Neuroanesthesia and Intensive Care

Best evidence in critical care medicine

Selective digestive decontamination decreases mortality and morbidity in the intensive care

Article appraised

de Jonge E, Schultz MJ, Spanjaard L, et al. Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. *Lancet* 2003; 362: 1011–6.

Clinical issue

Selective digestive decontamination (SDD) has been used as a prophylactic measure to prevent nosocomial infections in critically ill patients. Arguments against wide spread use of this strategy are the absence of definite mortality reduction; the fear of emergence of multi-resistance organisms and finally its cost.

Methodology

Design: Prospective, controlled, randomized, unblinded clinical trial.

Setting: Two separate intensive care units (ICU) in a single academic centre. Each ICU had a similar case mix of medical and surgical patients. Randomly, one unit was designated to be the intervention unit with the provision of SDD and the other the control unit to prevent cross-colonization between groups. The study was unblinded.

Participants: One thousand ninety consecutive patients were randomized using computer-generated codes to admission to the intervention or control ICU. Sealed envelopes were used to conceal allocation. Nine hundred thirty-four patients gave consent; SDD group $n = 466$, control group $n = 468$. Baseline characteristics were comparable; mean APACHE II score (SD) 18.7 (7.4). There was complete follow-up of all consented patients. The mortality analysis included all consented patients.

Interventions: Patients in the SDD unit were treated with a combination of oral and enteral polymyxin E, tobramycin and amphotericin B four times daily until discharge from the ICU. In addition, an initial

four-day course of *iv* cefotaxime was given. When applicable, antibiotic paste and suppositories were used for tracheostomy sites and blind-bowel loops respectively. Finally, nebulized polymyxin E or amphotericin B was administered to eradicate documented colonization of the tracheobronchial tree.

Selective cultures for resistant micro-organisms were taken from the patients (sputum, throat, rectum, axilla, and wounds) and from each ICU sink. Patients in the control ICU had standard oropharyngeal care, early enteral nutrition and the administration of systemic antibiotics for proven or suspected infections as clinically indicated.

Outcomes: Primary end-points were ICU and hospital mortality and the acquisition of resistant bacteria. Secondary outcomes were the length-of-stay in the ICU and the total costs of antibiotic treatment.

Results

TABLE The major outcomes

Outcomes	SDD <i>n</i> /total	Controls <i>n</i> /total	RR (95% CI)	ARR	NNT	<i>P</i> value
ICU mortality	69/466 (14.8%)	107/468 (22.9%)	0.65 (0.49-0.85)	8.1%	12	$P = 0.002$
Hospital mortality	113/466 (24.2%)	146/468 (31.2%)	0.78 (0.63-0.96)	7.0%	14	$P = 0.02$
Acquisition of resistance GNB	61/378 (16%)	104/395 (26%)	0.61 (0.46-0.81)	10%	10	$P = 0.001$
Acquisition of VRE	4/378 1.1%	5/395 1.3%	0.8 (0.2-3.1)			$P = 1.0$
Acquisition of MRSA	None	None				
Median ICU stay (IQR)	6.8 days (3.7-12.8)	8.5 days (4.8-15.7)				$P < 0.0001$
Costs	Total costs of antibiotics were 11% lower in the SDD unit than in the control unit.					

RR = relative risk; ARR = absolute risk reduction; NNT = number-needed-to-treat; GNB = gram-negative bacteria; VRE = vancomycin-resistant enterococcus; MRSA = methicillin-resistant *Staph aureus*; IQR = interquartile range; CI = confidence intervals.

Conclusions

SDD reduces ICU and in-hospital mortality, the length-of-stay in the ICU, the frequency of colonization with resistant GNB, and the total costs of antibiotic treatment. This supports the use of SDD in all patients expected to be on mechanical ventilation for at least two days in ICUs that have low prevalence of VRE and MRSA.

Commentary by O. Almuslim and R. Butler

Ventilator associated pneumonia (VAP) is the leading cause of nosocomial infections in critically ill patients.¹ It is associated with a substantial increase in mortality, morbidity, intensive care unit (ICU) length of stay and health care costs. Hence, effective measures to prevent VAP are of paramount importance. Since the pathogenesis of VAP is linked to aspiration of the oropharyngeal microbial flora, various strategies have been evaluated to minimize the acquisition and the aspiration of these pathogenic organisms.² Currently, these strategies include effective hand washing techniques, semirecumbent positioning of patients and endotracheal tubes with a subglottic suctioning lumen.²

In the early 1980s, Stoutenbeek and co-workers started to study a novel prophylactic measure known as selective decontamination of the digestive tract (SDD). By using various combinations of nonabsorbable enteral with and without parenteral antibiotics, it might be possible to reduce nosocomial infection by eradicating potentially pathogenic micro-organisms from the oropharynx, stomach, and gut.¹ Although multiple SDD studies have shown reduction in nosocomial infections, no single trial found a clear reduction in mortality. However, systematic reviews and meta-analyses have shown interesting findings. van Nieuwenhoven and co-workers found a small but significant reduction in mortality when analyzing SDD studies of high quality.³ Moreover, by pooling data of SDD trials which used a combination of parenteral and nonabsorbable enteral antibiotics, D'Amico and colleagues found that the number-needed-to-treat was five and 23 patients to prevent one respiratory tract infection and one death respectively.⁴ A third meta-analysis showed a 30% reduction in ICU mortality by using SDD in the critically ill surgical patients.⁵

Despite two decades of extensive clinical research, experts continue to be skeptical about SDD.⁶ Uncertainties of meta-analyses findings, the fear of emergence of resistance micro-organisms, SDD costs and potential adverse effects are obstacles to widespread acceptance of SDD as the standard care in North American ICUs. The need for well designed randomized clinical trials to answer these questions is obvious.

The study by de Jonge *et al.*, is unique amongst other SDD trials. This is the first and largest trial to show an overall mortality reduction in a mixed population of critically ill patients. In addition, the reduction in the acquisition of resistant aerobic gram negative bacteria challenges a long-standing argument against the SDD strategy. The secondary findings of lower total antibiotic costs and shorter ICU stay also favour the SDD regimen. Nevertheless, the study has limitations. First, it is not known if the results are sustainable beyond the two-year follow-up, especially regarding the emergence of resistant microbes. Second, the low prevalence of vancomycin-resistant enterococcus and meticillin-resistant *Staph aureus* might limit the generalizability of the study. Thus, surveillance cultures to monitor antibiotic resistance should be an integral part of any SDD strategy.

Finally, we have pooled the data from D'Amico *et al.*⁴ and the recently published trials⁷⁻⁹ which used both enteral and parenteral antibiotics as the SDD intervention. Using the random effects model, this meta-analysis gives a very impressive mortality reduction (Figure; relative risk = 0.81; 95% confidence interval = 0.74–0.89). The number-needed-to-treat with SDD to prevent one death is only 20 patients. We conclude that a combination of enteral and parenteral SDD strategy is an effective infection prophylaxis to reduce mortality in critically ill patients.

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