CORE
Metadata, citation and similar papers at core.ac.uk
Provided by University of Groningen

University of Groningen

SDD

Benus, R. F.; Harmsen, H. J.; van der Werf, T. S.

Published in:
Intensive Care Medicine

DOI:
10.1007/s00134-010-1947-9

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2010

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Benus, R. F., Harmsen, H. J., & van der Werf, T. S. (2010). SDD: don't be selective in considering pros and cons. Intensive Care Medicine, 36(10), 1785-1786. https://doi.org/10.1007/s00134-010-1947-9

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 12-11-2019

Intensive Care Med (2010) 36:1785–1786
DOI 10.1007/s00134-010-1947-9

R. F. Benus
H. J. Harmsen
T. S. van der Werf

SDD: don't be selective in considering pros and cons

Accepted: 2 May 2010
Published online: 7 July 2010
© The Author(s) 2010. This article is published with open access at Springerlink.com

Dear Editor,

We thank Dr. Zandstra and colleagues [1] for their interest in our work [2]. Although in their scientific careers they have amassed impressive data on selective digestive microbial decontamination (SDD), they have not fully appreciated what our paper adds to this large body of knowledge.

The intestinal microbiota contains many more cells than the human body itself. Furthermore the intestinal microbial gene set is approximately 150 times larger than the human genome [3]. Last year marked the 150th anniversary of Darwin's *On the Origin of Species*. How can we explain any genetic advantage for humans to carry so many microbes along? What benefit does our microbiome provide us during health? And what happens during critical illness? How does the intensive care unit (ICU) environment impact on our microbiota? What impact does SDD have on our microbiota? And what is the impact of SDD on the emergence of resistant bacteria in the ICU?

Zandstra et al. rightly allude to the fact that *Enterobacteriaceae* increase during critical illness—we also found a more than tenfold relative increase (as a percentage of total bacteria) compared to data from healthy volunteers [4, 5]. To fight overgrowth of *Enterobacteriaceae* seems like a good idea—but is there a trade-off? Why did SDD—though providing a small but significant survival advantage compared to a control group—fail to further reduce mortality compared with patients receiving only oral topical antimicrobial products, even though these study participants had similarly increased percentages of *Enterobacteriaceae*?

A potential advantage of having such massive numbers of anaerobic bacteria in the colon is that colonocytes feed on bacterial products. Indeed colonocytes feed on butyrate, produced by a limited number of colonic bacterial species. The *Faecalibacterium prausnitzii* group is predominant amongst these butyrate-producing groups. This group is already reduced during tube feeding, resulting in a significantly reduced concentration of butyrate [4]. We describe a significant reduction in two groups of microbiota that help in maintaining the integrity of the large intestinal mucosa. Quoting Vollaard's and Donskey's work, Zandstra et al. agree that SDD is a contradiction in terms. We apparently disagree in our concern that SDD might have a "dark side", i.e. that some important beneficial microbiota are harmed by SDD. Besides, there is additional collateral damage: in the analysis of point-prevalence cultures from the de Smet study [6], an increase of intestinal colonisation by resistant organisms was observed after cessation of SDD [7].

None of the articles cited by Zandstra et al. describe the use of molecular methods for detection and/or enumeration of the intestinal microbiota. Bacteria from the *F. prausnitzii* group are highly sensitive to oxygen and require very specific growth media. Culture-based quantification yields a high degree of culture bias. These limitations of culture-based microbiological techniques have precluded reliable testing of the effects of antibiotics (i.e. SDD) on the intestinal microbiota. We are obviously not the first to claim that SDD is not selective. We are, however, the first to back up these claims using absolute numbers of faecal bacteria derived from a quantitatively reliable, molecular method.

Referring to Wensinck as an argument that not *F. prausnitzii* but clostridia contribute to colonisation resistance (CR), Zandstra et al. display a misunderstanding of the composition of the intestinal microbiota. Although phenotypically Gram-negative, *F. prausnitzii* are genetically closely related to the Gram-positive clostridia Zandstra et al. refer to. In fact, they belong to clostridial cluster IV [8]. These phylogenetic relations have only been discovered since the dawn of the molecular era.

We agree that the clinical impact of *F. prausnitzii* reduction in the critically ill is unclear—at least, that this should be further studied; we do not know whether there is a critical threshold of butyrate substrate for colonocytes to survive, or to maintain the integrity of the large intestinal mucosa. Recent studies have shown an anti-inflammatory effect of *F. prausnitzii* in Crohn's disease that could also be beneficial for the critically ill [9]. We have, however, provided novel information that may explain the discrepancy of effective reduction of *Enterobacteriaceae* by SDD, which fails to translate into further survival benefit in comparison with selective oropharyngeal decontamination (SOD).

Open Access This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

References

1. Zandstra DF, Petros AJ, Silvestri L, de la Cal MA, Taylor N, Damjanovic V, van Saene HKF (2010) Selective decontamination of the digestive tract (SDD): selectivity is not required. Intensive Care Med. doi: 10.1007/s00134-010-1945-y
2. 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. doi:10.1007/s00134-010-1826-4
3. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, Nielsen T, Pons N, Levenez F, Yamada T, Mende DR, Li J, Xu J, Li S, Li D, Cao J, Wang B, Liang H, Zheng H, Xie Y, Tap J, Lepage P, Bertalan M, Batto JM, Hansen T, Le Paslier D, Linneberg A, Nielsen HB, Pelletier E, Renault P, Sicheritz-Ponten T, Turner K, Zhu H, Yu C, Li S, Jian M, Zhou Y, Li Y, Zhang X, Li S, Qin N, Yang H, Wang J, Brunak S, Doré J, Guarner F, Kristiansen K, Pedersen O, Parkhill J, Weissenbach J, MetaHIT Consortium, Bork P, Ehrlich SD, Wang J (2010) A human gut microbial gene catalogue established by metagenomic sequencing. Nature 464:59–65
4. Benus RF, van der Werf TS, Welling GW, Judd PA, Taylor MA, Harmsen HJ, Whelan K (2010) Association between *Faecalibacterium prausnitzii* and dietary fibre in colonic fermentation in healthy human subjects. Br J Nutr 29:1–8
5. Harmsen HJ, Raangs GC, He T, Degener JE, Welling GW (2002) Extensive set of 16S rRNA-based probes for detection of bacteria in human feces. Appl Environ Microbiol 68:2982–2990
6. de Smet AM, Kluytmans JA, Cooper BS, Mascini EM, Benus RF, van der Werf TS, van der Hoeven JG, Pickkers P, Bogaers-Hofman D, van der Meer NJ, Bernards AT, Kuijper EJ, Joore JC, Leverstein-van Hall MA, Bindels AJ, Jansz AR, Wesselink RM, de Jongh BM, Dennesen PJ, van Asselt GJ, te Velde LF, Frenay IH, Kaasjager K, Bosch FH, van Iterson M, Thijsen SF, Kluge GH, Pauw W, de Vries JW, Kaan JA, Arends JP, Aarts LP, Sturm PD, Harinck HI, Voss A, Uijtendaal EV, Blok HE, Thieme Groen ES, Pouw ME, Kalkman CJ, Bonten MJ (2009) Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med 360:20–31
7. Oostdijk EA, de Smet AM, Blok HE, Thieme Groen ES, van Asselt GJ, Benus RF, Bernards SA, Frénay IH, Jansz AR, de Jongh BM, Kaan JA, Leverstein-van Hall MA, Mascini EM, Pauw W, Sturm PD, Thijsen SF, Kluytmans JA, Bonten MJ (2010) Ecological effects of selective decontamination on resistant gram-negative bacterial colonization. Am J Respir Crit Care Med 181:452–457
8. Duncan SH, Hold GL, Harmsen HJ, Stewart CS, Flint HJ (2002) Growth requirements and fermentation products of *Fusobacterium prausnitzii*, and a proposal to reclassify it as *Faecalibacterium prausnitzii* gen. nov., comb. nov. Int J Syst Evol Microbiol 52:2141–2146
9. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán LG, Gratadoux JJ, Blugeon S, Bridonneau C, Furet JP, Corthier G, Grangette C, Vasquez N, Pochart P, Trugnan G, Thomas G, Blottière HM, Doré J, Marteau P, Seksik P, Langella P (2008) *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A 105:16731–16736

R. F. Benus · H. J. Harmsen · T. S. van der Werf (✉)
University Medical Center Groningen, Internal Medicine, Hanzeplein 1, P.O. Box 30001, 9700 RB Groningen, The Netherlands
e-mail: t.s.van.der.werf@int.umcg.nl
Tel.: +31-50-3611501
Fax: +31-50-3613216