Medical News

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Frequency and Determinants of Drug Administration Errors in the ICU

van den Bemt and colleagues from The Netherlands conducted a study to identify both the frequency and the determinants of drug administration errors in the intensive care unit (ICU). Administration errors were detected in two Dutch hospitals using the disguised-observation technique (observation of medication administrations by nurses, without revealing the aim of this observation to the nurses). The drug administrations to patients in the ICUs of the hospitals were observed during 5 consecutive days.

A total of 233 medications for 24 patients were observed to be administered (whether ordered or not) or omitted. When wrong time errors were included, 104 administrations with at least 1 error were observed (frequency, 44.6%); when they were excluded, 77 administrations with at least 1 error were observed (frequency, 33.0%). When wrong time errors were included, day of the week (Monday: odds ratio [OR], 2.69; 95% confidence interval [CI_{95}], 1.42 to 5.10), time of day (6 to 10 pm: OR, 0.28; CI_{95}, 0.10 to 0.78), and drug class (gastrointestinal: OR, 2.94; CI_{95}, 1.48 to 5.85; blood: OR, 0.12; CI_{95}, 0.03 to 0.54; and cardiovascular: OR, 0.38; CI_{95}, 0.16 to 0.90) were associated with the occurrence of errors. When wrong time errors were excluded, day of the week (Monday: OR, 3.14; CI_{95}, 1.66 to 5.94), drug class (gastrointestinal: OR, 3.47; CI_{95}, 1.76 to 6.82; blood: OR, 0.21; CI_{95}, 0.05 to 0.91; and respiratory: OR, 0.22; CI_{95}, 0.08 to 0.60), and route of administration (oral by gastric tube: OR, 5.60; CI_{95}, 1.70 to 18.49) were associated with the occurrence of errors.

In the hospital without full-time specialized intensive care physicians (which also lacks pharmacy-provided protocols for the preparation of parenteral drugs), more administration errors occurred, both when the investigators included (OR, 5.45; CI_{95}, 3.04 to 9.78) and when the investigators excluded (OR, 4.22; CI_{95}, 2.36 to 7.54) wrong time errors.

The authors concluded that efforts to reduce drug administration errors in the ICU should be aimed at the risk factors identified in this study. Specifically, focusing on system differences between the two ICUs (eg, the presence or absence of full-time specialized intensive care physicians and the presence or absence of protocols for the preparation of all parenteral drugs) may help reduce suboptimal drug administration.

FROM: van den Bemt PM, Fijn R, van der Voort PH, Gossen AA, Egberts TC, Brouwers JR. Frequency and determinants of drug administration errors in the intensive care unit. *Crit Care Med* 2002;30:846-850.

Gastrointestinal Colonization and VRE in a Hemodialysis Unit

The transmission dynamics of vancomycin-resistant enterococci (VRE) and factors contributing to their dissemination are complex. D'Agata and colleagues from Vanderbilt University, Nashville, Tennessee, used mathematical modeling to simulate patterns of dissemination among patients and healthcare workers and to quantify the contribution of specific factors and infection control interventions to the endemic prevalence of VRE in a long-term hemodialysis unit.

The model predicted that (1) an endemic prevalence of 12% would be reached over time, regardless of the number of patients initially colonized; (2) endemicity would be sustained by the constant influx of newly colonized patients discharged from the hospital; (3) the duration of VRE gastrointestinal colonization would have the most impact on the number of secondary cases, increasing the endemic prevalence to a maximum of 70%; and (4) decreasing the patient-to-healthcare worker ratio or improving hand hygiene would decrease the endemic prevalence to 3%.

Decreasing the duration of colonization, limiting hospital acquisition of VRE, and improving compliance with hand hygiene in the hemodialysis unit may decrease the rapidly rising rates of VRE in this patient population.

FROM: D'Agata EM, Horn MA, Webb GF. The impact of persistent gastrointestinal colonization on the transmission dynamics of vancomycin-resistant enterococci. *J Infect Dis* 2002;185:766-773.

Locally Delivered Polyclonal Antibodies for Abdominal Implant Infections

The increasing clinical incidence and host risk of biomaterial-centered infections, as well as the reduced effectiveness of clinically relevant antibiotics to treat such infections, provide compelling reasons to develop new approaches for treating implanted biomaterials in a surgical context. Poelstra and colleagues from the Gristina Institute for Biomedical Research, Herndon, Virginia, describe the direct local delivery of polyclonal human antibodies to abdominal surgical implant sites to reduce infection severity and mortality in a lethal murine model of surgical implant-centered peritoneal infection.

Surgical implant-centered peritonitis was produced in 180 female CF-1 mice by the direct inoculation of surgical-grade polypropylene mesh disks placed in the peritoneal cavity with lethal doses of either methicillin-resistant

Staphylococcus aureus (MRSA) or *Pseudomonas aeruginosa*. Mice randomly received a resorbable antibody delivery vehicle at the implant site: a blank carboxymethylcellulose (CMC) aqueous gel or the same CMC gel containing 10 mg of pooled polyclonal human immunoglobulin G locally on the implant after infection, either alone or in combination with systemic doses of cefazolin or vancomycin antibiotics. Human antibodies were rapidly released (first-order kinetics) from the gel carrier to both peritoneal fluids and serum in both infection scenarios. Inocula required for lethal infection were substantially reduced by surgery and the presence of the implant versus a closed lethal peritonitis model. Survival to 10 days with two different *P. aeruginosa* strains was significantly enhanced ($P < .01$) by the direct application of CMC gel containing antibodies alone to the surgical implant site.

Human-equivalent doses of systemic vancomycin provided a significantly improved benefit ($P < .01$) against lethal, implant-centered, gram-positive MRSA infection. However, locally delivered polyclonal human antibodies in combination with a range of systemic vancomycin doses against MRSA failed to improve host survival. Successful antibody therapy against gram-negative, implant-centered infections complements the clinically routine use of systemic antibiotics, providing a mechanism of protection independent of antibiotic resistance.

FROM: Poelstra KA, Barekzi NA, Rediske AM, Felts AG, Slunt JB, Grainger DW. Prophylactic treatment of gram-positive and gram-negative abdominal implant infections using locally delivered polyclonal antibodies. *J Biomed Mater Res* 2002;60:206-215.

Fibrin Sheath Enhances Central Venous Catheter Infection

Mehall and colleagues from the University of Arkansas for Medical Sciences, Little Rock, Arkansas, conducted a study to determine whether fibrin-coated central venous catheters have a higher infection rate, and spawn more septic emboli, than uncoated catheters after exposure to bacteremia. The study compared catheter infection and blood cultures of fibrin-coated and uncoated catheters exposed to bacteremia using adult male Sprague–Dawley rats.

A total of 210 rats had catheters placed with the proximal end buried subcutaneously. Rats were divided into three groups: tail vein bacterial injection on day 0 (no fibrin group) or on day 10 (fibrin group), or no injection/saline injection (control, n = 40). Bacterial injections were 1×10^8 colony-forming units of either *Staphylococcus epidermidis* (n = 100) or *Enterobacter cloacae* (n = 60). Animals were killed 3 days after injection. Blood cultures were obtained via cardiac puncture, and catheters were removed via the chest. Half of the catheter was rolled onto agar and the other half was placed in trypticase soy broth. Plates and broth were incubated at 37°C for 48 hours. The presence of more than 15 colonies on roll plates, or growth in broth, was accepted as a positive sign of infection. Thirty animals without catheters had bacterial injections and had blood cultures 3 days after injection.

Catheter infection with *S. epidermidis* occurred in 32% of roll plates and 80% of broth from the fibrin group versus 4% of roll plates and 20% of broth from the no fibrin group ($P < .01$ for each). Catheter infection with *E. cloacae* occurred in 50% of roll plates and 80% of broth from the fibrin group versus 0% of roll plates and 12% of broth from the no fibrin group ($P < .01$ for each). Positive blood cultures occurred in 47 of 68 animals from the fibrin group versus 8 of 68 from the no fibrin group ($P < .01$). Microscopy showed a fibrin sheath on 20 of 20 catheters. Without catheters, 30 of 30 blood cultures were negative.

The authors concluded that the fibrin sheath significantly enhanced catheter-related infection and persistent bacteremia.

FROM: Mehall JR, Saltzman DA, Jackson RJ, Smith SD. Fibrin sheath enhances central venous catheter infection. *Crit Care Med* 2002;30:908-912.

P. aeruginosa Cells Adapted to Benzalkonium Chloride Are Not Antibiotic Resistant

Loughlin and colleagues from the United Kingdom conducted studies to determine whether strains of *Pseudomonas aeruginosa* can adapt to growth in increasing concentrations of the disinfectant benzalkonium chloride, and whether co-resistance to clinically relevant antimicrobial agents occurs. Attempts were made to determine what phenotypic alterations accompanied resistance and whether these explained the mechanism of resistance. Strains were serially passaged in increasing concentrations of benzalkonium chloride in static nutrient broth cultures. Serotyping and genotyping were used to determine the purity of the cultures. Two strains were examined for cross-resistance to other disinfectants and antibiotics by broth dilution minimum inhibitory concentration determination. Alterations in outer membrane proteins and lipopolysaccharide expressed were determined, as well as cell surface hydrophobicity and charge, uptake of disinfectant, and proportion of specific fatty acid content of outer and cytoplasmic membranes.

Two *P. aeruginosa* strains showed a stable increase in resistance to benzalkonium chloride. Co-resistance to other quaternary ammonium compounds was observed in both strains; chloramphenicol and polymyxin B resistance was observed in one and a reduction in resistance to tobramycin was observed in the other. However, no increased resistance to other biocides (chlorhexidine, triclosan, and thymol) or antibiotics (ceftazidime, imipenem, ciprofloxacin, and tobramycin) was detected. Characteristics accompanying resistance included alterations in outer membrane proteins, uptake of benzalkonium chloride, cell surface charge and hydrophobicity, and fatty acid content of the cytoplasmic membrane, although no evidence was found for alterations in lipopolysaccharide. Each of the two strains had different alterations in pheno-