Intensive Care Med (2016) 42:1270–1275
DOI 10.1007/s00134-015-4009-5

Jozef Kesecioglu
Philippe Eggimann

What is new in selective decontamination of the digestive tract?

Received: 20 May 2015
Accepted: 26 July 2015
Published online: 18 May 2015

J. Kesecioglu (✉)
Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, The Netherlands
e-mail: j.kesecioglu@umcutrecht.nl

P. Eggimann
Department of Intensive Care Medicine, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland
e-mail: philippe.eggimann@chuv.ch

Selective decontamination of the digestive tract (SDD) and selective oropharyngeal decontamination (SOD) are among the few interventions in intensive care medicine that have been shown to improve patient survival, but their use is limited to a minority of European intensive care units (ICUs) (Tables 1, 2) [1].

In addition, when the microbiological data of patients receiving SDD or SOD were compared with those receiving standard care, ICU-acquired bacteremia was significantly reduced for *Staphylococcus aureus*, glucose-non-fermenting Gram-negative rods, and *Enterobacteriaceae* [4], In particular, the use of SDD was associated with a lower incidence of acquired bacteremia with Enterobacteriaceae. Similarly, ICU-acquired candidemia was lower in the SDD group than in the SOD group or standard care group, but the difference was not significant. These findings were confirmed in a recent study comparing SDD and SOD on antibiotic resistance. The incidence of ICU-acquired bacteremia was also lower for aminoglycoside-resistant Gram-negative bacteria in the SDD group [5]. Although the survival rate of ICU patients remains similar in both studies, the lower incidence of antibiotic resistance and nosocomial bacteremia as consistent findings are in favour of SDD.

Common reasons for the reluctance to use SDD or SOD are related to only a few arguments regularly mentioned in editorials and by expert opinion expressing the fear that their use may promote antibiotic resistance and the possible increase of methicillin-resistant *S. aureus* [15]. These can be summarized as follows:

1. The absence of emergence of resistance is against current microbiological concepts and contradicts the worldwide pandemic of multidrug-resistant microorganisms demonstrated to be directly related to the use of antibiotics. In a recent meta-analysis, no relation was observed between the use of SDD and the development of antimicrobial resistance, thus confirming earlier reports [16]. Recent studies have demonstrated similar findings (Table 2). In a large study showing lower mortality with the use of SDD or SOD compared with standard care, patients treated with SDD and SOD had a significantly lower incidence of carriage and infections with antibiotic-resistant bacteria [4]. Moreover, when compared with SOD, SDD was related with lower rectal carriage of antibiotic-resistant Gram-negative bacteria [5]. By contrast, the continuous application of antibiotics included in the paste, as well as the aerosolized colistin applied in the case of emergence of Gram-negative bacilli in the respiratory samples, may largely contribute to the absence of the documented emergence of resistance (footnote Table 1).
2. One of the main reasons of bacterial resistance to antibiotics is the widespread use of antimicrobial agents. This represents the main reluctance for the use of SDD. Surprisingly, some investigators have even advocated for the use of SOD due to the absence of widespread systemic prophylaxis with cephalosporins

Table 1 Large studies comparing SDD and SOD

References	Design	Results				Comments
Krueger [2]	Single centre, 2 ICUs (Tübingen University Hospital) 30 months. Placebo-randomized standard care (SC) or SDD	ICU mortality	APACHE II ≤ 19	APACHE II 20–29	APACHE II ≥ 29	SDD lowered ICU mortality
		SC	23/121 (19 %)	20/122 (16.4 %)	15/23 (62.5 %)	
		SDD	17/120 (14.2 %)	38/115 (33.0 %)	14/26 (53.8 %)	
		RR (95 % CI)	0.885 (0.472–1.659)	0.508 (0.295–0.875)	1.593 (0.767–3.306)	
		Infections	Pneumonia	Bloodstream	Urinary tract	SDD decreased nosocomial infections
		SC	29 (11.1)	36 (13.7)	60 (22.9)	
		SDD	6 (2.3)	14 (5.3)	36 (13.6)	
		RR (95 % CI)	0.205 (0.072–0.587)	0.384 (0.176–0.836)	0.593 (0.357–0.985)	
de Jonge et al. [3]	Single centre (AMC, Amsterdam) 9/1999–12/2001	ICU mortality		Hospital mortality		SDD lowered ICU and hospital mortality
		SC	107/468 (22.9 %)	SC	146/468 (31.2 %)	
		SDD	69/466 (14.8 %)	SDD	113/466 (24.2 %)	
		RR (95 % CI)	0.65 (0.49–0.85)	RR (95 % CI):	0.78 (0.63–0.99)	
		Acquisition of resistance by Gram-negative pathogens				SDD decreased colonizationby Gram-negative pathogens
		SC	104 (26 %)			
		SDD	61 (16 %)			
		RR (95 % CI)	0.61 (0.46–0.81)			
de Smet et al. [4]	13 Dutch ICUs cluster-randomized to SC, SDD and SOD. 05/2004–07/2006 5939 ICU patients	ICU mortality		Hospital mortality:		SDD lowered ICU and hospital mortality
		SC: 443/1990 (22.3 %)		632/1990 (31.8 %)		
		SDD: 440/2045 (21.5 %)	OR 0.81 (0.69–0.94)	665/2045 (32.6 %)	OR 0.88 (0.76–1.01)	
		SOD: 416/1904 (21.8 %)	OR 0.87 (0.74–1.02)	584/1904 (30.7 %)	OR 0.85 (0.74–0.98)	
		Bacteremia (any)[b]				SDD > SOD decreased bacteremia
		SC: 186/1990 (9.3 %)				
		SDD: 88/2045 (4.3 %)	OR 0.44 (0.34–0.57)			
		SOD: 124/1904 (6.5 %)	OR 0.68 (0.53–0.86)	SDD vs SOD	OR 0.65 (0.49–0.85)	
		Antibiotic-resistant bacteria:				SDD decreased colonization
		Global decrease of antibiotic-resistant bacteria in rectal samples and respiratory samples in SDD recipients in point-prevalence surveys performed in 6–8 % of patients				
Oostdijk et al. [5]	16 ICUs randomized to 12 months SDD and 12 months SOD or the opposite 08/2009–01/2011	ICU mortality		Hospital mortality		SDD = SOD mortality
		SOD: 1165/5881 (19.8 %)		1625/5881 (27.6 %)		
		SDD: 1138/6116 (18.6 %)	OR 0.96 (0.86–1.05)	1929/6116 (26.6 %)	OR 0.99 (0.90–1.08)	
		ICU-acquired bacteremia				SDD > SOD decreased bacteremia
		SOD: 319/5442 (5.9 %)				
		SDD: 253/5549 (4.6 %)	OR 0.77 (0.65–0.91)			
		Monthly acquisition of rectal carriage of aminoglycoside-resistant bacteria				SDD > SOD acquisition of aminoglycoside resistance carriage
		SOD: 4 %				
		SDD: 7 %	$P = 0.046$			

SDD Selective decontamination of the digestive tract. The SDD regimen consists of 4 days of intravenous cefotaxime, the oropharyngeal application (every 6 h) of a paste containing colistin, tobramycin, and amphotericin B, each in a 2 % concentration, and the administration (every 6 h) of a 10-mL suspension containing colistin (100 mg), tobramycin (80 mg as sulfate), and amphotericin B (500 mg) via a nasogastric tube. Topical antibiotics are applied until ICU discharge (Oostdijk EAN et al. JAMA 2014;312:1427–1431). SOD: selective oropharyngeal decontamination. The SOD regimen consists of only the oropharyngeal application (every 6 h) of the paste described above (Oostdijk EAN et al. JAMA 2014;312:1427–1431). During SOD, application of oropharyngeal paste is increased to eight times daily if the first surveillance culture of the throat yields yeasts, until two consecutive surveillance cultures are negative. There are no restrictions in physicians' choices of systemic antibiotic therapy

APACHE II acute physiology and chronic health evaluation II score, *ICU* intensive care unit, *SC* standard care, *OR* odds ratio, *RR* relative risk, *vs* versus, *95 % CI* 95 % confidence intervals

[a] During SDD, several adaptations are possible: (1) application of oropharyngeal paste is increased to 8 times daily if the first surveillance culture of the throat yields yeasts, until two surveillance cultures are negative; (2) 5 ml (5 mg) amphotericin B is nebulized 4 times daily if a sputum surveillance culture (not admission culture) yields yeasts, until two sputum cultures become negative; (3) 5 ml (80 mg) colistin is nebulized 4 times daily if a sputum surveillance culture (not admission culture) yields Gram-negative bacteria, until two sputum cultures are negative

[b] During SDD, it is recommended to avoid antibiotics that have anaerobic activity as much as possible so as to leave the anaerobic flora undisturbed and preserve the so-called colonization resistance. The "to be avoided" antibiotics are penicillin, amoxicillin-clavulanic acid, flucloxacillin, piperacilline ± tazobactam, carbapenem, clindamycin. Metronidazole is the antibiotic of choice when the coverage of anaerobics is intended for clinical reasons

Table 2 Post hoc analyses and secondary studies on SDD and SOD

References	Design	Main results				Comments
de Smet et al. [6]	2 centres among 13 Dutch ICUs (NEJM 2009)	Post-ICU rate of nosocomial infection (/1000 days at-risk)				No impact of SDD/SOD on post-ICU infection rates
		SC: 8.3				
		SOD: 11.2	RR 1.44 (0.87–2.39)			
		SDD: 12.9	RR 1.49 (0.90–2.47)			
Oostdijk et al. [7]	13 Dutch ICUs (NEJM 2009) Samples from 6 point-prevalence surveys before, during and after SDD/SOD	Respiratory samples ($n = 2304$):	Pre-intervention	Intervention	Post-intervention	SDD/SOD decreased resistance in respiratory and rectal samples, followed by a rebound effect after stopping it
		Ceftazidime-resistant	10 % (7.6–13.3 %)	4 % (2.6–4.6 %)	10 % (7.4–13.0 %)	
		Tobramycin-resistant	10 % (6.9–12.5 %)	6 % (4.5–6.9 %)	12 % (8.8–14.6 %)	
		Ciprofloxacin-resistant	14 % (10.4–17.0 %)	5 % (3.5–5.7 %)	12 % (9.0–14.9 %)	
		Rectal samples ($n = 2963$)	Pre-intervention	Intervention	Post-intervention	
		Ceftazidime-resistant	6 % (4.7–7.5 %)	5 % (3.9–6.7 %)	15 % (12.4–17.0 %)	
		Tobramycin-resistant	9 % (7.7–11.2 %)	7 % (5.5–8.7 %)	13 % (10.4–14.7 %)	
		Ciprofloxacin-resistant	12 % (9.7–13.5 %)	7 % (5.1–8.2 %)	13 % (10.8–15.2 %)	
Benus et al. [8]	1 of 13 Dutch ICUs (NEJM 2009) Fluorescent in situ hybridization analysis of the intestinal microbiota	Total number of bacteria cultured from the faeces				SDD/SOD reduced the bacterial count of the faeces
		SC: (21 out of 121 patients): 3.7×10^9 (2.2–6.2)				
		SOD: (19 out of 111 patients): 1.6×10^9 (0.8–3.4)				
		SDD: (19 put of 86 patients): 1.9×10^9 (0.9–4.3)				
		Enterococcus faecalis		*Enterococcus faecium*	*F. prausnitzii*	SDD/SOD significanty increased enterococci
		SC:	2.6×10^6	6.3×10^6	5.5×10^7	
		SOD	7.6×10^6 $P < 0.05$	9.8×10^6 NS	4.0×10^7 NS	
		SDD	69×10^6 $P < 0.05$	54×10^6 $P < 0.05$	0.1×10^7 $P < 0.05$	
Oostdijk et al. [9]	13 Dutch ICUs (NEJM 2009) and 1 ICU (UMC Utrecht: 08/2008–08/2010)	Cumulative rate of bacteremia according to respiratory colonization status:				SDD decreased bacteremia only in patients successfully decolonized
		SC: 4.5/1000 patient-days				
		SOD: 3.0/1000 patient-days				
		SDD: 3.0/1000 patient-days in patients remaining colonized by enterobacteriae				
		SDD: 1.0/1000 patient-days in patients successfully decolonized				
de Smet et al. [10]	13 Dutch ICUs (NEJM 2009) Rate of bacteremia and respiratory tract acquisition of microorganisms in patients staying >3 days	Any bacteremia (except Coagulase-negative *Staphylococci)* microorganisms		Bacteremia with highly-resistant microorganisms		SDD > SOD decreased bacteremia
		SC: 239/1837 (13 %)		19/1837 (0.10 %)		
		SOD: 158/1758 (9 %)	OR: 0.66 (0.53–0.82) NNT: 25	20/1758 (1.03 %)	NS	
		SDD: 124/1868 (7 %)	OR: 0.48 (0.38–0.60) NNT: 16	8/1868 (0.04 %)	OR:0.41 (0.18–0.94) NNT:170	
		Respiratory tract acquisition of any microorganisms		Of highly-resistant microorganisms		SDD > SOD decreased respiratory colonization
		SC: 867/881 (98 %)		128/881 (15 %)		
		SOD: 862/886 (97 %)	NS	88/886 (10 %)	OR: 0.65 (0.49–0.87) NNT: 22	
		SDD: 800/828 (97 %)	OR: 0.46 (0.24–0.88)	74/828 (9 %)	OR: 0.58 (0.43–0.78) NNT: 18	
		Respiratory tract acquisition of *Enterococcus* spp		Of *Candida* spp		SDD > SOD increased respiratory colonization by enterococci *Candida* spp and *Psedomonas aeruginosa*
		SC: 37/881 (4 %)		393/881 (45 %)		
		SOD: 32/886 (3 %)	NS	476/886 (53 %)	OR: 1.44 (1.20–1.74)	
		SDD: 93/828 (11 %)	OR: 2.89 (1.95–4.29)	465/828 (56 %)	OR: 1.59 (1.31–1.93)	
		Respiratory tract acquisition of tobramycin-resistant non-fermenting Gram-negative pathogens (such as *P. aeruginosa*)				
		SC: 18/881 (2 %)				
		SOD: 20/886 (2 %)	NS			
		SDD: 49/828 (6 %)	OR: 3.02 (1.74–5.20)			

Table 2 continued

References	Design	Main results						Comments
Oostdijk et al. [11]	13 Dutch ICUs (NEJM 2009) Patients receiving SDD with rectal sampling and 1 single centre cohort; UMC Utrecht 01/2008–08/2009	Proportion of successful decontamination under SDD						SDD less successfully decolonized the digestive tract from resistant microorganisms
		Patients with digestive enterobacteriaceae at ICU admission			399/507 (79 %)			
		Patients with cephalosporin-susceptible microorganisms			343/430 (80 %)			
		Patients with cephalosporin-resistant microorganisms			56/77 (73 %)	$P < 005$		
		Patients with aminoglycoside-susceptible microorganisms			368/457 (81 %)			
		Patients with aminoglycoside-resistant microorganisms			31/50 (62 %)	$P < 0.05$		
		Patients with any resistant microorganism at ICU entry			23/109 (21 %)			
		Patients with any resistant microorganism at ICU discharge			24/109 (22 %)	NS		
Melsen et al. [12]	13 Dutch ICUs (NEJM 2009) post hoc analysis of surgical ($n = 2762$) versus non-surgical ($n = 3165$) patients	28-day mortality in surgical patients			28-day mortality in non-surgical patients			SDD decreased mortality in non-surgical patients
		SC: 209/973 (21.6 %)			335/1016 (33.2 %)			
		SOD: 194/866 (22.6 %)	OR: 0.97 (0.77–1.22)		308/1038 (30.0 %)	OR: 0.77 (0.63–0·94)		
		SDD: 191/923 (20.8 %)	OR: 0.86 (0.69–1.09)		349/1111 (31.7 %)	OR: 0.85 (0.70–1·03)		
		Bacteremia in surgical patients			Bacteremia in non-surgical patients			SDD/SOD decreased bacteremia in all patients
		SC: 86/973 (8.8 %)			84/1016 (8.3 %)			
		SOD: 50/866 (5.8 %)	$P < 0.05$		60/1038 (5.8 %)	$P < 0.05$		
		SDD: 39/923 (4.2 %)	$P < 0.05$		41/1111 (3.7 %)	$P < 0.05$		
Oostdijk et al. [13]	9 of 13 Dutch ICUs (NEJM 2009) with colistin susceptibility testing	Colistin susceptibility testing ($n = 1022$ patients)						Medium-term (24 months) acquisition of colistin-resistance
		Acquisition of rectal colistin-resistant microorganisms			2.4 (2.5–4.2)/1000 patient-days			
		Evolution from colistin-susceptible to colistin-resistant			1.7 % (1.0–2.7)			
Wittekamp et al. [14]	5 of 13 Dutch ICUs participating in 2 large studies: I: SC, SOD-I, SDD-I (NEJM 2009) 1007 respiratory and 1093 rectal samples obtained from 1189 patients II: SOD-II, SDD-II (JAMA 2014) 1755 respiratory and 1808 rectal samples obtained from 1865 patients		SC	SDD-I	SOD-I	SDD-II	SOD-II	Long-term SDD/SOD (over 7 years) decreased tobramycin resistance in rectal and respiratory samples
		Tobramycin resistance in rectal samples: [1] SDD-I vs SC: RR 0.54 (0.34–0.87) [2] SDD-I vs SOD-I: RR 0.46 (0.29–0.72) [3] SDD-II vs SDD-I: RR 0.64 (0.40–1.04) [4] SDD-II vs SC: RR 0.35 (0.23–0.53) [5] SOD-II vs SOD-I: RR 0.56 (0.39–0.78) [6] SOD-II vs SC: RR 0.66 (0.47–0.95)	12.1 %	6.6 %[1,2]	14 %	4.2 %[3,4]	8 %[5,6]	
		Tobramycin resistance in respiratory samples [1] SDD-I vs SC: RR 0.61 (0.38–1.00) [2] SDD-II vs SC: RR 0.48 (0.32–0.73) [3] SOD-II vs SOD-I: RR 0.48 (0.30–0.76) [4] SOD-II vs SC: RR 0.42 (0.27–0.64)	10.9 %	6.7 %[1]	9.7 %	5.3 %[2,3]	4.5 %[3,4]	
		Colistin resistance in rectal samples [1] SOD-II vs SC: RR 0.41 (0.17–0.98)	2.7 %	2.8 %	1.2 %	1.7 %	1.1 %[1]	Long-term SDD/SOD (over 7 years) did not increase resistance to colistin
		Colistin resistance in respiratory samples	0.9 %	2.1 %	1.7 %	1.1 %	0.6 %	

SDD selective decontamination of the digestive tract, *SOD* selective oropharyngeal decontamination, *SC* standard care, *NS* not significant, *APACHE II* acute physiology and chronic health evaluation II score, *ICU* intensive care unit, *OR* odds ratio, *RR* relative risk, *vs* versus, *95 % CI* 95 % confidence interval

and a lower volume of topical antibiotics [4]. Indeed, when SDD was compared with standard care, the use of cephalosporins was increased due to the SDD regimen, but the use of antimicrobial agents was reduced significantly for broad-spectrum penicillins, carbapenems, lincosamides, and quinolones [4]. This was also true for SOD, but the difference with standard care was less pronounced [4].

3. Recent SDD/SOD studies were all performed in the Netherlands where antimicrobial resistance is a minor concern with a low reported use of broad-spectrum antibiotics, such as piperacillin/tazobactam, cefepime, and carbapenems. Hence, a more pronounced gradual increase was observed with aminoglycoside-resistant Gram-negative bacteria with SDD [5]. The effects of the prolonged use of SDD and SOD on colistin resistance have been determined in a study performed on two different large ICU cohorts [13]. No association was observed between the use of SDD or SOD and increased acquisition of colistin-resistant Gram-negative bacteria in the respiratory tract. In another study performed on patients colonized with Enterobacteriaceae in the intestinal tract at ICU admission, SDD was shown to eradicate cephalosporin-resistant Enterobacteriaceae from the intestinal tract [11]. These findings are usually related to the fact that the studies are performed in environments with a lower incidence of highly-resistant microorganisms. By contrast, studies performed in countries with a higher incidence of highly-resistant microorganisms have also reported similar effects [17, 18].
4. Some observations were performed over a short period of time and resistance may not have been immediately apparent. Hence, a rebound effect after stopping SDD/SOD has been suggested in one of the post hoc analyses, as well as the emergence of colistin-resistant strains during persistent Gram-negative bacteria colonization over the study period (24 months) [13, 7]. Indirect evidence suggests that SDD/SOD is associated with the long-term alteration of the microbiota of the digestive tract and a potential increase in the associated resistome, but this remains largely speculative at the present time [19]. However, these effects were not confirmed in a very recent report on continuous surveillance of the impact of SDD and SOD up to 7 years [14]. This large study confirmed a continuous reduction of the rate of tobramycin resistance and the absence of emergence of resistance to colistin in both respiratory and rectal samples (Table 2). The occurrence of a rebound effect after the discontinuation of SDD/SOD use in these centres remains to be determined.

In conclusion, SDD and SOD are used in a minority of ICUs, despite the available data on survival benefit. Although antibiotic resistance is not shown to be associated with the use of SDD and SOD in the particular setting of experienced Dutch ICUs, some ecological changes in ICUs have been reported (Table 2). SDD has resulted in lower rectal carriage of antibiotic-resistant Gram-negative bacteria compared to SOD. SDD has demonstrated superiority over SOD, but both are related to a lower use of systemic antibiotics, other than those used during the first 4 days of SDD, and result in a lower mortality in ICU patients compared to standard care. Therefore, SOD can be viewed as a good alternative to SDD. However, the lower rate of bacteremia and bacterial resistance observed with SDD pleads in favor of this regimen. Further studies are planned in higher endemic resistance regions to assess the effect of SDD or SOD on long-term resistance development.

Compliance with ethical standards

Conflicts of interest JK has received honorarium from B&D and QXV Communications Ltd. PE has no conflict of interest.

References

1. Reis Miranda D, Citerio G, Perner A, Dimopoulos G, Torres A, Hoes A, Beale R, De Smet AM, Kesecioglu J (2015) Use of selective digestive tract decontamination in European intensive cares: the ifs and whys. Minerva Anestesiol 81:734–742
2. Krueger WA, Lenhart FP, Neeser G, Ruckdeschel G, Schreckhase H, Eissner HJ, Forst H, Eckart J, Peter K, Unertl KE (2002) Influence of combined intravenous and topical antibiotic prophylaxis on the incidence of infections, organ dysfunctions, and mortality in critically ill surgical patients: a prospective, stratified, randomized, double-blind, placebo-controlled clinical trial. Am J Respir Crit Care Med 166:1029–1037
3. de Jonge E, Schultz MJ, Spanjaard L, Bossuyt PM, Vroom MB, Dankert J, Kesecioglu J (2003) Effects of selective decontamination of digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. Lancet 362:1011–1016

4. de Smet AM, Kluytmans JA, Cooper BS et al (2009) Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med 360:20–31
5. Oostdijk EA, Kesecioglu J, Schultz MJ, et al. (2014) Effects of decontamination of the oropharynx and intestinal tract on antibiotic resistance in ICUs: a randomized clinical trial. JAMA 312:1429–1437
6. de Smet AM, Hopmans TE, Minderhoud AL, Blok HE, Gossink-Franssen A, Bernards AT, Bonten MJ (2009) Decontamination of the digestive tract and oropharynx: hospital acquired infections after discharge from the intensive care unit. Intensive Care Med 35:1609–1613
7. Oostdijk EA, de Smet AM, Blok HE, et al. (2010) Ecological effects of selective decontamination on resistant Gram-negative bacterial colonization. Am J Respir Crit Care Med 181:452–457
8. Benus RF, Harmsen HJ, Welling GW, Spanjersberg R, Zijlstra JG, Degener JE, van der Werf TS (2010) Impact of digestive and oropharyngeal decontamination on the intestinal microbiota in ICU patients. Intensive Care Med 36:1394–1402
9. Oostdijk EA, de Smet AM, Kesecioglu J, Bonten MJ, Dutch SOD-SDD Trialist Group (2011) The role of intestinal colonization with Gram-negative bacteria as a source for intensive care unit-acquired bacteremia. Crit Care Med 39:961–966
10. de Smet AM, Kluytmans JA, Blok HE, et al. (2011) Selective digestive tract decontamination and selective oropharyngeal decontamination and antibiotic resistance in patients in intensive-care units: an open-label, clustered group-randomised, crossover study. Lancet Infect Dis 11:372–380
11. Oostdijk EA, de Smet AM, Kesecioglu J, Bonten MJ, Dutch SOD-SDD Trialist Group (2012) Decontamination of cephalosporin-resistant Enterobacteriaceae during selective digestive tract decontamination in intensive care units. J Antimicrob Chemother 67:2250–2253
12. Melsen WG, de Smet AM, Kluytmans JA, Bonten MJ, Dutch SOD-SDD Trialist Group (2012) Selective decontamination of the oral and digestive tract in surgical versus non-surgical patients in intensive care in a cluster-randomized trial. Br J Surg 99:232–237
13. Oostdijk EA, Smits L, de Smet AM, Leverstein-van Hall MA, Kesecioglu J, Bonten MJ (2013) Colistin resistance in Gram-negative bacteria during prophylactic topical colistin use in intensive care units. Intensive Care Med 39:653–660
14. Wittekamp BH, Oostdijk EA, de Smet AM, Bonten MJ (2015) Colistin and tobramycin resistance during long-term use of selective decontamination strategies in the intensive care unit: a post hoc analysis. Crit Care 19:113
15. Vincent JL, Jacobs F (2011) Effect of selective decontamination on antibiotic resistance. Lancet Infect Dis 11:337–338
16. Daneman N, Sarwar S, Fowler RA, Cuthbertson BH, Su DCSG (2013) Effect of selective decontamination on antimicrobial resistance in intensive care units: a systematic review and meta-analysis. Lancet Infect Dis 13:328–341
17. de La Cal MA, Cerda E, Garcia-Hierro P, van Saene HK, Gomez-Santos D, Negro E, Lorente JA (2005) Survival benefit in critically ill burned patients receiving selective decontamination of the digestive tract: a randomized, placebo-controlled, double-blind trial. Ann Surg 241:424–430
18. Ochoa-Ardila ME, Garcia-Canas A, Gomez-Mediavilla K, Gonzalez-Torralba A, Alia I, Garcia-Hierro P, Taylor N, van Saene HK, de la Cal MA (2011) Long-term use of selective decontamination of the digestive tract does not increase antibiotic resistance: a 5-year prospective cohort study. Intensiv Care Med 37:1458–1465
19. Buelow E, Gonzalez TB, Versluis D et al (2014) Effects of selective digestive decontamination (SDD) on the gut resistome. J Antimicrob Chemother 69:2215–2223