

Controlled Intervention Trials

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The Effects of Selective Digestive Decontamination (SDD) and Selective Oropharyngeal Decontamination (SOD) on Patient Survival in ICU

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Background:

Critically ill patients are at risk to develop nosocomial infections, most notable respiratory tract infections, which are assumed to have attributable mortality. Both Selective Decontamination of the Digestive tract (SDD) and Selective Oropharyngeal decontamination (SOD) reduce incidences of respiratory infections, but current data on the effects of SDD and SOD on patient survival are conflicting.

Objective:

To determine the effects of SDD and SOD, as compared to standard care, on patient survival.

Methods:

This was a randomized multi-center crossover open study in 13 ICUs. In each unit, the three regimens (SDD, SOD and standard care) were applied during 6 months. All patients with an expected duration of intubation >48 hours or with expected ICU-stay >72 hours were eligible. The order of periods was randomized per unit. ICU-mortality was the primary endpoint of the study. SDD consisted of four days of intravenous cefotaxim and topical application of antimicrobial agents (tobramycin, colistin and amphotericin B) in oropharynx and stomach during the duration of ICU-stay. SOD consisted only of oropharyngeal application of the same antibiotics, without systemic prophylaxis. No antibiotic-containing prevention measures were applied in the control period. Monthly point prevalence studies were performed to analyze antibiotic resistance of Gram-negative bacteria.

Results:

We enrolled 5943 patients (1990 control; 2050 SDD; 1903 SOD). Average inclusion rates were >85% of all eligible patients in each study period and baseline characteristics of groups were comparable. There was no significant difference in the primary outcome (ICU-mortality) between the three study groups (22,3%, 21,5% and 21,8% for control, SDD and SOD, respectively), nor in any of the secondary outcomes (hospital-mortality, length of ICU-stay and hospital-stay). Prevalence rates of Gram-negative bacteria in rectal swabs were significantly lower during SDD (as compared to SOD and control) and were equally reduced in respiratory specimens during SDD and SOD (as compared to control). 5 patients were colonized with methicillin-resistant *Staphylococcus aureus* and 3 patients with vancomycin-resistant enterococci, all without infection. A significant reduction in multiple antibiotic-resistant Gram-negative bacteria was observed in SDD-patients.

Conclusions:

There was no effect of SDD and SOD on patient outcome among critically ill patients.

Daily Bathing with Chlorhexidine Reduces the Incidence of Methicillin Resistant *Staphylococcus Aureus* (MRSA), Vancomycin Resistant Enterococci (VRE) and Healthcare-Associated Bloodstream Infections (HABSI): Results of a Multicenter Trial

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Background:

MRSA and VRE are important pathogens causing HABSI. Chlorhexidine is a widely used topical disinfectant that reduces residual skin organisms including MRSA and VRE and has been demonstrated to reduce HABSI in comparison to other skin disinfectant products such as povidone-iodine when used during skin preparation in central venous catheter insertion. Although the selective use of chlorhexidine as it relates to catheter site preparation and in the selective treatment of MRSA colonized patients during outbreaks has received preliminary study, there is little study of the potential utility of more wide scale use of chlorhexidine in daily bathing routines within the Intensive Care Unit (ICU) and hospital.

Objective:

The purpose of this study was to determine if the use of daily chlorhexidine bathing among ICU patients decreased the incidence of MRSA and VRE colonization and HABSI.

Methods:

Six ICUs at four academic centers, measured the incidence of MRSA and VRE colonization and HABSI during 2 periods: one of standard unit bathing with hospital approved soap for six months and a subsequent six month period where all admitted patients received daily bathing with chlorhexidine.

Results:

After the introduction of daily chlorhexidine bathing, acquisition of MRSA decreased 32% (5.04 cases per 1000 pt-days vs 3.44 cases per 1000 pt-days, $p=0.046$) and VRE acquisition decreased 50% (4.35 cases per 1000 pt-days vs 2.19 cases per 1000 pt-days, $p=0.008$). Incident BSI decreased 21% (10.92 cases per 1000 pt-days vs 8.66 cases per 1000 pt-days, $p=0.046$). The decrease occurred because of a reduction of BSI caused by Gram-positive organisms, particularly VRE. Among VRE colonized patients, bathing with chlorhexidine significantly reduced the risk of progression to VRE bacteremia (RR 3.35; 95% CI 1.13-9.87; $P=0.035$) compared to regular bathing.

Conclusions:

We conclude daily chlorhexidine bathing among ICU patients significantly reduces MRSA and VRE acquisition and the incidence of HABSI. The approach is simple to implement, inexpensive, and may be an important adjunctive intervention to barrier precautions to reduce acquisition of VRE, MRSA and the subsequent development of

HABSI. However, the study is limited by its before and after study design. Further confirmatory data is needed

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Computer-Assisted Antimicrobial Recommendations for Optimal Therapy (CAROT): Analysis of Prescribing Errors in a Randomized Trial of Antimicrobial Stewardship Programs

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Background:

The relative effectiveness of interventions to improve inpatient antimicrobial therapy is unclear.

Objective:

To compare the effects of separate interventions to improve antimicrobial therapy on rates of antimicrobial prescribing errors (APEs) among three inpatient medicine firms in an urban teaching hospital.

Methods:

We randomized three medicine inpatient firms to one of three interventions implemented concurrently over a 24-week period: 1) pharmacist review of all antimicrobial recipients using a computerized surveillance tool, with concurrent feedback to prescribing physicians in cases of inappropriate use (Ph-firm); 2) biweekly, case-based, interactive education sessions on optimal management of common infection syndromes (Ed-firm); and 3) comprehensive institutional guidelines on infection management, available to all clinicians via the hospital's clinical computer system (C-firm). We ascertained APEs retrospectively among a randomly selected sample of 504 patients using a two-step process of computer-assisted case vignette assembly by trained assistants followed by vignette review by an infectious diseases MD who was blinded to medicine firm assignment. We used the infection management guidelines as a gold standard for appropriateness and a hierarchical system to classify APEs.

Results:

Errors were identified in 353 (70.0%) of 504 antimicrobial starts; the prevalence of errant starts did not vary significantly among the three firms (72%, 71% and 66%, respectively; $p=0.4$). The 504 cases accrued 2300 inpatient-days on antimicrobials (mean 4.6 per patient) during which one or more APEs were detected in 1181 (51.3%); APEs occurred during significantly fewer inpatient-days on antimicrobials among patients on the C-firm (46.7%) than on the Ph-firm (53.8%) or the Ed-firm (52.2%; $p=0.03$). APEs involving the use of inappropriately narrow-spectrum therapy were more frequent among patients on the Ed-firm (17.0%) than among those on the Ph-firm (9.5%) or the C-firm (11.2%; $p<0.001$), possibly reflecting over-reaction to education appeals for more prudent antimicrobial use. APEs involving redundant, superfluous or overly expensive or broad-spectrum regimens were most frequent among Ph-firm patients (29.2% versus 19.1% for Ed-firm and 20.2% for C-firm; $p<0.001$), possibly a surveillance artifact from more frequent pharmacist-directed regimen changes.

Conclusions:

None of our interventions was clearly more effective in reducing APEs overall though the Ed-firm was associated with more frequent use of inadequate therapy, suggesting that the education intervention may have had unforeseen consequences. Given our high APE rates, more effective interventions are needed.

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A Crossover Intervention Trial Evaluating the Efficacy of a Chlorhexidine-Impregnated Sponge (BIOPATCH®) to Reduce Catheter-Related Bloodstream Infections in Hemodialysis Patients

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Background:

Introduction: Catheter-related bloodstream infections (BSI) account for majority of hemodialysis-related infections. There are limited data on the efficacy of the chlorhexidine-impregnated sponge to reduce catheter-related BSIs in ICU settings however, there is currently no published data in hemodialysis patients.

Objective:

To determine the efficacy of a chlorhexidine-impregnated sponge (Biopatch®) to reduce catheter-related BSI in hemodialysis patients.

Methods:

Patients: Endstage renal disease (ESRD) patients who are dialyzed through a central venous catheter.

Setting: Two outpatient dialysis centers affiliated with Washington University School of Medicine in Saint Louis, Missouri, USA.

Design: Cross-over controlled intervention trial conducted over 12 months. Crossover occurred at the 6-month interval. A nested cohort study of all patients who received the Biopatch® Antimicrobial Dressing was also conducted. Backward stepwise logistic regression analysis was used to determine independent risk factors for development of BSI.

Results:

121 patients were enrolled. 5764 dialysis sessions were included in the control period and 5847 in the intervention period. 37 bloodstream infections occurred in the intervention group for a rate of 6.3 BSIs/1000 dialysis sessions and 30 bloodstream infections in the control group for a rate of 5.2 BSIs/1000 dialysis sessions and [RR 1.22, CI (0.76, 1.97); $P=0.46$]. There were significantly less episodes of clinical sepsis in the intervention group [1.2 vs. 3.2 episodes/1000 dialysis sessions; RR 0.41 CI (0.17, 0.98); $P=0.04$]. The Biopatch® Antimicrobial Dressing was well-tolerated with only two patients (<2%) experiencing dermatitis that led to its discontinuation. Independent risk factors for development of BSI were a history of substance abuse[aOR 22.1 CI (1.85, 263); $P=0.01$]

and dialysis treatment at one dialysis center [aOR 4.4 (1.55, 12.7); $P=0.006$]. Age ≥ 60 years [aOR 0.26 (0.08, 0.82); $P=0.02$] and recent admission to the hospital [aOR 0.24 (0.06, 0.93); $P=0.04$] were associated with lower risks of BSI.

Conclusions:

Although the use of a chlorhexidine-impregnated sponge (Biopatch[®]) did not result in a decrease in catheter-related BSIs, there was a significant decrease in the incidence of clinical sepsis among hemodialysis patients. Risk factors for development of BSI were a history of substance abuse and treatment at one dialysis center. Older age and recent hospitalization were protective against development of BSI.

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A Randomized Controlled Trial of Urinary Catheter Stop Orders in Hospitalized Patients

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Background:

Urinary catheter use in hospital patients is common and is frequently inappropriate. Inappropriate use of urinary catheters may lead to urinary tract infections.

Objective:

To assess whether stop orders for indwelling urinary catheters reduces the duration of urinary catheterisation and the incidence of urinary tract infections in hospital patients.

Methods:

A randomized controlled trial was conducted in three tertiary care hospitals in Hamilton, Ontario, Canada. 692 medical patients admitted to hospital with indwelling urinary catheters inserted for ≤ 48 hours were randomized to either pre-written orders placed in patients' charts ordering removal of urinary catheters if specified criteria for a urinary catheter were not present or to usual care. The main outcome measures were days of indwelling catheter use, frequency of urinary tract infection, catheter reinsertions.

Results:

There were fewer days of indwelling urinary catheter use in the stop order group than in the usual care group (mean of 3.7 days versus 5.04 days; difference - 1.34 days, 95% confidence interval -0.64 to -2.05 days). The mean duration of inappropriate urinary catheter days was 2.20 days for the 347 participants in the stop order group and 3.89 days for the 345 in the usual care group (difference -1.69, 95% confidence interval -1.23 to -2.15). Urinary tract infections occurred in 19.0% of the stop order group and 20.2% of the usual care group, relative risk = 0.94 (0.66 to 1.33). In each study group 2.1% participants developed symptomatic urinary tract infections. Catheter reinsertion occurred in 8.6% of the stop order group and 7.0% in the usual care group, relative risk 1.23 (0.72 to 2.11).

Conclusions:

Stop orders for urinary catheterisation reduced the duration of urinary catheterisation but did not reduce urinary tract infections in hospital patients.