Propofol (2,6-diisopropylphenol) is a popular drug for the induction and maintenance of anesthesia. The emulsion contains propofol 10 mg/mL, soya bean oil 100 mg/mL, glycerol 22.5 mg/mL, egg lecithin 12 mg/mL, water, and sodium hydroxide to adjust the pH from 6.0 to 8.5 (1). Propofol in this formulation has the uncomfortable side effect of pain on IV injection. This adverse side effect occurs in up to 92% of patients (2). Many methods by which this discomfort may be reduced have been reported, the most common and effective of which is the addition of lidocaine to propofol (3–5).

Unfortunately, propofol supports the growth of many organisms (6–12). Crowther et al. (10) demonstrated that the addition of pentothal to propofol can suppress the growth of Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Candida albicans. The antimicrobial activity of local anesthetics was first reported by Jonnesco in 1909. Investigators later confirmed the antimicrobial activity of local anesthetics and lidocaine in particular (13,14). Consequently, the question arose as to whether the addition of clinically appropriate concentrations of lidocaine to propofol would confer antimicrobial activity to the resulting mixture.

The purpose of this study was to determine the potential for growth of four microorganisms (S. aureus, E. coli, P. aeruginosa, and C. albicans) in propofol, 0.2% lidocaine and 0.5% lidocaine in propofol, and 0.5% lidocaine in isotonic sodium chloride solution. Nonbacteriostatic isotonic sodium chloride solution was used as a control.
Methods

The pH of all study solutions was measured using a Fisher Accumet® pH meter (Fisher Scientific Ltd., Pittsburgh, PA). Preservative-free 0.9% saline, preservative-free 2% lidocaine (Xylocaine®; Astra Pharma Inc., Mississauga, Ontario, Canada), and 1% propofol (Diprivan®; Zeneca Pharma Inc., Mississauga, Ontario, Canada) were used.

The methodology used was similar to that reported by Sosis and Braverman (9) and Crowther et al. (10). Overnight cultures of S. aureus (ATCC 25923), E. coli (ATCC 25922), P. aeruginosa (ATCC 27853), and C. albicans (ATCC 14053) were diluted to a density of 0.5 McFarland units with 0.9% sterile nonbacteriostatic saline using a Baxter Microscan® turbidity meter (Baxter Diagnostics, Inc., Deerfield, IL.). Each organism solution was further diluted 1:50 with sterile 0.9% saline. A 0.2-mL aliquot of each diluted organism was then added to sterile sealed culture vials containing 20 mL of the following solutions: 1) three vials of 0.9% sterile nonbacteriostatic saline, 2) three vials of 1% propofol, 3) three vials of 0.2% lidocaine in 1% propofol, 4) three vials of 0.5% lidocaine in propofol, and 5) three vials of 0.5% lidocaine in 0.9% sterile nonbacteriostatic isotonic sodium chloride solution. Each organism solution was vortexed before addition to the 20-mL vials. After the organisms were added, each vial was vortexed for 1 min and subplated to three plates of trypticase soy agar using a calibrated precision 1-μL loop. Vials were subplated at 0-, 3-, 6-, 12-, and 24-h intervals for a total of nine plates per solution per sampling period and were stored at 20°C between samplings. The plates were then incubated at 35°C for 24 h. Each plated medium was read, and the numbers of colony-forming units (CFUs) were counted and recorded by one investigator. For each microorganism, the number of CFUs per plate was averaged for each sample period.

Data are presented as the mean ± SEM of nine replicate assays. For each organism, comparisons among time periods for each treatment group were made by using repeated-measures analysis of variance followed by a pairwise multiple comparison test by using the Student-Newman-Keuls method. In addition, comparisons among treatment groups for each organism at each time interval were made by using analysis of variance followed by a Scheffé’s multiple comparison test. A probability of $P < 0.05$ was taken to indicate statistical significance.

Results

The pH of the 1% propofol emulsion was 7.98. The pH of the 0.2% and 0.5% lidocaine mixed with propofol solutions were 6.43 and 5.92, respectively. The pH of the 0.5% lidocaine solution was 6.62. The pH of the 0.9% isotonic sodium chloride solution was 7.01.

With S. aureus (Fig. 1), a significant decline ($P < 0.05$) in CFUs in 0.9% saline and 0.5% lidocaine was observed compared with baseline. The inoculated propofol emulsion showed no significant growth of S. aureus during the 24-h study period. Nonetheless, the number of CFUs of S. aureus in propofol was significantly greater at 12 and 24 h compared with the saline and 0.5% lidocaine solutions. The mixture of 0.2% lidocaine in propofol showed no significant change during the study period. When 0.5% lidocaine in propofol was studied, a 37% increase in CFUs was noted at 24 h ($P < 0.05$).

With E. coli (Fig. 2) in 0.9% isotonic sodium chloride solution and in 0.5% lidocaine, significant reductions ($P < 0.05$) in the mean numbers of CFUs were observed at 12 and 24 h. Propofol emulsion inoculated with E. coli supported a significant ($P < 0.05$) growth of this microorganism at 12 and 24 h. Compared with baseline (time 0) there was a 3-and a 14-fold increase at these times. The mixtures of lidocaine 0.2% and 0.5% in propofol showed significant growth ($P < 0.05$) at 24 h compared with baseline. Respectively, there was an eightfold and a threefold increase in the mean CFUs counts. Compared with propofol alone at 24 h, the mixture of 0.2% lidocaine in propofol showed a 32% reduction ($P < 0.05$) in E. coli CFUs. Likewise, the mixture of 0.5% lidocaine in propofol showed a 50% and 62% reduction in CFUs at 12 and 24 h ($P < 0.05$) compared with propofol. Inhibition of E. coli growth was observed with the lidocaine mixtures, which suggests a concentration-related effect attributable to lidocaine. Neither of these mixtures suppressed the growth of E. coli as effectively as 0.9% saline or 0.5% lidocaine alone.

With P. aeruginosa (Fig. 3) in 0.9% saline and 0.5% lidocaine, a significant ($P < 0.05$) reduction in CFUs was observed over the study period. The inoculated propofol emulsion showed a rapid decline ($P < 0.05$) in P. aeruginosa CFUs beginning at 3 h. Similarly, the mixtures of 0.2% and 0.5% lidocaine in propofol significantly ($P < 0.05$) suppressed the formation of P.
aeruginosa CFUs at 3, 6, 12 and 24 h. The addition of lidocaine to propofol did not enhance the ability of propofol to suppress the formation of *P. aeruginosa* CFUs. The saline control group and 0.5% lidocaine alone did not inhibit the formation of *P. aeruginosa* CFUs as well as propofol alone.

With *C. albicans* (Fig. 4), static levels were observed in both 0.9% saline and 0.5% lidocaine during the study period. The propofol emulsion, however, substantially increased the formation of CFUs at 24 h (*P < 0.05*) compared with baseline. A 15-fold increase in CFUs was observed. The mixtures of 0.2% and 0.5% lidocaine in propofol both demonstrated significant (*P < 0.05*) growth of *C. albicans* at 24 h. Compared with the propofol emulsion for the same time period, 0.2% lidocaine in propofol had twice the number of CFUs (*P < 0.05*), whereas 0.5% lidocaine in propofol had less than half the number of CFUs (*P < 0.05*). Propofol with 0.2% lidocaine enhanced the growth of *C. albicans*, whereas 0.5% lidocaine in propofol had an inhibitory effect. Nevertheless, the mixture of 0.5% lidocaine in propofol still had a sevenfold increase in the mean number of CFUs at 24 h compared with baseline (*P < 0.05*).

**Discussion**

Propofol emulsion is an excellent vehicle for supporting the growth of some microorganisms, but it is not a universal growth medium. Propofol strongly supports the growth of *E. coli* and *C. albicans*. In contrast, propofol inhibits the growth of *P. aeruginosa*. Our study failed to demonstrate that propofol promoted the growth of *S. aureus* at room temperature (20°C), a temperature selected because it represents the normal environmental temperature of our surgical suites. Sosis and Braverman (9) demonstrated that propofol promoted the growth of *S. aureus* at 27°C. Taki et al. (15) showed that temperature has important effects on the growth of *S. aureus*, even in the presence of lidocaine. Consequently, the reported outbreaks of postsurgical infections secondary to the extrinsic contamination of propofol emulsion with *S. aureus* (6,16) implies that although propofol may not promote the growth of *S. aureus* at room temperature, a propofol emulsion may harbor static levels of the contaminating bacteria sufficient to pose a significant risk when introduced IV into a patient.

Infections related to extrinsically contaminated propofol continue to be a problem. In 1990, the Centers for Disease Control (CDC) reported four clusters of suspected propofol-acquired postsurgical infections involving *S. aureus*, *C. albicans*, and *Moraxella osloensis* (6). From June 1990 to February 1993, the CDC subsequently investigated seven hospitals because of unexpected outbreaks of bloodstream infection, surgical-site infection, and acute febrile episodes related to the use of propofol for anesthesia (17). In 1993, another outbreak linked to the use of propofol from a 50-mL rubber-topped vial resulted in two deaths (17). In 1993, Veber et al. (18) also reported four patients who experienced severe sepsis after the IV injection of a propofol emulsion contaminated with *Klebsiella pneumonia*. The Food and Drug Administration documented 38 clusters of fever and/or infections involving 155 patients from 20 states between July 1989 and May 1994. Four additional deaths were documented (17). In 1997, Kuehnert et al. (16) documented *S. aureus* bloodstream infections in five patients...
who had received propofol for electroconvulsive therapy. Lapses in infection control and the possible extrinsic contamination of propofol were implicated.

It has become a common anesthetic practice to add lidocaine to the propofol emulsion in an attempt to reduce the discomfort associated with the IV administration of propofol. The concentration of 0.2% lidocaine used in this study was based on clinical reports that confirmed that this concentration consistently ameliorated the pain associated with the administration of propofol (3,5). The concentration of 0.5% lidocaine in 20 mL of propofol corresponds to a dose of 1.5 mg/kg lidocaine for an average-weight (70-kg) patient. A dose of 1.5 mg/kg lidocaine improves intubating conditions (19). Therefore, lidocaine 0.5%, alone or mixed with propofol, was selected as the remaining solution to be investigated.

The antimicrobial activity of lidocaine is well documented (13,14). However, not all organisms are susceptible to its antimicrobial properties (20). The antimicrobial activity of lidocaine is rapidly attenuated as its concentration is reduced (13,14). In our study, lidocaine 0.5% alone was not statistically different from saline in suppressing the growth of the microorganisms studied. In addition, neither 0.9% saline nor 0.5% lidocaine contains nutrients to support microbial growth. Furthermore, the possibility of an interaction between lidocaine and the propofol emulsion must be considered. This could explain the enhanced growth of S. aureus at 24 h in the mixture of 0.5% lidocaine in propofol and the enhanced growth of C. albicans in the mixture of 0.2% lidocaine in propofol.

Strong alkalis exert marked antimicrobial effects. Thiopental with a pH of 10.5 is markedly bactericidal (10). Propofol is formulated to have a pH between 6.0 and 8.5. Most pathogenic bacteria prefer a narrow pH range of 6.0–8.0 (10). None of the solutions we studied had a pH >7.98 or <5.92. Gudmundsson et al. (21) demonstrated that the growth of S. aureus (ATCC 25923), E. coli (ATCC 25922), and P. aeruginosa (ATCC 27853) was not affected by pH of 5.0–8.0. Consequently, the pH values documented in this study are unlikely to confound the reported results.

We conclude that clinically relevant concentrations of lidocaine, when mixed with the propofol emulsion, do not prevent the growth of S. aureus, E. coli, and C. albicans. Propofol’s intrinsic ability to suppress the growth of P. aeruginosa is not enhanced by the addition of lidocaine. The implication of this study is that scrupulous aseptic techniques must be used in the handling and administration of propofol. The addition of lidocaine to propofol does not confer any bactericidal or fungicidal properties to the propofol emulsion. We conclude that the addition of lidocaine to propofol in clinically relevant concentrations offers no antimicrobial protection to the patient and therefore cannot be used as a means of decreasing the risk of propofol-acquired infections.

References