Selective decontamination of the digestive tract reduces pneumonia and mortality without resistance emerging

To the Editor:

We welcome the review by Flanders et al.[1] on the pathogenesis, diagnosis, treatment, and prevention of nosocomial pneumonia, including ventilator-associated pneumonia (VAP); however, we do not agree completely with the section on selective decontamination of the digestive tract (SDD). Although Flanders et al. are correct in saying that the evidence suggests that SDD significantly reduces the risk for VAP and mortality in patients who are receiving both parenteral and enteral antimicrobials, they cited Dodek et al.'s[2] practice guidelines and Collard et al.'s[3] systematic review to sustain that evidence.[4,5] We would like to support authors' assertion providing more updated informations.

Fifty-six randomized controlled trials (RCTs)[6-8]and 12 meta-analyses of RCTs[9-20] have been published during 20 years of clinical research on SDD. The main morbidity end point was pneumonia in 9 meta-analyses,[9-16,18] whereas in the remaining 3 meta-analyses it was infection in liver transplantation,[17] yeast carriage and infection,[19] or bloodstream infections.[20] Those 9 meta-analyses consistently demonstrated a significant reduction in pneumonia (Table 1). The recent Cochrane meta-analysis that was published in 2004, which included 6922 patients, showed that SDD with parenteral and enteral antimicrobials reduced the odds ratio (OR) for pneumonia to 0.35 (95% confidence interval [CI], 0.29-0.41).[18]

Mortality was the outcome measure in 9 of 12 meta-analyses (Table 2).[9-15,17,18,20] There was a consistent survival benefit in all meta-analyses that evaluated SDD with parenteral and enteral antimicrobials.[10,12,14,15,18,20,26] The most recent Cochrane meta-analysis demonstrated that parenteral and enteral antimicrobials reduced the OR for mortality to 0.78 (95% CI, 0.68-0.89); 21 patients need to be treated with SDD to save one life.[18] Vandenbroucke-Grauls and Vandenbroucke's[9] and Kollef's[11] meta-analyses in surgical/medical patients, and Safdar's[17] meta-analysis in recipients of liver transplants showed an impact on mortality; however, it was not significant because the sample size was small.

We disagree with the authors' claim that ''the results of meta-analyses may overstate the benefit'' based on ''an inverse relationship between reported benefit and methodologic quality'' found in a recent review.[21] That review has several limitations, including identification of studies, choice of the instrument for assessing trial quality, and presentation and interpretation of the results.[22] Notwithstanding, the same review confirmed the evidence of the effectiveness of SDD in significantly reducing respiratory tract infections and mortality.

An appropriate analysis of resistance should include multi-resistant aerobic gram-negative bacilli (AGNB), and the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE). A French RCT showed that SDD controlled infections that were due to extended-spectrum β-lactamase–producing *Klebsiella*,[23] and a large Dutch RCT demonstrated that carriage of multi-resistant AGNB was reduced significantly in patients who had SDD, compared with controls (risk ratio, 0.61; 95% CI, 0.46-0.81).[24] The emergence of resistance was virtually absent in the remaining RCTs of SDD.[25] Additionally, resistance was not a clinical problem in 10 SDD studies that monitored resistance over a period of 2 to 9 years.[26] Therefore, SDD does not increase resistance, but it does solve the problem of endemicity of resistant AGNB.

The parenteral and enteral antimicrobials of the full SDD package are intrinsically inactive against VRE and MRSA, and they may promote gut overgrowth of these microorganisms.[27] Of the 56 RCTs, 7 were undertaken in intensive care units (ICUs) when MRSA was endemic in the unit, and they reported a trend toward higher MRSA carriage or infection rates.[28] In these circumstances, enteral vancomycin needs to be added to the SDD protocol.[29-32] Three studies that used oropharyngeal or intestinal vancomycin added to the nonabsorbable polymyxin-tobramycin-amphotericin B component of SDD, demonstrated that the prevention and the eradication of carriage and overgrowth of MRSA were followed by the control of MRSA infection, transmission, and outbreaks.[29-31] In 2 RCTs, severe infections, including MRSA pneumonia, were reduced significantly by using enteral vancomycin.[32,33]

SDD has been evaluated in two American ICUs with VRE endemicity;[34,35] carriage and infections that were due to VRE were similar in the test and control groups. None of the eight RCTs that evaluated SDD, which included enteral vancomycin, reported a problem with VRE.[36] Interestingly, recent literature demonstrated

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Table 1. Results of the nine meta-analyses of randomized controlled trials of SDD with the end point of pneumonia

Investigators	Number of RCTs	Aggregate number of patients	Number of RCTs by outcome	Number of patients by outcome	End point of pneumonia and subgroup analyses	Odds ratio	95% confidence interval
Vandenbroucke-Grauls & Vandenbroucke[9]	6	491	6	491	Overall	0.12	0.08-0.19
SDD Trialists' Collaborative Group[10]	22	4142	22	3836	Overall	0.37	0.31-0.43
			NR	2283	Parenteral and enteral	0.33	0.27-0.40
			NR	1553	Enteral	0.43	0.33-0.56
Kollef[1]	16	2270	16	2128	Overall	0.145*	0.116-0.174
			7	1043	Trachebronchitis	NR	NR
Heyland et al.[12]	25	3395	20	3395	Overall	0.46†	0.39-0.56
			12	NR	Parenteral and enteral	0.48	0.39-0.60
			8	NR	Enteral	0.43	0.32-0.59
Hurley[13]	26	NR	25	NR	Overall	0.35	0.30-0.42
D'Amico et al.[14]	33	5727	16	2883	Parenteral and enteral	0.35	0.29-0.41
			16	2377	Enteral	0.56	0.46-0.68
Nathens et al.[15]	22	NR	11	NR (surgical)	Overall	0.19	0.15-0.26
			11	NR (medical)	Overall	0.45	0.33-0.62
Redman et al.[16]	NR	NR	NR	NR	Parenteral and enteral	0.31	0.20-0.46
			NR	NR	Enteral	0.40	0.29-0.55
Liberati et al.[18]	36	6922	15	2883	Parenteral and enteral	0.35	0.29-0.41
			16	2664	Enteral	0.52	0.43-0.63

AGNB, Aerobic gram-negative bacilli; NR, not reported.
*Risk difference.
†Relative risk.

Table 2. Results of the ten meta-analyses of RCTs of SDD including the analysis of mortality

Investigators	Number of RCTs	Aggregate number of patients	Number of RCTs	Number of patients by outcome	End point of mortality and subgroup analyses	OR	95% CI
Vandenbroucke-Grauls & Vanderbroucke[9]	6	491	6	491	Overall	0.70	0.45-1.09
SDD Trialists' Collaborative Group[10]	22	4142	22	4142	Overall	0.90	0.79-1.04
			NR	2450	Parenteral and enteral	0.80	0.67-0.97
			NR	1692	Enteral	1.07	0.86-1.32
Kollef[11]	16	2270	16	2270	Overall	0.019*	−0.016-0.054
			7	778	Related to nosocomial acquired infection	0.051*	0.015-0.089
Heyland et al.[12]	25	3395	24	3395	Overall	0.87†	0.79-0.97
			14	NR	Parenteral and enteral	0.81†	0.71-0.95
			10	NR	Enteral	1.00†	0.83-1.19
Hurley[13]	26	NR	25	NR	Overall	0.86	0.74-0.99
D'Amico et al.[14]	33	5727	16	3581	Parenteral and enteral	0.80	0.69-0.93
			17	2543	Enteral	1.01	0.84-1.22
Nathens et al.[15]	22	NR	11 (surgical)	NR	Overall	0.70	0.52-0.93
					Parenteral and enteral	0.60	0.41-0.88
					Enteral	0.86	0.51-1.45
			11 (medical)	NR	Overall	0.91	0.71-1.18

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