SELEKTİF BARSAK DEKONTAMİNASYONU

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Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

Sunum planı

- SDD nedir?
  - Neden verilir?
  - Kimlere verilir?
  - Ne verilir?
- SDD çalışmaları
- Cerrahide SDD'nin yeri
- SDD neden yaygınlaşmadı?

Tanım

- SDD; endojen veya ekzojen enfeksiyon gelişimini önlemek için parenteral, enteral ve/veya topikal olarak uygulanan *antimikrobiyal profilaksi!!!*

SDD'nin amacı

- Aerobik Gram negatif bakteriler, S. aureus, mantarlar gibi potansiyel patojenik bakterilerin, orofarengeal veya intestinal taşıyıcılığını önlemek veya varsa eradike etmek!!!

SDD'nin felsefesi

- Özellikle YBÜ'de izlenen hastalarda florada normal taşıyıcılıktan anormal taşıyıcılığa, düşük düzey taşıyıcılıktan yüksek düzey taşıyıcılığa kayma olur.
- GIS aşırı üremesi (feçes veya tükrükte $>10^5$ cfu/ml); hem endojen enfeksiyon gelişimi hem de AB direnci için önemli bir risk faktörüdür.
- YBÜ'deki enfeksiyonların çoğundan 15 potansiyel patojen mikroorganizma sorumludur.
- YBÜ enfeksiyonlarının çoğu primer endojen enfeksiyonlar olup bunu sekonder endojen ve ekzojen enfeksiyonlar izler.

Enfeksiyon tipleri

Enfeksiyon tipi	Potansiyel patojenler	Başlangıç	İnsidans
Primer endojen	N /aN		
Sekonder endojen	aN		
Ekzojen	aN		

- **Taşıyıcılık:** 3-7 gün ara ile, boğaz ve/veya rektumdan alınan 2 ardışık sürveyans kültüründe aynı patojenin izole edilmesi
- Normal taşıyıcılık: S. pneumoniae, H. İnfluenzae, M. catarrhalis, S. aureus, E. coli, C. albicans
- Anormal taşıyıcılık: Klebsiella, Proteus, Morganella, Citrobacter, Enterobacter, Serratia, Acinetobacter, Pseudomonas spp, MRSA

Silvsetri L et al. Int Care Med 2012;38:1728-50.

SDD'nin felsefesi

Enfeksiyon tipi	Potansiyel patojenler	Başlangıç	İnsidans	Kontrol manevrası = SDD
Primer endojen	N /aN	< 1 hafta	% 55	Parenteral ABler
Sekonder endojen	aN	> 1 hafta	% 30	Hijyen + oral/enteral ABler
Ekzojen	aN	Herhangi bir zaman	% 15	Hijyen + topikal ABler

Silvsetri L et al. Int Care Med 2012;38:1728-50.

Kolonizasyon rezistansı

- Bağırsaklardaki olağan anaerobik flora, aerobik gram-negatif bakterilerin kolonizasyonuna engel olmaktadır.
- Anaerobik floranın ortadan kalkması ise aerobik bakterilerin kolonizasyonunun, takiben de bunlarla oluşan infeksiyonların artmasına neden olmaktadır.

Waay D et al. J Hyg 1969; 405:71

- SDD uygulamasındaki temel amaç; bağırsaklardaki anaerobik floraya zarar vermeden sindirim sistemindeki gram-negatif bakterilerin ve mantarların elimine edilmesidir.

Table 1. Description of selective decontamination of the digestive tract and selective oropharyngeal decontamination regimens

Intervention	Timing	Purpose
SDD and SOD regimens		
0.5 g of a paste containing polymyxin E, tobramycin and amphotericin B each in a 2% concentration applied in oropharynx	Four times daily until ICU discharge	Selective decontaminaton of the oropharynx
10 ml of a suspension containing 100 mg polymyxin E, 80 mg tobramycin and 500 mg amphotericin B via the nasogastric tube	Four times daily until ICU discharge	Selective decontaminaton of the gut from stomach to rectum
Cefotaxime 1 g i.v. during the first 4 days of study (or other third-generation cephalosporins)	Four times daily during the first 4 days	Preemptive treatment of primary infections
Avoidance of (systemic) antibiotics that might impair the colonization resistance, that is, with antianaerobic activity	During treatment with SDD, until ICU discharge	Avoidance of penicillins, carbapenems and so on
		No addition of antibiotics for patients with colonization without clinical signs suggestive for infection
Oropharyngeal endotracheal, and rectal cultures	On admission and twice weekly	Determination of colonization pattern at admission and during treatment, including monitoring of effectiveness of SDD

De smet AM et al, Cur Opp Infect Dis 2012; 25:211-17.

Parenteral Antibiyotikler

- Primer endojen enfeksiyonların önlenmesinde parenteral AB olarak *sefotaksim* tercih edilmesinin nedenleri;
  - Etki spektrumunun hem "normal" hem "anormal" bakterileri içermesi
  - Tükrük ve safraya yüksek oranda ekskresyonunu sağlayan farmakokinetik özellikleri

  (+Kolonizasyon rezistansında önemli yer tutan enterik anaerobik flora üzerinde etkisiz!)

Oral /Enteral Antibiyotikler

- Sekonder endojen enfeksiyonların önlenmesinde oral ve/veya enteral olarak uygulanan:

  *Polimiksin ve tobramisin kombinasyonu;

  - Pseudomanas spp dahil tüm anormal Gram negatif basilleri kapsaması
  - Sinerjistik etkili olması nedeniyle!

  *Amfoterisin B; mayaların eradikasyonunu sağlamak için!

  * MRSA endemik ise; enteral vankomisin eklenebilir.

Table 3 Full four component-strategy of SDD

Target PPM and antimicrobials	**Total daily dose [4 x daily]**		
	<5 years	5 – 12 years	>12 years
1. parenteral antimicrobials: 'normal' PPM cefotaxime (mg)	150/Kg	200/Kg	4000
2. enteral antimicrobials: 'abnormal' PPM A. oropharynx • AGNB : polymyxin E with tobramycin • MRSA : vancomycin • Yeasts : amphotericin B or nystatin	2 g of 2% paste or gel 2 g of 4% paste or gel 2 g of 2% paste or gel		
B. gut • AGNB : polymyxin E (mg) with tobramycin (mg) • MRSA : vancomycin (mg) • Yeasts : amphotericin B (mg) or nystatin (units)	100 80 20-40/Kg 500 2×10^6	200 160 20-40/Kg 1000 4×10^6	400 320 500-2000 2000 8×10^6
3. topical antimicrobials: 'abnormal' PPM	2% and 4% paste or gel on tracheostoma, wound		
4. surveillance cultures of throat and rectum on admission, Monday, Thursday	'Abnormal' PPM in overgrowth concentrations		

PPM = potentially pathogenic micro-organism; AGNB = aerobic Gram-negative bacilli;

Table 3 Antimicrobials selected for SDD to control overgrowth of both 'normal' and 'abnormal' flora

Antimicrobials selected for SDD	Concentrations (mg/L)		
	Saliva	Bile	Faeces
'Normal' flora			
Bacterial overgrowth Cefotaxime	6	20	
Yeast overgrowth amphotericin B or nystatin			60 <100
'Abnormal' flora			
AGNB overgrowth polymyxin E with tobramycin			16–1,000 100
MRSA overgrowth vancomycin			3,000–24,000

SDD selective digestive decontamination, *AGNB* aerobic Gram-negative bacilli, *MRSA* methicillin-resistant *Staphylococcus aureus*

Silvsetri L et al. Int Care Med 2012;38:1728-50.

SDD çalışmaları

- 1980'ler: 2 önemli çalışma!!!
  - Stoutenbeek CP et al.

    A new technique of infection prevention in the ICU by selective decontamination of the digestive tract.

    Acta Anaesthesiol Belg 3:209;13
  - Stoutenbeek CP et al.

    The effect of selective decontamination of the digestive tract on colonization and infection rate in multiple trauma patients.

    Intensive Care Med 1984;10:185-192

Intensive Care Med (1984) 10:185 – 192

Intensive Care Medicine

The effect of selective decontamination of the digestive tract on colonisation and infection rate in multiple trauma patients

C. P. Stoutenbeek[1], H. K. F. van Saene[2], D. R. Miranda[1] and D. F. Zandstra[1]

Table 4. Infection rate during ICU-stay

Site	Group I (control) $n = 59$	Group II (SDD) $n = 63$	x^2-value p value df = 120
Respiratory tract	35 (59%)	5 (8%)	$x^2 = 34.2$
Gram +	24	3	$p < 0.001$
Gram −	25	3	
Urinary tract	19 (32%)	1 (2%)	$x^2 = 18.7$
Gram +	9	—	$p < 0.001$
Gram −	13	1	
Blood	25 (42%)	2 (3%)	$x^2 = 24.9$
Gram +	20	2	$p < 0.001$
Gram −	13	—	
Wounds	15 (25%)	3 (5%)	$x^2 = 8.8$
Gram +	10	—	$p < 0.01$
Gram −	8	3	
Total number of infections	94	11	
Total number of infected patients	48 (81%)	10 (16%)	$x^2 = 49.8$ $p < 0.001$

Intensive Care Med (1984) 10:185 – 192

Intensive Care Medicine

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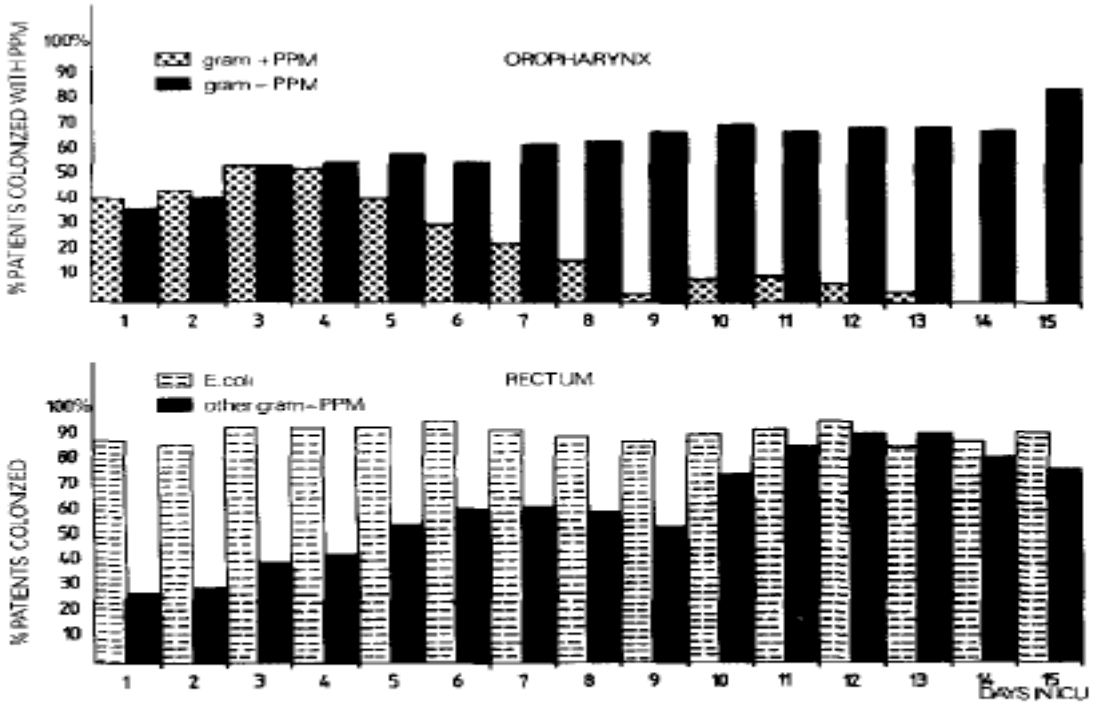


Fig. 1. Number of patients in group I (control) colonised by PPM in the oropharynx and intestines. The majority of patients was rapidly colonised by ICU-associated gram-negative bacilli in the oropharynx and later in the rectum

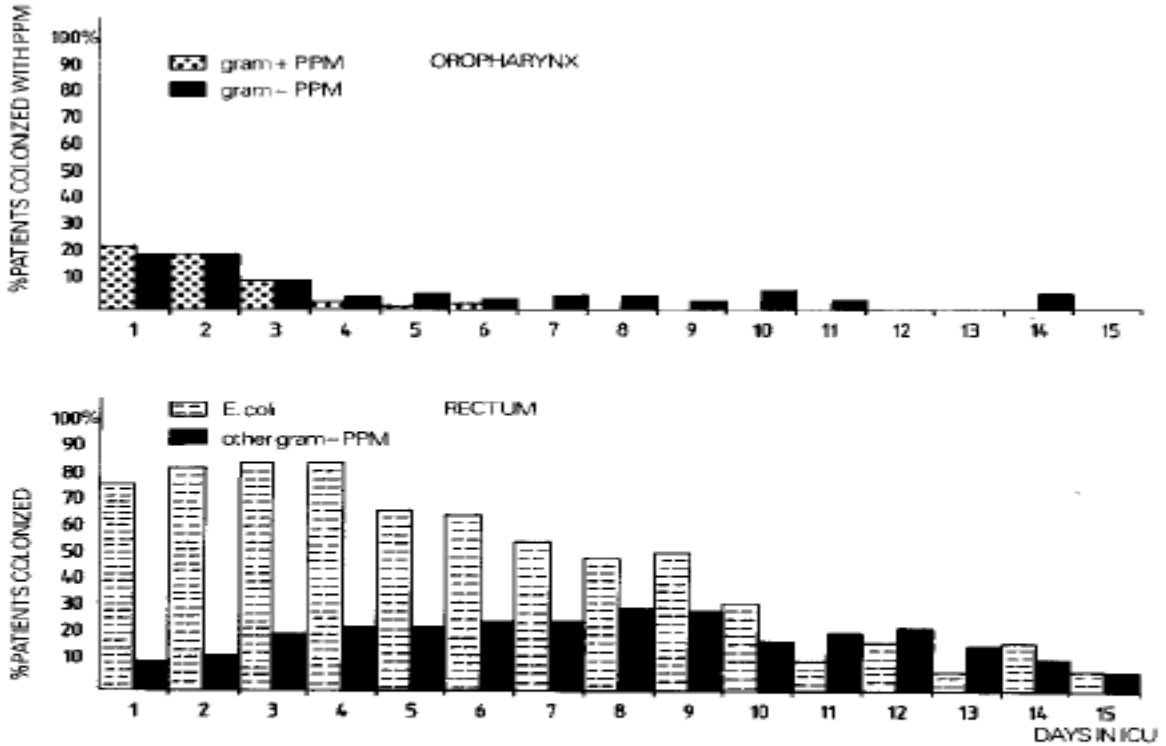


Fig. 2. Colonisation rate of selective decontaminated patients in group II (SDD). PPM were effectively eliminated from the oropharyngeal cavity, within 3 days. Secondary colonisation of the intestines was largely prevented. A significant reduction of rectal flora was achieved after 7 days ($p < 0.01$)

SDD çalışmaları

- 65 RCT
- 11 metaanaliz
- >15000 hasta
  - Çoğu çalışma YBÜ'de izlenen hastalarda
  - Çalışma sonlanım noktaları farklı

Table 1 Overview table efficacy of SDD: 65 RCTs and 11 meta-analyses

Author	No RCTs	Sample size	Lower airway infection OR (95 % CI)	Bloodstream infection OR (95 % CI)	Multiple Organ Dysfunction Syndrome OR (95 % CI)	Mortality OR (95 % CI)
Vandenbroucke-Grauls [68]	6	491	0.12 (0.08–0.19)	NR		0.92 (0.45–1.84)
D'Amico [69]	22	5,727	0.35 (0.29–0.41)	NR		0.80 (0.69–0.93)
Safdar						
Libera						
Silves						
Silves						
Silves						
G −v						
G +v						
Silves						
Libera						
Silves						
Silves						

SDD
G −v
[a] Yea
[b] Tra

- 11 metaanalizin sonlanım noktaları:
  - 6'sında pnömoni; hepsinde istatistiksel olarak anlamlı azalma!
  - 3'ünde kan dolaşımı enfeksiyonları
    - AGNB hepsinde istatistiksel olarak anlamlı azalma
    - Fungemi azalmış ama istatistiksel olarak anlamlı değil
    - Gr (+)ler artmış ama istatistiksel olarak anlamlı değil
  - 8'inde mortalite
    - 5'inde sağkalıma olumlu katkı,
    - 3'ünde hasta sayısının azlığına bağlı, istatistiksel olarak anlamlı azalma yok.
    - Tek tek RCTlerde de sağkalıma etki belirsiz

SDD-Mortalite

- SDD'nin sağkalıma etkisi tüm hastalara SDD uygulanan çalışmalarda daha belirgin;
  - Tüm hastalara SDD uygulandığında % 41
  - ½ hastaya SDD uygulandığında % 29
  - 1/3 hastaya SDD uygulandığında % 17

- Bu sonuç dekontaminasyon yapılan ve yapılmayan hastaların aynı ünitelerde izlenmesi sonucu temas yoluyla ekzojen enfeksiyonların önlenmesinin mümkün olmamasına ve SDDnin gerçek etkinliğinin dilüe olmasına bağlanmış.

De Jonge E et al. Lancet 2003;362:1011-16.

SDD-Direnç

- Bildiklerimiz:
  - Antibiyotiklerin yaygın kullanımı= Direnç!

- SDD ile ilgili çalışmalar:
  - Kullanılan ABlere direnç artışı yok
  - Hatta dirençte azalma var.

- Çekincemiz:
  - Direnç gelişimi için yeterli süre gözlem var mı?

SDD-Direnç

- 3 RCT'de sonlanım noktası AGNB direnci:
  - ESBL (+) Klebsiella'nın endemik olduğu bir hastanede
    - Kontrol grubunda kolonizasyon % 19.6, infeksiyon % 9
    - Enteral AB'lerin kullanımı ile oranlar %1 ve %0!
  - IMP, CAZ, CIP, TOB ve polimiksin'e dirençli AGNB taşıyıcılığı
    - Kontrol grubunda % 26, SDD grubunda % 16 ($p<0.05$)

- Parenteral ABler tek başına kullanıldıklarında safra ile barsağa ulaştıkları için letal konsantrasyonlara ulaşamamakta ve AGNB'nin aşırı üremesine neden olarak dirençli suşların seçimine neden olmaktalar.
- Enteral ABlerin eklenmesi yüksek düzey taşıyıcılığı dirençli mutantlar da dahil eradike etmekte!

De Smet AM et al. N Eng J Med 2009;360:20-31.

SDD-Direnç

- Enteral polimiksin/tobramisine dirençli AGNB varlığında;
  - Serratia spp polimiksin/tobramisin'e intrensek dirençli tek AGNB
    - Serratia endemisitesi varsa; polimiksin/paromisin veya gentamisin ile değiştirlmeli
  - ESBL (+) AGNBler polimiksine duyarlı olmakla birlikte tobramisine sıklıkla dirençli
    - ESBL (+) AGNB endemik ise; tobramisin, neomisin veya paromomisin gibi aktif bir aminoglikozidle değiştirilmeli

Direnç- Uzun dönem sonuçlar

Table 6 Long term studies of enteral polymyxin/tobramycin on AGNB resistance

Author	Study		Patients		% patients with carriage [surv] and/or infection [diag] due to resistant AGNB
	Type	Period	Type	Number	
Stoutenbeek [123]	Prosp observ	2½ years	Trauma	164	4% of patients carried E.coli resist to tobra Acinetob resist to tobra Pseudo resist to tobra
Leone [124]	Retrosp case-control	6 years	MV	720	No difference between test and control
Sarginson [125]	Prosp observ	4 years	Children ≥4 days of ventil	1241	4% of children were infected with resistant bacteria including MRSA
Heininger [126]	Prosp observ	5 years	MV >2 days	1913	0.05% of patients infected with E.coli resist to tobra

Surv = Surveillance samples; Diag = diagnostic samples

Direnç- Uzun dönem sonuçlar

Figure 1 Density of patients carrying resistant bacteria 1999-2004. No significant resistance patterns emerged over the five years,

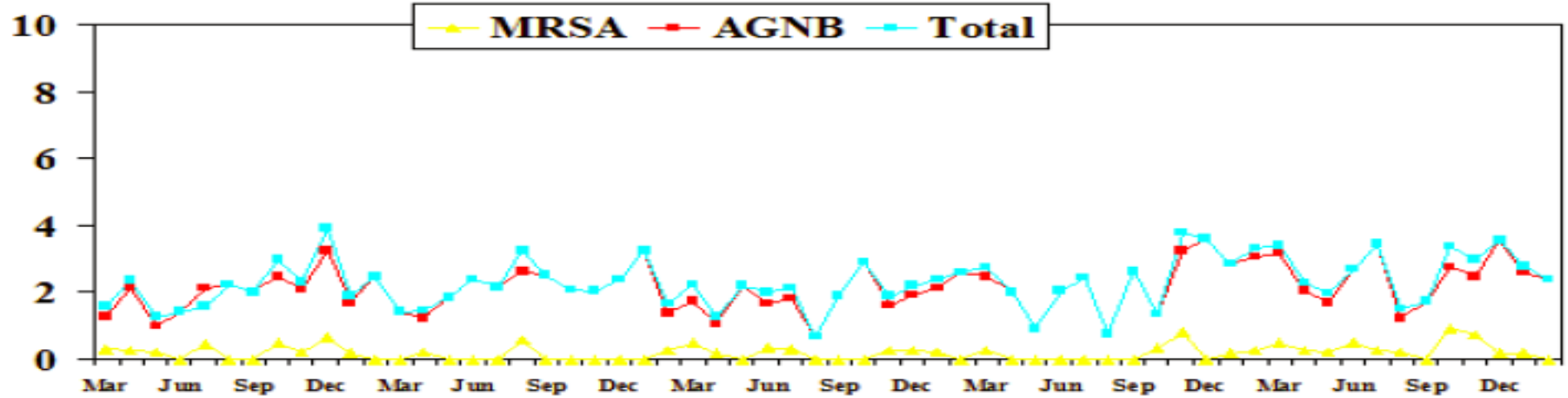
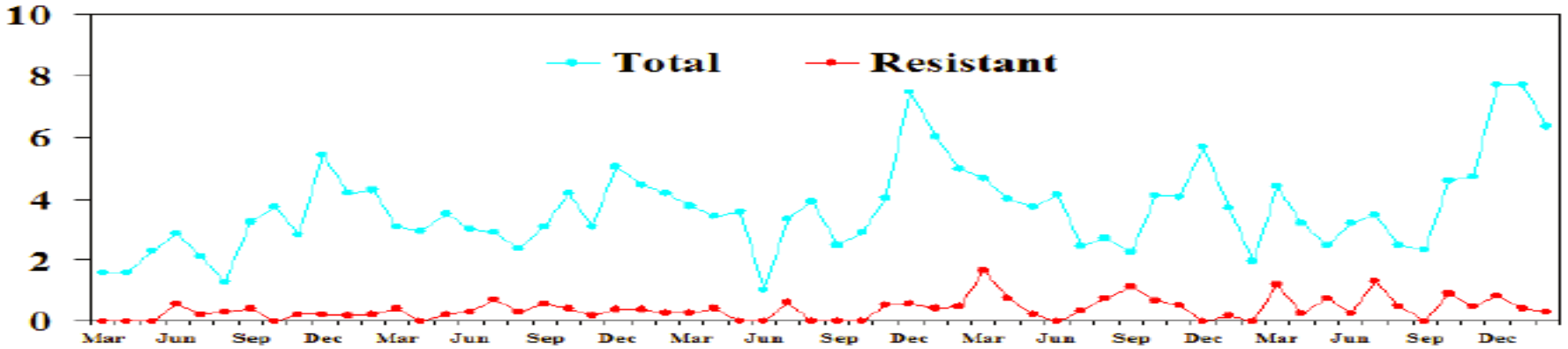


Figure 2 Density of patients with infections due to resistant micro-organisms 1999-2004



SDD- MRSA ve VRE

- 1980'lerde MRSA ve/veya VRE sorun patojen değil.
- 7 RCT'de çalışma sırasında MRSA endemik; SDD ile MRSA enfeksiyon oranlarında artış bildirilmiş.
  - Öneri: MRSA endemik ise enteral vankomisin eklenmeli.
- 2 RCT'de VRE endemik; taşıyıcılık ve enfeksiyon oranları SDD ve kontrol grubunda benzer

- Günümüzde; VISA?? VRE????

Silvestri L et al. Am J Infect Control 2002;30:391-99.

SDD- MRSA ve VRE uzun dönem sonuçlar

Table 7 Long term studies of enteral vancomycin on staphylococcal and enterococcal resistance

Author	Study		Patients		% patients with carriage [surv] and/or infection [diagn] due to VISA and/or VRE
	Type	Period	Type	Number	
de la Cal [127]	Prosp observ	4 years	Med/Surg >3 days of MV	799	13/799 [5%] carried VRE
Cerda [128]	Prosp observ	4 years	Burns	375	No emergence of VRE or VISA in either surv or diagn
					E or VISA in

- MRSAnın endemik olduğu YBÜ'lerde parenteral vanko kullanımı ile VISA suşlarının olması kaçınılmaz:
  - Enteral vankomisin kullanımı ile feçeste 3000mikrogram/ml'ye ulaşan konsantrasyonlarda var olan VISA suşları da eradike edilmekte.
- Bugüne kadar enteral vankomisinin VRE taşıyıcılığını önleme veya eradike etmesini değerlendiren bir çalışma yok.

SDD- Cerrahi

- SDD çalışmalarının çoğu YBÜ enfeksiyonlarının önlenmesi ile ilgili!

- Cerrahi ile ilgili çalışmaların da çoğu postoperatif dönemde YBÜ'de izlenen hastalarda yapışmış.

- Cerrahi alan enfeksiyonlarını önlemesi ile ilgili sınırlı sayıda çalışma var.

SDD – Kardiyak cerrahi

- SDD'nin kardiyak cerrahi hastalarında etkinliğinin değerlendirildiği 3 RCT'de
  - Enfeksiyon oranlarında azalma saptanırken, mortalitede istatistiksel olarak anlamlı azalma saptanmamış.

Nathens AB. Arch Surg 1999;134:170-76..

J Gastrointest Surg (2013) 17:2172–2178
DOI 10.1007/s11605-013-2379-y

REVIEW ARTICLE

Selective Decontamination of the Digestive Tract in Gastrointestinal Surgery: Useful in Infection Prevention? A Systematic Review

Gabor S. A. Abis · Hein B. A. C. Stockmann · Marjolein van Egmond · Hendrik J. Bonjer · Christina M. J. E. Vandenbroucke-Grauls · Steven J. Oosterling

Abstract

Introduction Gastrointestinal surgery is associated with a high incidence of infectious complications. Selective decontamination of the digestive tract is an antimicrobial prophylaxis regimen that aims to eradicate gastrointestinal carriage of potentially pathogenic microorganisms and represents an adjunct to regular prophylaxis in surgery.

Material and Methods Relevant studies were identified using bibliographic searches of MEDLINE, EMBASE, and the Cochrane database (period from 1970 to November 1, 2012). Only studies investigating selective decontamination of the digestive tract in gastrointestinal surgery were included.

Results Two randomized clinical trials and one retrospective case–control trial showed significant benefit in terms of infectious complications and anastomotic leakage in colorectal surgery. Two randomized controlled trials in esophageal surgery and two randomized clinical trials in gastric surgery reported lower levels of infectious complications.

Conclusion Selective decontamination of the digestive tract reduces infections following esophageal, gastric, and colorectal surgeries and also appears to have beneficial effects on anastomotic leakage in colorectal surgery. We believe these results provide the basis for a large multicenter prospective study to investigate the role of selective decontamination of the digestive tract in colorectal surgery.

SDD – GIS cerrahisi

Table 1 Summary of available studies on selective decontamination of the digestive tract (SDD) in gastrointestinal surgery

Author	Type of study	Type of surgery	Primary endpoint	Number (*N*, SDD)	Number (*N*, Control group)	Infection rate (SDD, %)	Infection rate (no SDD, %)	Anastomotic leakage (%)	SDD regimen
Roos et al. 2009	Retrospective analysis, prospective 3-year cohort	Colorectal surgery	Infection rate	76	86	7.9*	19.8*	11 (SDD) vs 26 (no SDD)*	Polymyxin B, tobramycin, amphotericin B
Taylor et al. 1994	RCT	Colorectal surgery	Infection rate	159	168	11.3*	23.2*	NR	Ciprofloxacin 500 mg orally
Roos et al. 2011	RCT	Colorectal surgery	Infection rate	143	146	19.6*	30.8*	6.3 (SDD) vs 15.1 (no SDD)*	Polymyxin B, tobramycin, amphotericin B
Schardey et al. 1997	RCT	Gastrectomy	Infection rate	102	103	30.4 *	44.7 *	2.9 (SDD) vs 10.6 (no SDD)*	Polymyxin B, tobramycin, amphotericin B, vancomycin
Farran et al. 2008	RCT	Esophagectomy and Gastrectomy	Infection rate	40	51	12.5 NS	19.6 NS	2.5 (SDD) vs 5.9 (no SDD) NS	Erythromycin, gentamicin, nystatin
Tetteroo et al. 1990	RCT	Esophagectomy	Infection rate	56	58	18 infections in 12 patients *	51 infections in 32 patients *	NR	Polymyxin E, tobramycin, amphotericin B

NA non-applicable, *NR* not reported, *NS* not significant

*Significant

Abis GS et al. J Gastrointest Surg 2013;17:2171-78.

SDD – Ösefageal & Gastrik cerrahi

- Ösefagektomi uygulan 112 hasta, SDD vs standart pre-op profilaksi:
  - SDD grubunda 12 hastada 18 enf
  - Kontrol grubunda 32 hastada 51 enf ($p<0.001$)
  - Daha az ASYE ve yara enf bildirmişler.
- Gastrektomi uygulanan 205 hasta, SDD vs plasebo;
  - Anostomoz kaçağı % 2.9 vs %10.6 ($p<0.05$)
  - Pnömoni % 8.8 vs % 22.3 ($p<0.05$)
  - Mortalite %4.9 vs %10.6 ($p>0.05$)

Abis GS et al. J Gastrointest Surg 2013;17:2171-78.

SDD- Kolorektal cerrahi

Table 1 Summary of available studies on selective decontamination of the digestive tract (SDD) in gastrointestinal surgery

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Abis GS et al. J Gastrointest Surg 2013;17:2171-78.

J Gastrointest Surg (2009) 13:1839–1844
DOI 10.1007/s11605-009-0970-z

ORIGINAL ARTICLE

Perioperative Selective Decontamination of the Digestive Tract (SDD) in Elective Colorectal Surgery

Daphne Roos · Lea M. Dijksman · Brigitte M. Sondermeijer · Heleen M. Oudemans-van Straaten · Laurens T. de Wit · Michael F. Gerhards

Table 3 Endpoints

	SDD (n=76)	Control (n=86)	p value
Hospital stay in days, median (IQR)	10 (8–13)	10 (7–13)	0.980
Patients with infectious complications[a], n (%)	6 (8)	17 (20)	0.031
Urinary tract infection	2 (3)	9 (11)	0.048
Pneumonia	3 (4)	5 (6)	0.724
Wound infection	0	4 (5)	0.123
Intra-abdominal abscess	2 (3)	1 (1)	0.601
Patients with anastomotic leakage, n (%)	2 (3)	6 (7)	0.284
Patients with infectious complications and anastomotic leakage (combined endpoint), n (%)	8 (11)	22 (26)	0.014
Patients with non-infectious complications, n (%)[a]	15 (20)	19 (22)	0.713
Cardiopulmonary[b]	9(12)	10(12)	0.966
Neurologic (CVA, delier)	2 (3)	3 (4)	1.00
Abdominal (non-infectious)[c]	7 (9)	13 (15)	0.254
Patients with a relaparotomy, n (%)	6 (8)	7 (8)	0.937
No. of patients with complications, n (%)	19 (25)	32 (38)	0.085
Mortality, n (%)	0	3 (4)	0.248

Randomized clinical trial

Randomized clinical trial of perioperative selective decontamination of the digestive tract *versus* placebo in elective gastrointestinal surgery

D. Roos[1], L. M. Dijksman[2], H. M. Oudemans-van Straaten[3], L. T. de Wit[1], D. J. Gouma[4] and M. F. Gerhards[1]

Table 2 Effect of selective decontamination on primary and secondary endpoints

	SDD ($n = 143$)	Placebo ($n = 146$)	P**
Total no. of patients with complications	47 (32·9)	67 (45·9)	0·024
No. with infectious complications	28 (19·6)	45 (30·8)	0·028
Pneumonia	8 (5·6)	9 (6·2)	0·837
Urinary tract infection	3 (2·1)	11 (7·5)	0·031
Wound infection	10 (7·0)	19 (13·0)	0·089
Clostridium	1 (0·7)	1 (0·7)	1·000††
Anastomotic leakage†	9 (6·3)	22 (15·1)	0·016
No. with non-infectious complications	20 (14·0)	22 (15·1)	0·794
Cardiopulmonary‡	10 (7·0)	12 (8·2)	0·694
Neurological§	1 (0·7)	2 (1·4)	1·000††
Abdominal (non-infectious)¶	15 (10·5)	16 (11·0)	0·897
No. with one or more relaparotomies#	15 (10·5)	19 (13·0)	0·505
Hospital stay (days)*	11 (9–14)	12 (9–18)	0·055‡‡
Death	6 (4·2)	5 (3·4)	0·732††
Readmission	12 (8·4)	9 (6·2)	0·466

Roos D et al. British Journal of Surgery 2011;98:1365-72.

SDD- Cerrahi

- Kolorektal cerrahilerde sıklıkla uygulanan absorbe olmayan oral ABler (neomisin-eritromisin-metronidazol) + i.v. AB kombinasyonu;
  - Tek başına i.v. AB profilaksisi ile karşılaştırıldığında pek çok çalışmada CAE'yi azaltmada yararlı bulunmuş.
  - Bu kombinasyon hem aerop hem de anaerop bakteri yükünü azaltmakta.
  - Hiçbir çalışmada anostomoz kaçakları üzerine etki değerlendirilmemiş.
  - Absorbe olayan AB'ler ve SDD'nin karşılaştırıldığı çalışma yok!!!

- SDD özellikle kolorektal cerrahilerde umut verici!!!

SDD neden yaygınlaşmadı?

- Etkinlik?
- Maliyet?
- Direnç?
- Temin sorunu?

Etkinlik

Dekontaminasyon çalışmalarının etkinliğini değerlendirirken *optimal sonlanım noktası* belirsiz!!!!

- VİP:
  - Orofarengeal uygulanan ABler kültür sonuçlarını etkilemekte ve VİP tanısını zorlaştırmakta!
- Mortalite;
  - Mevcut çalışmalarda SDD'nin sağkalıma katkısını tam gösterebilmek için hasta sayıları yetersiz. (2000 hastalık gruplar ideal)
  - Mortalite analizlerinin çoğunda YBÜ mortalitesi veya 28 gün mortalitesi esas! Uzun dönem etki bilinmiyor!!!

Etkinlik

- SDD'nin etkinliğini değerlendiren ve etkili bulan çoğu çalışma AB direncinin düşük olduğu Avrupa ülkelerinde!!!
- Dirençli patojenlerin yüksek oranda görüldüğü merkezlerde SDD'nin etkinliğini değerlendiren çalışma yok.
- Kanıt düzeylerinin yüksek olaması için önerilen çift kör RCTler SDD çalışmalarında yapılamıyor.

- Sonuç: Gerçek etkinlik çelişkili!!!

Maliyet

- SDD ile standart tedavi maliyetini karşılaştıran çalışma sayısı az.

- Çalışmalarda bildirilen maliyetler değişken:
  - SDD 12 US $ vs SOD 1 US $
  - SDD 200 € vs SOD 40 €

- Mevcut çalışmaların çoğu AB direncinin düşük olduğu ülkelerde.

Oostdijk EAN et al. Intensive Care Med 2012;38:533-38.
De Smet AM et al. N engl J Med 2009;360:20-31

BMJ open
accessible medical research

Selective decontamination of the digestive tract and selective oropharyngeal decontamination in intensive care unit patients: a cost-effectiveness analysis

Evelien A N Oostdijk,[1,2] G A de Wit,[3,4] Marina Bakker,[1] Anne Marie G A de Smet,[5] M J M Bonten,[1,3] on behalf of the Dutch SOD-SDD trialists group

Table 1 Costs used per unit

Category	Prices per unit
Length of stay	
Day in ICU	€2183[11]
Day in hospital ward	€505[11]
Mechanical ventilation, additional costs	€327.45[15–17]
Topical antibiotics	
Cost of SOD per day	€0.87[3 42]
Cost of SDD per day	€10.48[3 42]
Microbiology	
Blood culture	€11.89 per culture+€12.90 order rate*
Throat culture	€7.78 per culture+€12.90 order rate*
Sputum culture	€7.78 per culture+€12.90 order rate*
Bronchoalveolar lavage	€7.78 per sample+€12.90 order rate*
Rectum culture	€7.78 per sample+€12.90 order rate*
Species determination	Extra €13.00 per isolate+€18.52*
Resistance profile determination	8.96 per isolate
Antibiotics	According to GIP database[18]

*UMCU costs.
SC, standard care; SDD selective decontamination of the Digestive tract; SOD, selective oropharyngeal decontamination.

Table 3 Total costs (2009 €) per patient

	SC N=1990	SOD N=1904	SDD N=2045
Length of stay			
ICU	€29553.45 (€28152.40 to €30954.49)	€28684.46 (€27412.05 to €29956.87)	€29069.78 (€27636.40 to €30503.16)
Hospital	€8621.85 (€8059.10 to €9184.61)	€7830.55 (€7345.91 to €8315.20)	€7963.94 (€7476.75 to €8451.13)
MV	€3225.06 (€3045.61 to €3404.51)	€3316.36 (€3151.14 to €3481.58)	€3308.18 (€3116.09 to €3500.27)
Total	€41400.36 (€39672.04 to €43128.68)	€39831.37 (€38261.92 to €41400.82)	€40341.90 (€38599.66 to €42084.14)
Study medication	–	€3.48 (€3.47 to €3.49)	€41.35 (€41.07 to €41.62)*
Systemic Antibiotics	€358.29 (€321.34 to €395.24)	€317.65 (€280.89 to €354.42)	€439.14 (€406.69 to €471.59)
Microbiology			
Rectal swabs	–	–	€102.75 (€97.64 to €107.86)
BAL	€6.44 (€5.42 to €7.46)	€4.70 (€3.92 to €5.49)	€4.77 (€4.01 to €5.53)
Sputum	€114.83 (€106.87 to €122.79)	€135.85 (€127.99 to €143.71)	€117.57 (€110.78 to €124.36)
Throat	€8.12 (€6.39 to €9.84)	€86.66 (€83.07 to €90.25)	€89.65 (€85.68 to €93.63)
Blood	€52.61 (€48.74 to €56.49)	€53.72 (€49.64 to €57.79)	€45.45 (€41.87 to €49.04)
Total	€182.15 (€170.60 to €193.69)	€280.93 (€267.00 to €294.87)	€360.73 (€343.69 to €377.76)
Total	€41940.79 (€40183.93 to €43697.66)	€40433.42 (€38837.50 to €42029.35)	€41183.12 (€39408.39 to €42957.85)

Mean (95% CI)*Excluding cefotaxim. Cefotaxim use is included in total systemic antibiotic use.
BAL, Brancheoalveolar Lavage; ICU, intensive care unit; MV, mechanical ventilation; SC, standard care; SOD, Selective Oropharyngeal Decontamination; SDD, Selective Decontamination of the Digestive tract.

Table 4 Outcomes of cost-effectiveness comparisons across groups

	LYG*	Cost difference	ICER
SOD vs SC (95% CI)	+0.25 (−0.05 to 0.55)	−€1507.37 (−€3186.45 to €171.72)	SOD dominates SC
SDD vs SC (95% CI)	+0.04 (−0.26 to 0.34)	−€757.67 (−€2522.56 to €1007.21)	SDD dominates SC
SOD vs SDD (95% CI)	+0.21 (−0.09 to 0.51)	−€749.69 (−€2439.35 to €939.97)	SOD dominates SDD

*Effects are discounted at 1.5% a year.
ICER, incremental costs effectiveness ratio (costs/LYG); LYG, life years gained; SC, Standard Care; SDD, Selective Decontamination of the Digestive tract; SOD, Selective Oropharyngeal Decontamination.

Oostdijk EAN et al. BMJ open 2013;3:e002529

Direnç

- SDD'nin direnci arttırmadığı, hatta azalttığı yönündeki verilerin aksini savunanların görüşü:
  - Bu konudaki kanıtlar sıradışı olarak düşük direnç profiline sahip YBÜ'lerden gelmekte
  - Gözlem süreleri çok kısa
  - SDD profilaksisi ile pekçok dirençli patojen kapsanamakta.
  - SDD'yi kestikten sonra rekolonizasyon olup olmadığı bilinmiyor.

Effect of selective decontamination on antimicrobial resistance in intensive care units: a systematic review and meta-analysis

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Summary

Background Many meta-analyses have shown reductions in infection rates and mortality associated with the use of selective digestive decontamination (SDD) or selective oropharyngeal decontamination (SOD) in intensive care units (ICUs). These interventions have not been widely implemented because of concerns that their use could lead to the development of antimicrobial resistance in pathogens. We aimed to assess the effect of SDD and SOD on antimicrobial resistance rates in patients in ICUs.

Methods We did a systematic review of the effect of SDD and SOD on the rates of colonisation or infection with antimicrobial-resistant pathogens in patients who were critically ill. We searched for studies using Medline, Embase, and Cochrane databases, with no limits by language, date of publication, study design, or study quality. We included all studies of selective decontamination that involved prophylactic application of topical non-absorbable antimicrobials to the stomach or oropharynx of patients in ICUs, with or without additional systemic antimicrobials. We excluded studies of interventions that used only antiseptic or biocide agents such as chlorhexidine, unless antimicrobials were also included in the regimen. We used the Mantel-Haenszel model with random effects to calculate pooled odds ratios.

Findings We analysed 64 unique studies of SDD and SOD in ICUs, of which 47 were randomised controlled trials and 35 included data for the detection of antimicrobial resistance. When comparing data for patients in intervention groups (those who received SDD or SOD) versus data for those in control groups (who received no intervention), we identified no difference in the prevalence of colonisation or infection with Gram-positive antimicrobial-resistant pathogens of interest, including meticillin-resistant *Staphylococcus aureus* (odds ratio 1·46, 95% CI 0·90–2·37) and vancomycin-resistant enterococci (0·63, 0·39–1·02). Among Gram-negative bacilli, we detected no difference in aminoglycoside-resistance (0·73, 0·51–1·05) or fluoroquinolone-resistance (0·52, 0·16–1·68), but we did detect a reduction in polymyxin-resistant Gram-negative bacilli (0·58, 0·46–0·72) and third-generation cephalosporin-resistant Gram-negative bacilli (0·33, 0·20–0·52) in recipients of selective decontamination compared with those who received no intervention.

Interpretation We detected no relation between the use of SDD or SOD and the development of antimicrobial-resistance in pathogens in patients in the ICU, suggesting that the perceived risk of long-term harm related to selective decontamination cannot be justified by available data. However, our study indicates that the effect of decontamination on ICU-level antimicrobial resistance rates is understudied. We recommend that future research includes a non-crossover, cluster randomised controlled trial to assess long-term ICU-level changes in resistance rates.

	Year	Country	Study design	Number of ICUs	Number of patients			
					SDD	SOD	Control	Total
Melsen et al[85]*	2012	Netherlands	RCT (cluster/crossover)	13	2034	1904	1989	5927
Oostdijk et al[84]*	2011	Netherlands	RCT (cluster/crossover)	14	2667	2166	1945	6778
Ochoa Ardilla et al[83]	2011	Spain	Prospective cohort	1	1588	0	0	1588
De Smet et al[82]*	2011	Netherlands	RCT (cluster/crossover)	13	2034	1904	1989	5927
Abecasis et al[81]	2011	UK	Prospective cohort	1	39	0	0	39
Oudhuis et al[87]	2011	Netherlands	RCT (crossover)	1	124	0	130	254
Oostdijk et al[86]*	2010	Netherlands	Before and after	13	2034	1904	1989	5927
Benus et al[80]*	2010	Netherlands	RCT (cluster/crossover)	13	86	111	140	397
De Smet et al[32]*	2009	Netherlands	RCT (cluster/crossover)	NA	335	331	327	993
Koeman et al[78]	2008	Netherlands	RCT (parallel)	NA	0	128	257	385
De Smet et al[79]*	2008	Netherlands	RCT (cluster/crossover)	13	2034	1904	1989	5927
Heininger et al[76]	2006	Germany	Prospective cohort	1	1913	0	5357	7270
al Naeimi et al[77]	2005	Netherlands	Case series	1	4	0	0	4
Leone at al[75]‡	2005	France	Prospective cohort	1	159	0	0	159
de La Cal et al[74]†	2005	Spain	RCT (parallel)	1	53	0	54	107
Camus et al[73]	2005	France	RCT (parallel)	3	0	389	127	515
Van Der Voort et al[72]	2004	Netherlands	Before and after	1	529	0	513	1042
Garbino et al[64]	2004	Switzerland	RCT (parallel)	NA	110	0	110	220
de La Cal et al[71]†	2004	Spain	Before and after	1	401	0	398	799
Leone et al[70]‡	2003	France	Retrospective cohort	1	369	0	360	720
De Jonge et al[69]	2003	Netherlands	RCT (cluster)	2	466	0	468	934
Damjanovic et al[84]	2003	UK	Retrospective cohort	1	76	0	30	106
Rayes et al[67]	2002	Germany	RCT (parallel)	1	32	0	63	95
Pneumatikos et al[68]	2002	Greece	RCT (parallel)	1	30	0	31	61
Leone et al[66]‡	2002	France	Case control	1	159	0	163	324
Krueger et al[65]	2002	Germany	RCT (parallel)	2	265	0	262	527
Nardi et al[63]	2001	Italy	RCT (parallel)	1	223	0	0	223
Bergmans et al[62]	2001	Netherlands	RCT (cluster/parallel)	3	0	87	139	226
Barret et al[61]	2001	USA	RCT (parallel)	1	11	0	12	23
Dahms et al[60]	2000	USA	Retrospective cohort	1	54	0	542	596
Sanchez-Garcia et al[59]	1998	Spain	RCT (parallel)	5	131	0	140	271
Ruza et al[58]	1998	Spain	RCT (parallel)	1	116	0	110	226
Varwaest et al[57]	1997	Belgium	RCT (parallel)	1	393	0	185	578
Lingnau et al[56]	1997	Austria	RCT (parallel)	1	162	0	148	310
Abele-Horn et al[55]	1997	Germany	RCT (parallel)	1	0	58	30	88
Quinio et al[54]	1996	France	RCT (parallel)	1	76	0	72	148
Wiener et al[53]	1995	USA	RCT (parallel)	1	30	0	31	61
Luiten et al[51]	1995	Netherlands	RCT (parallel)	16	50	0	52	102
Hammond et al[52]	1995	South Africa	Before and after	1	719	0	809	1528
Georges et al[50]	1994	France	RCT (parallel)	1	31	0	33	64
Ferrer et al[49]	1994	Spain	RCT (parallel)	1	51	0	50	101
Bion et al[48]	1994	UK	RCT (parallel)	1	32	0	27	59
Tetteroo et al[46]	1993	Netherlands	Prospective cohort	1	97	0	0	97
Smith et al[47]	1993	USA	RCT (parallel)	1	18	0	18	36
Korinek et al[45]	1993	France	RCT (parallel)	2	63	0	60	123
Winter et al[43]	1992	UK	RCT (parallel)	1	91	0	85	176
Rocha et al[42]	1992	Spain	RCT (parallel)	1	47	0	52	101
Hammond et al[41]	1992	South Africa	RCT (parallel)	1	114	0	125	239
Gastinne et al[40]	1992	France	RCT (parallel)	15	220	0	225	445
Cockerill et al[39]	1992	USA	RCT (parallel)	NA	75	0	75	150

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	Year	Country	Study design	Number of ICUs	Number of patients			
					SDD	SOD	Control	Total
Cerra et al[38]	1992	USA	RCT (parallel)	1	25	0	23	48
Zobel et al[37]	1991	Austria	RCT (parallel)	1	25	0	25	50
Pugin et al[36]	1991	Switzerland	RCT (parallel)	1	0	25	27	52
Fox et al[35]	1991	UK	Non-RCT	1	129	0	12	141
Aerdts et al[34]	1991	Netherlands	RCT (parallel)	1	21	17	18	56
Rodriguez-Roldan et al[33]	1990	Spain	RCT (parallel)	2	0	13	15	28
Godard et al[32]	1990	France	RCT (crossover)	1	112	0	97	209
Flaherty et al[31]	1990	USA	Non-RCT	1	0	51	56	107
Ulrich et al[30]	1989	Netherlands	RCT (parallel)	1	52	0	48	100
Brun-Buisson et al[29]	1989	France	RCT (parallel)	1	26	0	174	210
Ledingham et al[28]	1988	UK	Before and after	1	161	0	163	324
Kerver et al[27]	1988	Netherlands	RCT (parallel)	1	49	0	47	96
Unertl et al[26]	1987	Germany	RCT (parallel)	1	20	0	19	39
Stoutenbeek et al[25]	1987	Netherlands	Before and after	1	105	0	59	164

ICU=intensive care unit. NA=data not available. SDD=selective decontamination of the digestive tract. SOD=selective oropharyngeal decontamination. *Group of studies re-examining study population from De Smet et al.[79] †Group of studies re-examining study population from de La Cal et al.[71] ‡Group of studies re-examining study population from Leone et al.[66]

Table 1: General characteristics of identified studies

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Short Communication

Rapid emergence of secondary resistance to gentamicin and colistin following selective digestive decontamination in patients with KPC-2-producing *Klebsiella pneumoniae*: a single-centre experience

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ABSTRACT

After a single patient was transferred to Leipzig University Hospital from a hospital in Rhodes, Greece, KPC-2- October ecutive (SDD), pplying s were llowed od was f three hieved 5 (30%) istance ates. In in this pment.

- KPC-2 KP dekolonizasyonu;
  - SDD grubunda 6/14 (% 43) hastada,
  - Kontrol grubunda 23/76 (%30) hastada (p=0.102)
- SDD ile tedavi sonrası izolatlarda
  - kolistine % 19!!!!
  - gentamisine %45 direnç artışı!!!!
  - Kontrol grubunda sekonder direnç artışı yok

Ticari destek sorunu

- SDD'nin macun, jel veya süspansiyon formları hiçbir ilaç firması tarafından desteklenmemekte ve piyasada bulunmamakta!!!
- SDD'yi kullanan merkezler AB'lerin parenteral formlarını alarak kendi hastanelerindeki eczacılara uygun doz ve formlarda hazırlatmaktalar!!!

Sonuç

- SDD düşük AB direnç profiline sahip YBÜ'lerde VİP başta olmak üzere enfeksiyon oranlarını azalttığı gösterilmiş bir yaklaşım.

- Hastanede kalış süresi, mortalite gibi sonlanım noktalarındaki etkileri değişken.

- Dirençli patojenlerin endemik olduğu hastanelerde yapılacak çalışmalara ihtiyaç var.

- SDD'nin cerrahi alan enfeksiyonlarının önlenmesindeki etkinliği ile ilgili daha çok yolumuz var.


TEŞEKKÜR EDERİM