

Prevention of HAI in Burns Patients

Issues of Infection in Burns Patients

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Introduction

- Burn
 - Severe trauma
 - Fourth most common trauma type in the world, getting behind traffic accidents, crashes and interpersonal violence
 - Social, economic and public health repercussions
 - Great complexity
 - Treatment difficult (multidisciplinary)
 - High rates morbimortality

Carolina Oliveira de Souza: Caracterização do perfil epidemiológico dos queimados do Brasil: Revisão sistemática da literatura, 2016

Brazil

ALAGOAS

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- 55 hospita
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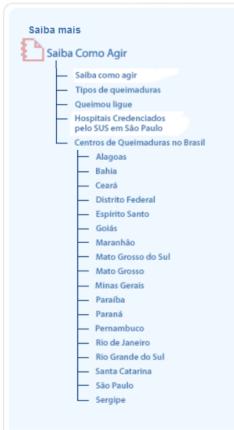
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Veja também



Manual de prevenção

Brazil

Carolina Oliveira de Souza: Characterization of the epidemiological profile of the burn patients in Brazil: systematic review of the literature, 2016

Tabela 1	: Resultae	dos das variá	iveis analis	sadas				
Autor (ano)	Região do Brasil	Mês Incidente	Idade	Sexo	SCQ / Profundidade	Agente Etiologico	Área corporal	Intenção/ Local
Leão <i>et al</i> (2011)	SE	-	29 anos	Masc	20,80%	Líquido Inflamável	Tórax anterior	Acidental
Biscegli <i>et</i> <i>al</i> (2014)	SE	-	< 6 anos	Masc	18%	Escaldadura	Tórax	Acidental/ domicílio
Fernandes et al(2012)	NE	Junho		Masc	2º grau	Escaldadura	Tórax	Acidental/ domicílio
Gawrysze wski <i>et al</i> (2012)	23 capitais e DF	-	20 a 29 anos	Masc	-	Escaldadura	MMSS	Acidental/ domicílio
Haack <i>et al</i> (2008)	S	Dezembro - Março	15 a 19 anos	Fem	1º grau	Solar	-	Acidental/ praia
De-Souza et al(1998)	SE	-	0 a 9 anos	Masc	20%	Chama direta	-	Acidental/ domicílio
Macedo <i>et</i> <i>al</i> (2011)	СО	-	24 anos	Masc	14%	Chama direta	-	Acidental/ domicílio
Silva <i>et al</i> (2009)	NE	-	< 3 anos	Masc	16,63% / 2º grau	Escaldadura	-	Acidental/ domicílio
Cruvinel <i>et</i> <i>al</i> (2005)	NE	-	22,66 anos	Masc	1º grau	Líquido Inflamável	MMSS	
Marques et al(2014)	S	-	35,4 anos	Fem	20,45%	Chama direta	-	Acidental/ domicílio
Marchesan et al (1997)	Bracil	-	<30 anos	Fem	52,40%	Alcool	-	Suicídio/ domicílio
Piccolo et al (1991)	СО	-	15-44 anos	Masc	<40%	Escaldadura	-	Acidental/ domicílio
Rossi <i>et al</i> (1998)	SE	-	<3 anos	Masc	>40% / 2º e 3º grau	Escaldadura	Cabeça e MMSS	Acidental/ domicílio

Brazil

- Mean age = 20 and 30 years for adults and below 9 years for children
- Only 1 study researched incidence according to the month (June more incidence due to parties)
- Areas most affected were thorax and upper limbs
- The most prevalent etiological agents were flammable liquids and scald, but in cases of self-extermination the direct flame was the most predominant.
- The total body surface area (TBSA) range for 14 to 20%
- Depth of the burn more prevalent were 1º and 2º degrees
- Most burns are accidental and occur at home

Carolina Oliveira de Souza: Caracterização do perfil epidemiológico dos queimados do Brasil: Revisão sistemática da literatura, 2016

Classification of Burn Wounds

- Depth
 - 1º, 2º, 3º, 4º degrees
- Extension
 - Total body surface area (%)

- Inhalatory injury
- Politrauma

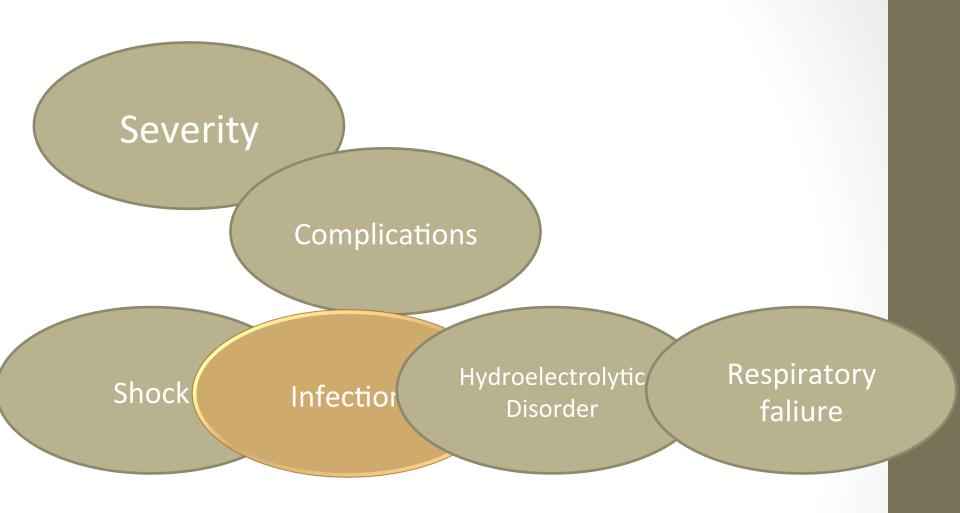
examples of burn degrees. First-degree burn (a). Second-degree burn (b). Third-degree burn (c). Fourthdegree burn (d). Histologic overview (e) Type (Degrees) of Burns Fourth Epidermii

Fig 1. Classification of burn wounds' depth. Clinical

Burn Severity

Conditions that classify severe burn:

- Extension greater than 20% TBSA in adults.
- Extension greater than 10% TBSA in children.
- Age less than 3 years or greater than 65 years.
- Presence of inhalation injury.
- Politrauma and associated prior diseases.
- Chemical burn.
- Electrical trauma.
- Noble / special areas (perineum).
- Violence, ill-treatment, self-extermination (suicide).



Besides the loss of skin function, burn injury provokes an inflammatory response leading to a state of immunologic dysfunction.

As a consequence, burn patients are at high risk of infection

Infection x Mortality

- Patients with TBSA > 40%
- 75% die due to infection
- Mortality => has been decreasing
 - New tecnologies
 - Early surgical procedures
 - Medicines/Treatments

Challenges ?







Challenges



- Diagnosis of burn infection
 - Clinical criteria
 - Microbiological criteria
- Use of antiseptics / antimicrobials
 - Topic
 - Systemic (prophylactic)
- Contact Precautions
- Therapeutic drug monitoring of antimicrobials
- Selective digestive decontamination (SDD)

Clinical Criteria – Wound Burn

Signs and Symptoms of Burn Infection:

- Change in the color of the lesion.
- Edema of edges of the wounds or **
- Deepening of the lesions.
- Change of odor (formall)
- Early dippin escharge eschar

egment.

- E
- Ce ne lesion.
- Vasion (reddish spots).
- Increased or modified painful complaint.

Sometimes difficult!









How about Microbiological Criteria?

Rational

- Use of burn wound biopsies for histological and quantitative assessment of the burn wound originates from Teplitz et al (1964!!!)
- Using a rat model, he found that increasing numbers of Pseudomonas aeruginosa on a burn wound were followed by invasion of the underlying viable tissue and clinical infection.
- A clinical method for quantitative biopsy in burns patients was first described by Loebl et al. and subsequently modified (1974!)
- Consequently, exist a variety of quantitative methods, but no universally accepted as a 'gold standard'.

Microbiological Criteria

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ARTICL

Article history Accepted 24) Available onl

Keywords: Burns Infection Systematic n Quantitative Biopsies Wound swab 26 studies

- 12 investigated clinical outcomes
- Great heterogeneity
 - Patients
 - Samples collection and processing
 - Methods

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- More than one quantitative microbiology sample is required to obtain reliable estimates of bacterial load;
- Biopsies are more sensitive than swabs in diagnosing or predicting sepsis;
- 3) High bacterial loads may predict worse clinical outcomes;
- 4) Both quantitative and semiquantitative culture reports need to be interpreted with caution and in the context of other clinical risk factors.

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iology en poc

Antiseptics Use

Rational = topic agents => prevent growth of microorganisms => prevent infection => promoting healing of burn wounds



Cochrane Database of Systematic Reviews

Antiseptics for burns (Review)

Norman G, Christie J, Liu Z, Westby MJ, Jefferies JM, Hudson T, Edwards J, Mohapatra DP, Hassan IA, Dumville JC

Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD011821. DOI: 10.1002/14651858.CD011821.pub2.

www.cochranelibrary.com

Antiseptic Use

- 56 RCTs with 5807 randomised participants. Almost all trials had poorly reported methodology
- In many cases the primary review outcomes, wound healing and infection, were not reported or were reported incompletely.
- Most trials enrolled people with recent burns, described as seconddegree and less than 40% TBSA; most participants were adults.
- Antiseptic agents assessed were: silver-based, honey, Aloe Vera, iodine-based, chlorhexidine or polyhexanide (biguanides), sodium hypochlorite, merbromin, ethacridine lactate, cerium nitrate and Arnebia euchroma.
- Most studies compared **antiseptic** with a **topical antibiotic silver sulfadiazine (SSD)**; others compared antiseptic with a non-antibacterial treatment or another antiseptic.

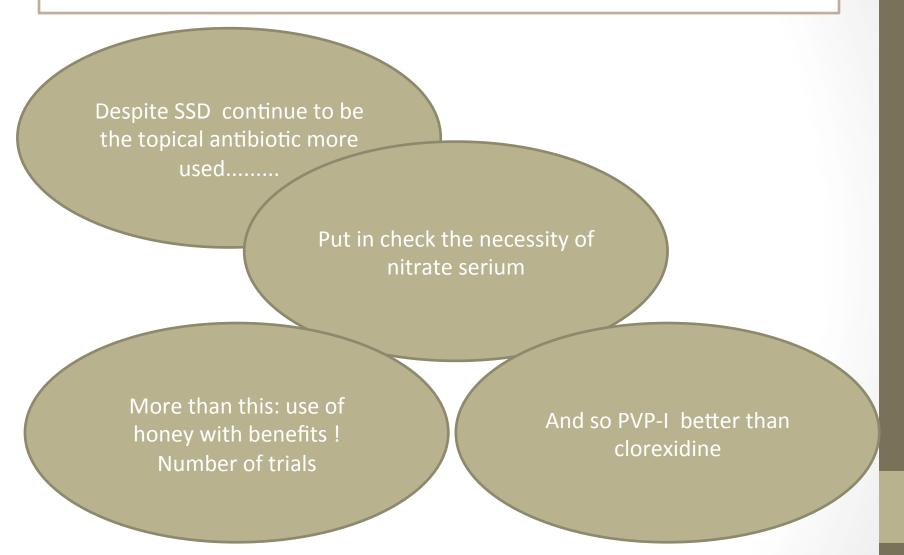
Antiseptic Use

- Compared with the topical antibiotic SSD there is no clear difference in the hazard of healing
- There is moderate certainty evidence that, on average, burns treated with honey are probably more likely to heal over time compared with topical antibiotics (HR 2.45, 95% CI 1.71 to 3.52; I2 = 66%; 5 studies; 140 participants).
- Most comparisons did not report data on infection. Based on the available data we cannot be certain if antiseptic treatments increase or reduce the risk of infection compared with topical antibiotics (very low certainty evidence).

Antiseptic Use

- There may be some reduction in mean time to healing for wounds treated with povidone iodine compared with chlorhexidine (MD 2.21 days, 95% CI 0.34 to 4.08).
- It is also uncertain whether infection rates differ for SSD plus cerium nitrate, compared with SSD alone (low certainty evidence).
- There may be fewer deaths in groups treated with cerium nitrate plus SSD compared with SSD alone (RR 0.22, 95% CI 0.05 to 0.99; I2 = 0%, 2 studies, 214 participants) (low certainty evidence).

What is surprising!!



Rational

- Burn wounds provide an ideal medium for bacterial proliferation and a portal of entry into the bloodstream.
- As nosocomial infections in burn patients are prevalent and dangerous, systemic antibiotic prophylaxis is often considered, alongside other infection prevention and control interventions.
- However, the use of prophylaxis => controversy
 - Risk-benefit => benefits of prophylaxis X drug toxicity and development of multi-drug resistance

- Two meta-analysis
 - One showed clearly that the use of systemic antibiotic prophylaxis after burn injury was beneficial, lessening pneumonia mortality and burn wound infections
 - 2. A Cochrane review concluded that the benefits of prophylaxis in preventing burn wound infections was unclear

^{1.} Avni T, Levcovic A, Ad-El D, Leibovici L, Paul M. Prophylactic antibiotics for burns patients: systematic review and meta-analysis. BMJ 2010;340:c241.

^{2.} Barajas-Nava L, Lo´pez-Alcalde J, Roque´i Figuls M, Sola` I, Bonfill Cosp X. Antibiotic prophylaxis for preventing burn wound infection. Cochrane Database Syst Rev 2013;6:CD008738

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Review

Systemic antimicrobial prophylaxis in burn patients: systematic review

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SUMMARY

Objective: To review studies of systemic antibiotic prophylaxis in burn patients. Methods: Electronic databases were searched for human clinical trials performed between 1966 and 2016 that compared prophylactic systemic antibiotics with placebo or no intervention.

Results: Nineteen trials met the selection criteria. Early postburn prophylaxis was assessed in non-severe burn patients (six trials) and severe burn patients (seven trials). Antimicrobial prophylaxis showed no effectiveness for the prevention of toxic shock syndrome or burn wound infection (Grade 1C), but could be useful in patients with severe burns and requirement for mechanical ventilation (Grade 2B). Perioperative prophylaxis was assessed in six trials. Antimicrobial prophylaxis during resection of devitalized tissue is of no benefit in most burn patients (Grade 2B); however, there is insufficient evidence to make a recommendation for patients with extensive burns. Antibiotic prophylaxis may also be effective in preventing split-thickness skin graft infections in selected procedures (Grade 2B).

Conclusions: The available evidence does not support the role of systemic antibiotic prophylaxis in the management of the majority of burn patients. Nevertheless, it may be useful in patients with severe burns who require mechanical ventilation, and in selected split-thickness skin grafting procedures.

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- 53 publications
- Between 1982 and 2016
- 12 randomized prospective trials
- 4 retrospective studies
- 12 trials assessed early postburn prophylaxis
- 6 trials assessed
 perioperative
 prophylaxis
- 1 trial assessed both.

- Systemic antibiotic prophylaxis during the early post-burn period is not indicated in most burn patients (Grade 1C), but could be useful in patients with severe burns and the requirement for mechanical ventilation (Grade 2B).
- Perioperative prophylaxis during resection of devitalized tissue is not indicated in most burn patients (Grade 2B), but there is insufficient evidence for a recommendation for extensive burns, and it could be useful for the prevention of split-thickness skin graft infection in selected procedures (Grade 2B).

Rational

- Center for Disease Control and Prevention (CDC) widely implemented contact precautions in modern burn care to prevent transmission of microorganisms
- However, the use of isolation rooms is labour intensive and expensive, while these techniques are only based on a scarce number of scientific studies for evaluating their effectiveness.

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Review

Protective isolation precautions for the prevention of nosocomial colonization and infection in burn patients: A systematic review and meta-analysis*

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Meta-analysis

ABSTRACT

Objectives: To assess the impact of protective isolation precautions on nosocomial colonization and infection rates in burn patients.

Research methodology: A systematic review and meta-analysis were performed of studies identified through Pubmed and Web of Science. Only articles in English were considered. The Downs and Black tool was used to evaluate their methodological quality. Random-effects meta-analysis obtained pooled risk ratios (RRs) and 95% confidence intervals (CIs) of nosocomial colonization and infection rates.

Results: Five eligible before-after studies were identified, encompassing a total of 3033 patients (1192 in the experimental group; 1841 in the control group). Varying protective isolation precautions were investigated, resulting in high clinical heterogeneity. Quality assessment revealed overall poor methodological quality. Protective isolation significantly reduces combined colonization and infection rates compared to baseline care (RR 0.52, 95% CI 0.40–0.69; P< 0.0001). Subgroup analyses indicated significant reductions in both nosocomial colonization (RR 0.65, 95% CI 0.51–0.83; P=0.02) and infection rates (RR 0.53, 95% CI 0.49–0.58; P< 0.0001).

Conclusions: Protective isolation precautions appear to decrease the risk of colonization and infection in burn patients. Because of the absence of higher quality study designs, clinical heterogeneity and the small number of studies involved, these results must be interpreted cautiously.

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• 5 estudos

• N e n h u m randomizado

Fig. 1. PRISMA flowchart.

	Isolation Cont		rol	Risk Ratio			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Lee et al., 1990	28	38	42	43	30.2%	0.75 [0.62, 0.92]	1990	-
McManus et al., 1994	342	914	1117	1605	34.3%	0.54 [0.49, 0.59]	1994	•
Matsumura et al., 1996	23	116	57	115	19.9%	0.40 [0.27, 0.60]	1996	
Thompson et al., 2002	9	58	8	17	9.1%	0.33 [0.15, 0.72]	2002	
Weber et al., 2002	5	66	13	61	6.5%	0.36 [0.13, 0.94]	2002	
Total (95% CI)		1192		1841	100.0%	0.52 [0.40, 0.69]		•
Total events	407		1237					
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 16.16$, $Chi^2 =$								
Test for overall effect: Z =	4.63 (P	< 0.00	001)					Favours isolation Favours control

Fig. 2. Meta-analysis Forest plot summarizing the preventive effect of isolation precautions on nosocomial colonization and infection rates in burn patients.

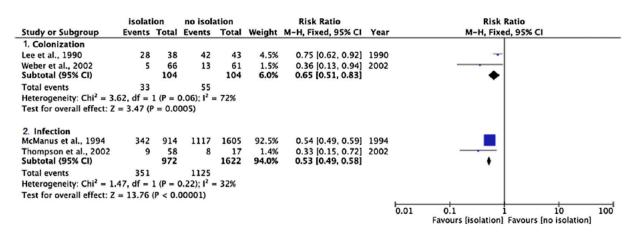


Fig. 3. Meta-analysis Forest plot summarizing the preventive effect of isolation precautions on respectively nosocomial colonization and infection rates in burn patients. Fig. Legend Studies reporting colonization rates (Lee et al. and Weber et al.) and studies reporting infection rates (McManus et al. and Thompson et al.) were separately pooled to assess the effect of protective isolation on colonization and infection rates distinctly. The study by Matsumura et al. is not considered in this subgroup analysis as it only focused on methicillin-resistant Staphylococcus aureus (MRSA) colonization.

 Implementation of protective isolation precautions does lead to a reduction in both colonization and infection rates in burn patients.

- Isolation precautions can be recommended for the treatment of burn patients, although the evidence is rather weak
 - lack of high quality study designs
 - limited number of studies available
 - clinical heterogeneity between studies.

Therapeutic drug monitoring

Rational

- A large number of factors may affect the pharmacokinetics (PK) of drugs in burn patients
 - TBSA and depth, sepsis, hydration, serum protein concentrations, age, creatinine clearance and time after injury.
- These factors lead to changes in antimicrobial plasma concentrations and, consequently, antimicrobial killing activity may be altered
- The PK/PD relationship => may improve patient outcome

Therapeutic drug monitoring

ARTICLE IN PRESS

Clinical Therapeutics/Volume I, Number I, 2017

Clinical Outcome and Antimicrobial Therapeutic Drug Monitoring for the Treatment of Infections in Acute Burn Patients

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Retrospective, observational study comparing 2 groups of patients: 1) the conventional treatment group (May 2005 to October 2008) and 2) the monitored treatment group (November 2008 to June 2011) whose dosing regimen was determined by plasma drug monitoring.

Therapeutic drug monitoring

Clinical Therapeutics

Table II. Clinical outcome and mortality according to treatment group, Burn Intensive Care Unit, Hospital das Clinicas, University of São Paulo, Brazil (2005-2011). Values are given as number (%).

	Conventional Treatment	Monitored Treatment	All Patients	
Variable	Group $(n = 63)$	Group (n = 77)	(N = 140)	P
Hospital mortality	23 (36)	30 (39)	53 (38)	0.83
14-day mortality	9 (14)	12 (16)	21 (15)	0.99
Clinical outcome	(n = 56)	(n = 72)	(N = 128)	
Improvement	29 (52)	43 (60)	72 (56)	0.37
Worsening	27 (48)	29 (40)	56 (43)	

TDM of antimicrobial treatment, focused especially on dose adjustment to optimize PK/PD parameters, did not alter the prognosis of burn patients.

Rational

- It is well known that infections in burn patients are caused by potentially pathogenic microorganisms concomitantly isolated in digestive tract
- The effects of SDD have been evaluated in 67 different randomized clinical trials (RCT) in different critically ill patient populations and in 12 meta-analyses (ICU)
- Burns: Two different approaches have been used to prevent infections and decrease mortality and infection incidence -SDD and only the enteral administration of antibiotics (EA)

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BURNS XXX (2017) XXX-XXX

Study	Year	Type of study	Intervention	Patients (n)	Age (years)	TBSA (%)	Inhalation (%)
Jarret et al. [8]	1978	Observational	EA (neomycin, erythromycin, nystatin)	20	25	44	NA
			No treatment	10	40	43	NA
Deutsch et al. [9]	1990	RCT	EA (neomycin, erythromycina, nystatin)	15	45	50	27
			Placebo	15	35	45	41
Mackie et al. [31]	1992	Observational	SDD	31	38	46	32
			No treatment	33	38	44	42
Mackie et al. [32]	1994	Observational	SDD+nasal mupirocin	33	34	48	13
			SDD	34	38	43	12
Shalaby et al. [28]	1998	RCT	EA (colistin, co-trimoxazole, nystatin)	162	NA	Adults≥25	NA
			No treatment	85	NA	Children≥15	NA
Abdel-Razek et al.	2000	RCT	EA (colistin, co-trimoxazole, nystatin)	215	NA	Adults≥25	NA
[29]			No treatment	85	NA	Children≥15	NA
Barret et al. [30]	2001	RCT	EA (polymyxin, tobramycin, amphotericin)	11	9	67	75
			Placebo	12	8	58	64
De la Cal et al. [21]	2005	RCT	SDD	58	41	34	64
			Placebo	59	48	38	67
Cerdá et al. [22]	2007	Observational	SDD+vancomycin	402	46	30	41
			No treatment or SDD (54 patients)	375	46	26	40
Aboelatta et al. [33]	2013	Observational	EA (colistin, amikacin, miconazol) +ciprofloxaciniv	15	33	30-50	Excluded
			No treatment	15	23		Excluded

EA: enteral antibiotic. iv: intravenous. SDD: selective digestive decontamination (Four days of intravenous cefotaxime and tobramycin, polymyxin and amphotericin in oral paste and digestive solution.) TBSA: total body surface area.

- Outcomes
 - Mortality
 - Incidence of BSI and Pneumonia
 - Colonization of wound burn infection
 - Adverse effects (diarrhea but not C. difficile)

Table 2 – Mortality (%).							
Author	Non absorbable enteral antibiotics	Control					
Jarret et al. [8]	0	0					
Deutsch et al. [9]	8/15 (53)	4/12 (33)					
Shalaby et al. [28]	14/171 (8)	13/85 (15)					
Abdel-Razek et al. [29]	9/225 (4)	16/85 (12)					
Barret et al. [30]	2/11 (18)	1/12 (8)					
Aboelatta et al. [33]	4/15 (27)	8/15 (53)					
Author	Selective digestive decontamination	Control					
	/33 (3) /53 (9)	7/31(23) 15/54 (28)					

EA = OR: 0.62 (95% CI: 0.20–1.94) High heterogeneity (I^2 =71%)

SDD

RCT = OR: 0,27 (95% CI 0.09–0,81)

Obs = OR: 0.11 (95% CI 0.01–0,93)

Tabla 3 – Cumulative incidence of patients with bloodstream infection.					
Study	Treated (%)	Control (%)			
Global					
Jarret et al. [8]	3/20 (15)	3/10 (30)			
Mackie et al. [31]	1/33 (3)	8/31(26)			
Shalaby et al. [28]	15/171 (9)	41/85 (48)			
De la Cal et al. [20]	19/53 (36)	17/54 (31)			
Aboelatta et al. [33]	4/15 (27)	12/15 (80)			
Enterobacteriaceae					
Deutsch et al. [9]	6/15 (40)	6/12 (50)			
Mackie et al. [31]	0/33 (0)	4/31(13)			
Shalaby et al. [28]	4/171 (2)	9/85 (11)			
De la Cal et al. [20]	1/53 (2)	8/54 (15)			
Pseudomonas sp.					
Deutsch et al. [9]	4/15 (27)	4/12 (33)			
Mackie et al. [31]	0/33 (0)	4/31 (13)			
De la Cal et al. [20]	9/53 (17)	7/54 (13)			
S. aureus					
Jarret et al. [8]	1/20 (5)	2/10 (20)			
Deutsch et al. [9]	8/15 (53)	9/12 (75)			
Mackie et al. [31]	1/33 (3)	7/31 (23)			
Methicillin-resistant S. aureus					
De la Cal et al. [32]	13/53 (25)	5/54 (9)			
Enterococcus sp.					
Jarret et al. [8]	1/20 (5)	1/10 (10)			
Deutsch et al. [9]	6/15 (40)	1/12 (8)			
Mackie et al. [31]	0/33 (0)	4/31 (13)			
De la Cal et al. [18]	3/53 (6)	5/54 (9)			
Coagulase-negative Staphylococcus					
Jarret et al. [8]	2/20 (10)	1/10 (10)			
Deutsch et al. [9]	10/15 (67)	10/12 (83)			
De la Cal et al. [32]	13/53 (25)	5/54 (9)			

- The incidence of Enterobacteriaceae
 BSI was consistently reduced in 4
 studies
- In the two studies using SDD, the reduction was more marked
 - 0% vs. 13%
 - 2% vs. 11%
- A reduction in *Pseudomonas spp*.
 bloodstream infections was observed in one study
- MRSA bloodstream infection
 - 13 of 53 patients treated with SDD
 - 5 of 54 receiving placebo
- Candidemia = 0 in the SDD group and
 7% in the control group

Table 4 – Cumulative incidence of patients with pneumonia.

Study	Treated (%)	Control (%)
Enteral antibiotics		
Jarret et al. [8]	1/20 (5)	1/10 (10)
Barret et al. [30]	1/11(9)	0/11 (0)
Aboelatta et al. [33]	2/15 (13)	2/15 (13)
Selective digestive decontamination Mackie et al. [31] De la Cal et al. [20]	2/33 (6) 18/53 (34)	9/31(29) 26/54 (48)

- 3 studies using EA = no effect on the incidence of pneumonia
- 2 studies using SDD = a reduction in the incidence of pneumonia was reported in the group treated with SDD versus placebo (23% and 14%, respectively)

Burn wound colonization

- 3 studies
- no difference in 2
- 1 study = a nonsignificant reduction in the incidence of burn wound colonization noted in the SDD treated group (60% vs 93%; p=0.08)

Adverse Effects

- None of the selected studies showed an increased incidence of bacterial resistance associated with the use of SDD or EA
- 2 studies = high incidence of diarrhea in patients receiving EA
 - Incidence of diarrhea was 33% leading to the interrruption of treatment
 - Diarrhea developed in 82% of treated patients versus 17% of the control group
- Clostridium difficile toxin was not measured

Conclusion

SDD seems to improve the survival of severe burn patients and consistently reduces the incidence of infection such as pneumonia and bloodstream infections caused by Enterobacteriaceae as has been consistently found in other critically ill patients.

Butneed high quality RCTs with low risk of bias

Conclusion



- Diagnosis of burn infection
 - Clinical criteri
 - Microbic
- Use of ?
 - Top/
 - Syst
- Contact
- Therape
- Selective dis

Many papers published recently (in 2017) in different periodics!

All issues needs more research and studies of good quality of evidence

Our attention !!!!

Thank you!

