment were positive after transfer to the Blood agar medium. All four types of colonies from MacConkey selective agar and Blood agar medium were stained using Gram stain technique. After microscopic examination, the microorganisms present in the samples were classified as *Escherichia coli* (lactose positive) (1.1RF12') (Fig. 4), *Micrococcus* (1.1RF24') (Fig. 5) and the *genus Bacillus* in two samples (1.2 RF24' and 2.1RT0') (Fig. 6).

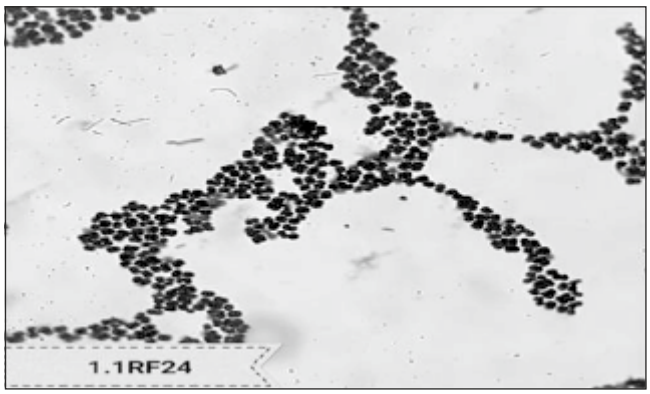

Fig. 5. *Micrococcus* in sample 1.1RF24'

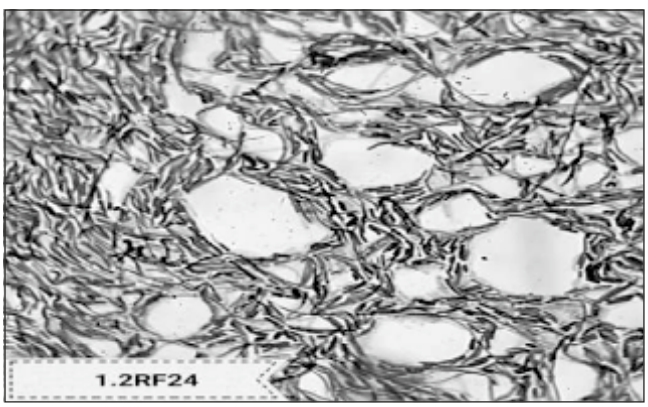

Fig. 6. *Genus Bacillus* in the sample 1.2RF24'

Of a total of 60 samples taken into the study, only four were contaminated (6.66%). This finding is consistent with other authors which have reported rates from 3%-6.3% (8, 16). Three of the samples were colonized after minimum 12-hour exposure in the refrigerator and one at the time of initial manipulation. Probably, with this last sample, the conditions of sterility in handling have not been effective despite our efforts. Even though there are no similar results between the two stages of the study, the fact that the contamination occurred both under room temperature and refrigeration conditions, plus that the propofol samples may be contaminated and the transfer after opening the vial, warrants us to conclude that propofol is an excellent medium of bacterial culture. The contamination of refrigerated samples was somewhat surprising because there is a widespread opinion among vets that keeping propofol in the refrigerator prevents its contamination after the bottle has been opened. Erden et al., (2013) pointed out that for propofol, low temperature does not guarantee safety in case contamination occurs. This contamination after a minimum of 12 hours of storage, are consistent with data from other studies and has formed the basis of recommendations in human hospitals that propofol should be used within six to 12 hours after the vial is first pierced after which time exponential growth of contaminant bacteria occurs (13).

Mama et al., (2013) suggest that the inclusion of benzyl alcohol in the a commercial formulation of propofol allowed the use of one propofol vial for up to 9 needle insertions for drug withdrawal over a period up to 17 days without contamination.

Especially in human medicine there is a growing concern about the risks for transmitting infections during routine health care procedures requiring IV medications. Outbreaks of infection have occurred with increasing regularity. The gap between what is recommended and what is actually done clinically regarding safe injection practices must be addressed (5).

Most common microorganisms that have been identified in contaminated propofol in other studies were *Staphylococcus aureus*, followed by *Enterococcus*, *Acinetobacter*, *Bacillus species*, *Pseudomonas* and *Staphylococcus citrus* (9).

CONCLUSIONS

In our study the number of the contaminated specimens of propofol represented 6.66% of the total number of samples. The contamination of the samples was achieved both during handling and especially at 12 hours after exposure. The microorganisms that have developed in the investigated samples are found in the everyday practice and are not uncommon at all. Keeping propofol in the refrigerator is not a solution to prevent its contamination.

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