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Contamination of Propofol Infusions in the Intensive Care Unit: Incidence and Clinical Significance

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SUMMARY

Epidemics of bacteraemia and wound infection have been associated with the infusion of bacterially contaminated propofol administered during anaesthesia. We conducted an observational study to determine the incidence and clinical significance of administration of potentially contaminated propofol to patients in an ICU setting. One hundred patients received a total of 302 infusions of propofol. Eighteen episodes of possible contamination of propofol syringes were identified, but in all cases contamination was by a low-grade virulence pathogen. There were no episodes of clinical infection or colonization which could be attributed to the administration of contaminated propofol. During the routine use of propofol to provide sedation in ICU patients the risk of nosocomial infection secondary to contamination of propofol is extremely low.

Key Words: ANAESTHETICS, INTRAVENOUS: propofol; COMPLICATIONS: nosocomial infection; INTENSIVE CARE: nosocomial infection

The intravenous anaesthetic agent propofol is commonly used to provide sedation in intensive care unit (ICU) patients. Serious nosocomial bacteraemias and wound infections related to the use of propofol which had become contaminated after vial-opening have been reported[1]. It is possible that infusion of propofol to ICU patients may contribute to the occurrence of nosocomial infections.

The need for propofol to be formulated in a lipid emulsion is largely responsible for its potential to introduce infectious agents. Lipid emulsions are capable of supporting bacterial growth[2-4] and several studies have demonstrated that propofol may host a wide variety of potentially pathogenic micro-organisms[5-11].

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In the United States, the use of propofol during anaesthesia has been associated with epidemics of post-surgical infections, especially bacteraemias and/or wound infections[1,12,13]. These reports provide overwhelming epidemiological evidence that extrinsic microbiological contamination of propofol was responsible for these outbreaks of infection.

Propofol infusions are commonly used to provide sedation for critically ill patients who are admitted to an ICU. Syringes of propofol being infused may not routinely be changed in some ICUs for much longer than the manufacturer's recommendations, which specify a maximum infusion time of twelve hours[14]. Relatively little is known about whether contamination of propofol infusions contributes to the occurrence of nosocomial infections in ICU patients. One study conducted in an ICU[10] failed to demonstrate significant contamination among 50 syringes of propofol administered for a mean duration of 5.16 hours.

The aims of this study were to identify the rate of contamination of propofol syringes used in an ICU setting, and if such contamination was demonstrated, to determine whether this resulted in any subsequent nosocomial infections.

METHODS

A prospective observational study was performed to determine the incidence and clinical significance of

contamination of propofol infusions in an ICU setting.

All patients receiving propofol infusions for sedation during a three-month study period were enrolled in the study. This study was registered as a Quality Assurance (QA) project with the appropriate institutional body. Patients who received boluses of propofol directly from a syringe, e.g. during procedures, were not included.

Propofol was prepared in 20 ml syringes by the bedside nursing staff using standard clean, but not sterile, techniques (i.e., clean surface, new sterile needle and syringe, prior handwashing) and administered using a syringe driver (Terufusion model STC–523, Terumo Corp, Japan). Each syringe was used only once. The most common indication for the use of propofol was to provide sedation for patients requiring short-term mechanical ventilation. For each administration the duration of infusion and the final volume delivered were recorded. At the completion of each administration the residual volume, which was set to be a minimum of 2 ml, was injected aseptically into an aerobic Bactec blood culture bottle (Becton Dickinson, Sparks, MD, U.S.A.). These were incubated at 37°C for five days and cultured organisms were identified and antibiotic sensitivities determined using standard microbiological techniques.

The age, gender and admission APACHE II score[15] of all patients who received propofol were recorded. All patients who received propofol from which any organism was cultured were observed for the remainder of their hospital admission to identify the occurrence of any nosocomial infections. Bacterial isolates obtained from clinically indicated cultures from patients who received contaminated propofol were compared using standard taxonomy and antibiograms to determine if any organism found in a propofol culture was associated with infection or colonization of a patient. Additionally, the tips of all intravenous cannulae, both central and peripheral, which were used for the administration of propofol were cultured using the technique of Maki et al[16].

Prospective definitions of the following outcome variables were used. A syringe of propofol was considered *culture positive* if a microorganism was identified. Positive cultures were further categorized as *probable contamination* if a recognized pathogen such as *Staphyloccocus aureus*, gram-negative bacilli, yeast, and nonviridans streptococci was cultured; or as *possible contamination* if a low virulence organism such as *Staphylococcus epidermidis*, coagulase negative staphylococci, diptheroid corynebacteria, propionibacteria, and viridans streptococci was identified. *Propofol associated infection* was defined as any nosocomial infection occurring after the administration of contaminated propofol in which the same organism was isolated from the propofol syringe as that isolated from a clinical isolate in the presence of infection. *Propofol associated colonization* was defined as the isolation of the same organism from a clinical specimen and a propofol syringe, in which the organism was not obviously associated with nosocomial infection. The definitions of the Centres for Disease Control[17] were used to differentiate colonization from infection.

Statistical Analysis

The cumulative incidence of probable propofol associated infection and colonization were estimated. The t-test was used to determine if there was a relationship between the duration of an infusion and the likelihood of a culture positive result.

RESULTS

Over the study period, 302 syringes of propofol were administered to 100 (71 male and 29 female) patients. Among study patients the mean age was 56 years, the mean admission APACHE II score was 13 (range 2 to 34), and the mean duration of ICU stay was 4.06 days (range 1 to 27 days). The mean duration for total administration of propofol per patient was 16.8 hours and the average duration of each syringe infusion was 5.30 hours (range 30 minutes to 64 hours).

Of the 302 syringes 18 were culture positive and had been administered to a total of 13 patients. The organisms identified were *S. epidermidis* from 13 syringes, and on one occasion each Corynebacterium species, Bacillus species, *Micrococcus kristinae*, Gemella species and *Streptococcus salivarius*. Using the predetermined definitions, there were no episodes of probable propofol contamination but the incidence of possible propofol contamination was 5.9%.

No episodes of propofol-associated infection or colonization were identified among the patients who received potentially contaminated propofol. Of the 13 patients who received culture positive propofol, two patients had no evidence of nosocomial infection or colonization. Among the remaining eleven there were three cases of pneumonia, four of respiratory tract colonization, two urinary tract infections, two wound infections, one episode of *Clostridium difficile* associated colitis, two episodes of meningitis, one colonized central venous catheter tip and one case of peritonitis. In only three cases was the same species of bacteria, *S. epidermidis*, isolated from both propofol and a clinical collection. The clinical sites

involved were a central venous catheter tip, the tip of a cerebral ventricular catheter and a wound swab. However, the antibiograms of the clinical and propofol isolates indicated that in none of these occasions was the clinical isolate the same as that obtained from culture of the propofol. The tips of all vascular devices that were used to infuse propofol were cultured, and on no occasion was the same organism cultured from the tip of a catheter as was found in the infused propofol. There was no association between the duration of propofol infusion and the likelihood of a positive culture. The mean duration for negative infusions was 5.35 hours and the mean duration for positive infusions was 4.49 hours (t-test $P=0.59$).

DISCUSSION

During a three-month period of observation of the routine use of propofol by continuous infusion to sedate patients in the ICU, only a low rate of contamination of propofol syringes was identified and high-grade virulent pathogens were never isolated from propofol. The number of true positive episodes of propofol contamination may have been even lower as some of the organisms that were cultured may have been introduced at the time of inoculation of the blood culture bottle. The study method of culturing the residual volume of propofol using a blood culture bottle technique is likely to be sensitive to the isolation of potential pathogens within the propofol. Lastly, even in patients who did receive potentially contaminated propofol, no episode of infection or colonization could be attributed to this cause.

We believe that the study duration and size were sufficiently large to exclude contamination of propofol as the explanation for any component of the background rate of nosocomial infection which occurs in ICUs. Although members of bedside staff were not explicitly aware of the study's aims, it is possible that drawing-up techniques and the care of lines and infusions may have improved during the study period, and this may have influenced the results. However, we observed no noticeable change in the pattern of use and administration of propofol during the study period.

Given that epidemics of serious nosocomial infections have been linked with the use of propofol during anaesthesia[1], it remains possible that such outbreaks could occur in an ICU setting. However, it would appear that such outbreaks would be most likely to occur in the context of breakdowns in clean technique for the preparation of infusions. Our current practice emphasizes the importance of attention to detail when preparing clean propofol syringes at the bedside. We also encourage the use of 20 ml syringes to limit the infusion times between syringe changes (average infusion time of 5.3 hours in this group of patients). This practice, as demonstrated by the current study, ensures that within our Intensive Care Units the risk of nosocomial infection during routine use of propofol is extremely low.

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