Intensive Care Med (2003) 29:1194–1195
DOI 10.1007/s00134-003-1771-6

Didier Pittet
Jorge Garbino
Stéphane Hugonnet
Jacques Romand
Daniel P. Lew

Reply to comment on "Prevention of severe *Candida* infections in non-neutropenic, high-risk, critically ill patients"

Received: 27 March 2003
Accepted: 30 March 2003
Published online: 14 May 2003

Sir: We read with interest the comments of van Saene et al. Their central argument concerns selective digestive decontamination (SDD)—once again. It seems important to recall the difference between the concept of this potentially effective prevention strategy and the so-called "SDD tetralogy," referred to by van Saene et al. The potential benefit of each of the distinct components of the selective decontamination approach remains a matter of debate both in the literature and among experts [1, 2, 3]. After almost 20 years of extensive research, no consensus exists on either the choice of antibiotics, the route of administration, or the necessity to combine intravenous and oral antimicrobials. The reason why SDD is currently not universally accepted is not due to its lack of efficacy to prevent ventilator-associated pneumonia (VAP) among some patient categories or even reduce mortality in some conditions, but because of its parenteral component and consequent concerns regarding short- and long-term emergence of antibiotic resistance, even following the "princeps" study [4, 5]. We are completely aware of the effect of selective decontamination given that our group was among the first to investigate its potential benefit [6], but we have always used it only in highly selected patients and without the parenteral component [6, 7]. We and others [1, 2, 3, 6, 7, 8, 9, 10] continue to challenge the overall appropriateness of the systematic use of intravenous antibiotics in ICU patients, used for as long as 3–5 days in most trials [11]. Such a duration is close to that of VAP treatment [12]. Let us recall that the "SDD tetralogy" is based on a nonrandomized trial with an historical control group [4], and that the impact of the strategy has been shown to be inversely related to the quality of the trial [13]. Using a focused hypothesis that colonization of the oropharynx only, and not of the stomach and gut, is responsible for subsequent VAP, Bergmans et al. [10] confirmed that a reduction in the orotracheal colonization without impact on the endogenic flora of the stomach and gut reduces the incidence of late-onset VAP. In their study no yeast overgrowth or increase in fungal infection was observed despite the absence of an antifungal. VAP prevention by modulating oropharyngal colonization and preserving the endogenous gut flora or minimizing the overgrowth of resistant organisms may impose as a primary measure in the future [3]. However, this could be achieved only with a strictly controlled and limited use of parenteral antibiotics which has been our strategy over two decades.

The incidence of late-onset pneumonia in our study [7] is among the lowest reported in the literature [14], without the use of any parenteral component. We agree with van Saene et al. that the addition of intravenous antibiotics could have further reduced the already low incidence of early-onset pneumonia, but at the cost of treating a large number of patients for a marginal benefit, and the likely risk of resistance acquisition. Assuming that prophylactic intravenous antibiotic would halve the incidence of early-onset pneumonia, 34 patients would need to be treated to prevent one case.

We agree that, unsurprisingly, the incidence of bacteremia in our study population was high due to the choice that we made to recruit patients at extremely high risk [7, 15], who represented only 4.2% of patients admitted in our ICUs over the study period [7]. Moreover, there was no expectation that the selective decontamination regimen used would impact on bacteremia rates [7]. Such a high infection rate cannot be compared with the rates reported in other SDD studies in which less stringent selection criteria were applied. Regarding prevention of bloodstream infection, we stress again that by far the leading source of primary infection, including candidemia, is vascular devices [16, 17]. Consequently, approaches to prevent gut translocation should only be considered in institutions where effective evidence-based strategies have been implemented [16].

We were surprised by the superficial understanding of the process of *Candida* infection. *Candida* infection arises from endogenous colonization [15]. In all studies appropriately designed to assess this process [7, 15, 18, 19, 20], *Candida* colonization has always preceded infection, with intensity of colonization being the prerequisite and the key predisposing factor for infection [7, 15]. Preventing colonization surely did contribute to the 90% reduction in candidemia incidence [7]. The high proportion of patients colonized with *Candida* certainly does not reflect cross-transmission but is an expected characteristic of highly selected patients at risk for endogenous colonization, as reported in other studies that have focused on high-risk patients only [19, 21, 22, 23, 24].

References

1. Kollef MH (1999) The prevention of ventilator-associated pneumonia. N Engl J Med 340:627–634
2. Pittet D, Eggimann P, Rubinovitch B (2001) Prevention of ventilator-associated pneumonia by oral decontamination: just another SDD study? Am J Respir Crit Care Med 164 338–339
3. Aarts MA, Marshall JC (2002) In defense of evidence: the continuing saga of selective decontamination of the digestive tract. Am J Respir Crit Care Med 166:1014–1015
4. Stoutenbeek CP, van Saene HKF, Miranda DR, Zandstra DF (1984) The effect of selective decontamination of the digestive tract on colonization and infection rate in multiple trauma patients. Intensive Care Med 10:185–192
5. Saene HK van, Stoutenbeek CP (1987) Selective decontamination. J Antimicrob Chemother 20:462–465
6. Pugin J, Auckenthaler R, Lew DP, Suter PM (1991) Oropharyngeal decontamination decreases incidence of ventilator-associated pneumonia. JAMA 265:2704–2710
7. Garbino J, Lew DP, Romand J-A, Hugonnet S, Auckenthaler R, Pittet D (2002) Prevention of severe Candida infections in non-neutropenic, high-risk, critically ill patients: a randomised, double-blind, placebo-controlled trial in patients treated by selective digestive decontamination. Intensive Care Med 28:1708–1717
8. Gastinne H, Wolff M, Delatour F, Faurisson F, Chevret S (1992) A controlled trial in intensive care units of selective decontamination of the digestive tract with nonabsorbable antibiotics. The French Study Group on Selective Decontamination of the Digestive Tract. N Engl J Med 326:594–599
9. Laggner AN, Tryba M, Georgopoulos A, Lenz K, Grimm G, Graninger W, Schneeweiss B, Druml W (1994) Oropharyngeal decontamination with gentamicin for long-term ventilated patients on stress ulcer prophylaxis with sucralfate? Wien Klin Wochenschr 106:15–19

10. Bergmans DCJJ, Bonten MJM, Gaillard CA, Paling JC, van der Geest S, van Tiel FH, Beysens AJ, de leeuw PW, Stobberingh EE (2001) Prevention of ventilator-associated pneumonia by oral decontamination: a prospective, randomised, double-blind, placebo-controlled study Am J Respir Crit Care Med 164:382–388
11. Heyland DK, Cook DJ, Jaeschke R, Griffith L, Lee HN, Guyatt GH (1994) Selective decontamination of the digestive tract. An overview. Chest 105:1221–1229
12. Chastre J, Wolff M, Fagon JY, et al for the groupe PneumA France (2002) Comparaison de deux durées d'antibiothérapie dans la prise en charge des pneumonies acquises sous ventilation mécanique. Réanimation 11:S3
13. van Nieuwenhoven CA, Buskens E, van Tiel FH, Bonten MJ (2001) Relationship between methodological trial quality and the effects of selective digestive decontamination on pneumonia and mortality in critically ill patients. JAMA 286:335–340
14. Eggimann P, Pittet D (2001) Infection control in the ICU. Chest 120:2059–2093
15. Pittet D, Monod M, Suter PM, Frenk E, Auckenthaler R (1994) Candida colonization and subsequent infection in critically ill surgical patients. Ann Surg 220:715–758
16. Eggimann P, Harbarth S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D (2000) Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. Lancet 355:1864–1868
17. Nucci N, Anaissie E (2002) Should vascular catheters be removed from all patients with candidemia? An evidence-based review Clin Infect Dis 34:591–599
18. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP (1989) Risk factors for hospital-acquired candidemia. A matched case-control study Arch Intern Med 149:2349–2353
19. Saiman L, Ludington E, Pfaller M, Rangel-Frausto S, Wiblin RT, Dawson J, Blumberg HM, Patterson JE, Rinaldi M, Edwards JE, Wenzel RP, Jarvis W (2000) Risk factors for candidemia in neonatal intensive care unit patients Pediatr Infect Dis J 19:319–324
20. Bross J, Talbot GH, Maislin G, Hurwits S, Strom BL (1989) Risk factors for nosocomial candidemia: a case-control study in adults without leukemia. Am J Med 87:614–620
21. Blot SI, Vandewoude KH, Hoste EA, Colardyn FA (2002) Effects of nosocomial candidemia on outcomes of critically ill patients. Am J Med 113:480–485
22. Petri MG, König J, Moecke HP, Gramm HJ, Barkow H, Kujath P, Dennhart R, Schafer H, Meyer N, Kalmar P, Thulig P, Muller J, Lode H (1997) Epidemiology of invasive mycosis in ICU patients: a prospective multicenter study in 435 non-neutropenic patients. Intensive Care Med 23:317–325
23. Rantala A, Niinikoski J, Lehtonen OP (1993) Early Candida isolations in febrile patients after abdominal surgery. Scand J Infect Dis 25:479–485
24. Borzotta AP, Beardsley K (1999) Candida infections in critically ill trauma patients: a retrospective case-control study. Arch Surg 134:657–664

This reply refers to the comment available at http://dx.doi.org/10.1007/s00134-003-1770-7

D. Pittet (✉) · J. Garbino · S. Hugonnet
J. Romand · D. P. Lew
Infection Control Program,
University of Geneva Hospitals,
24 Rue Micheli-du-Crest, 1211 Geneva 14, Switzerland
e-mail: didier.pittet@hcuge.ch
Tel.: +41-22-3729828
Fax: +41-22-3723987

D. Pittet · J. Garbino · D. P. Lew
Department of Infectious Diseases,
University of Geneva Hospitals,
Geneva, Switzerland

J. Romand
Surgical Intensive Care Department,
University of Geneva Hospitals,
Geneva, Switzerland