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BRIEF REPORT

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Decontamination of the digestive tract and oropharynx: hospital acquired infections after discharge from the intensive care unit

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Abstract *Objective:* To determine the incidence rates of hospital acquired infections (HAI) during the first 14 days after ICU discharge after treatment during ICU-stay with Selective Decontamination of the Digestive tract (SDD), Selective Oropharyngeal Decontamination (SOD) or Standard Care (SC). *Design:* Prospective observational study. *Setting:* ICUs in two tertiary care hospitals. *Patients:* Patients discharged from the ICU to the ward. *Interventions:* None. *Measurements and results:* Post-ICU incidences of HAI per 1,000 days at risk were 11.2, 12.9 and 8.3 for patients that had received SDD ($n = 296$), SOD ($n = 286$) or SC ($n = 289$) respectively in ICU, yielding relative risks, as compared to SC, of 1.49 (CI_{95} 0.9–2.47) for SOD and 1.44 (CI_{95} 0.87–2.39) for SDD. Incidences of surgical site infections (per 100 surgical procedures) were 4 after SC and 11.8 and 8 after SOD and SDD ($p = 0.04$). Among patients that succumbed in the hospital after ICU-stay ($n = 58$) eight (14%) had developed HAI after ICU discharge; 3 of 21 after SDD, 3 of 15 after SOD and 2 of 22 after SC. *Conclusions:* Incidences of HAI in general wards tended to be higher in patients that had received either SDD or SOD during ICU-stay, but it seems unlikely that these infections have an effect on hospital mortality rates.

Keywords SDD · SOD · Critically ill patients · Intensive care · Hospital acquired infections

Introduction

Prophylactic antibiotic regimens, such as Selective Decontamination of the Digestive tract (SDD) and Selective Oropharyngeal Decontamination (SOD), reduce the incidence of respiratory tract infections (RTI) in Intensive Care Unit (ICU) patients and improve survival [1–6]. The concept of SDD, developed in the 1980s [7, 8] consists of prevention of secondary colonization with Gram negative bacteria, *S. aureus*, and yeasts through application of non-absorbable antimicrobial agents in the oropharynx and gastrointestinal tract. Further it consists of pre-emptive treatment of possible infections due to commensal respiratory tract bacteria through systemic administration of cephalosporins during the first four days in ICU and maintaining the anaerobic intestinal flora through the use of antibiotics (both topically and systemically) not active against anaerobic bacteria [8]. In meta-analyses, three single center randomized studies and a recent multi-center trial, SDD was associated with improved patient survival [1, 4, 6, 9–11]. SOD (application of topical antibiotics in the oropharynx only) might be an alternative to SDD, as they are both effective in reducing day 28 mortality in a recent multi-center study [6].

SDD (and to lesser extent SOD) aim to extensively modulate the microbial ecology of patients. It is unknown how discontinuation of these interventions at ICU discharge changes the patients' microbial ecology and whether this influences their immediate risk of infections. The current study was motivated by the findings from de Jonge et al. [4]. In their SDD study the observed relative risk reduction (RRR) in ICU mortality of 35% reduced to 22% at hospital discharge. This reduction in survival benefit after ICU discharge might have been related to an increased incidence of hospital acquired infection (HAI) in those patients that had received SDD in ICU. Nested within a multi-center SDD–SOD trial we prospectively monitored the occurrence of HAI during the first 14 days after ICU discharge in all patients transferred to regular wards in two university hospitals.

Patients and methods

Setting

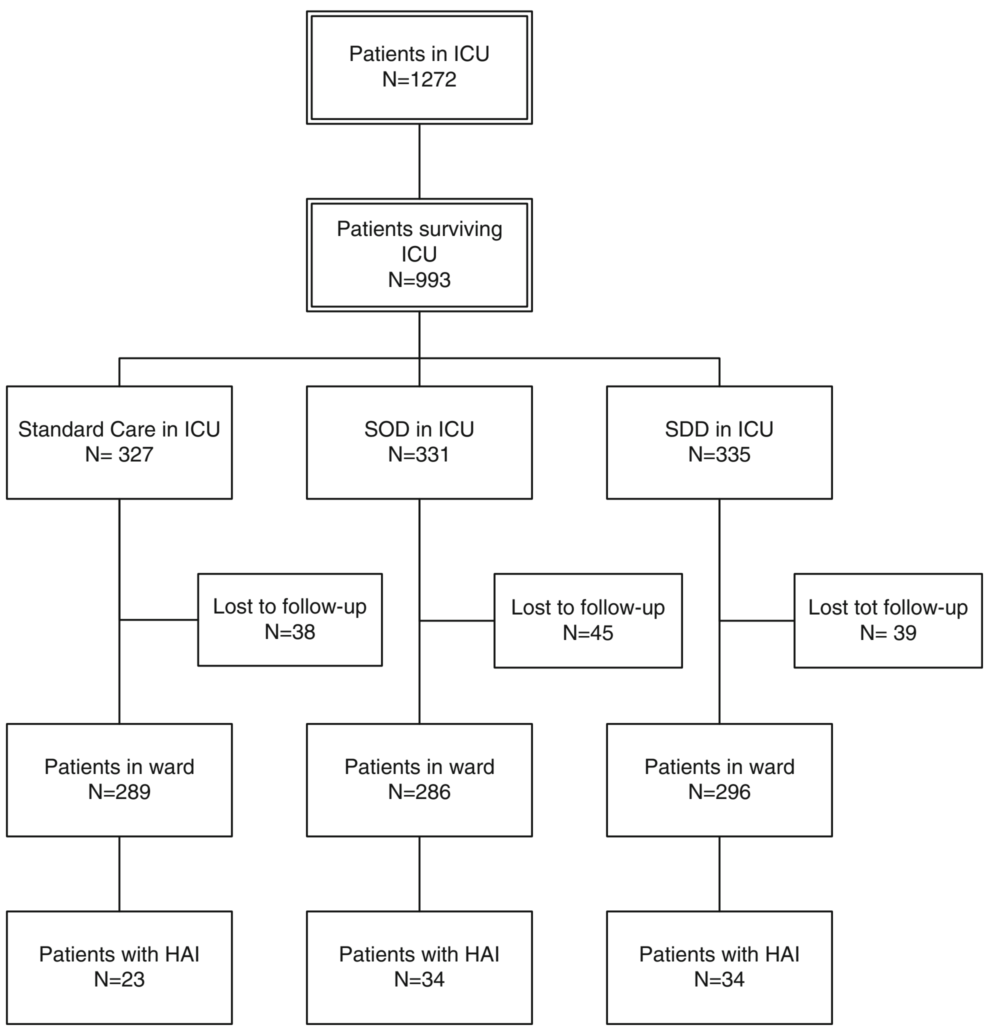
The study was conducted in two tertiary care hospitals: the University Medical Center Utrecht and the Leiden University Medical Center. Nested within a multi-center SDD–SOD trial [6], the occurrence of HAI during the first 14 days after ICU discharge was prospectively monitored in all patients transferred to regular wards.

Study design, data collection and definitions

In ICU, patients with an expected stay ≥72 h, or with an expected duration of mechanical ventilation ≥48 h, had received either SDD, SOD or standard care (SC), which rotated in 6-month periods, as described previously [6].

Data were collected from patient records for a maximum of 14 days post-ICU. The following data were recorded for each patient: gender, age, length of stay at

Fig. 1 Flowchart



the ICU, mechanical ventilation and APACHE II score at the ICU. At the wards, medical records were prospectively reviewed twice weekly by an Infection Control Professional for HAI according to the Centers for Disease Control and Prevention (CDC) definitions [12, 13].

In the surveillance period the following HAIs (and day of diagnosis) were registered in both hospitals: surgical site infections (SSI), bloodstream infections (BSI), and RTI. In one of the hospitals, oropharyngeal infections were also registered. Infection control policies (other than the subject of the study) did not change during the period of the study in either hospital.

Data analysis

The incidence of HAI was expressed per 1,000 days at risk, i.e. days until first HAI, day of discharge or end of observation period. The proportion of patients with HAI was expressed as the total number of patients with HAI per 100 patients surveyed post-ICU, with 95%-confidence interval (CI_{95}). The total number of SSIs was expressed per 100 patients with surgical procedures. Statistical analysis was performed with SPSS for Windows 12.0.1 (SPSS, Inc., Chicago, IL, USA). Differences in continuous variables between groups were determined by Student's t test. Differences in proportions of HAI (with CI_{95}) in the successive study periods were determined. Statistical significance was defined as a p value of less than 0.05.

Results

Patients

Between May 2004 and July 2006, 871 patients were included; 289 after SC, 286 after SOD and 296 SDD (Fig. 1). Reasons for patients being lost to follow-up ($n = 122$) mainly included their transfer to other hospitals after ICU discharge. Although fewer patients in the SC group had received mechanical ventilation in ICU (84% vs. 96% and 94% in SOD and SDD, respectively), other characteristics (such as age, sex, Apache II-score on ICU admission and surgical or non-surgical reasons for admission) were comparable for all three groups (Table 1).

End points

The numbers of patients with HAI were 23, 34 and 34 from the SC, SOD and SDD groups, respectively, yielding incidences per 1,000 days at risk of 8.3, 12.9 and 11.2 for SC, SOD and SDD, respectively (Table 2). As compared to SC, the relative risks for developing HAI in the first 14 days after ICU discharge were 1.49 (CI_{95} 0.9–2.47) after SOD and 1.44 (CI_{95} 0.87–2.39) after SDD. Oropharyngeal infections, only registered in one hospital, occurred in one patient after SC and in four patients after SOD.

Most infections were RTI, with similar incidences and similar time until diagnosis in all three study groups (Table 2). Adjustment for the difference in number of mechanically ventilated patients in ICU did not change these observations. Incidences of BSI were also similar between the three groups, but the duration until infection tended to be longer in the post-intervention groups (means of 4.8 for SC and 7.7 days for SOD and SDD combined, $p = 0.17$ when comparing SC to SDD and SOD combined). Incidences of SSI, expressed per 100 surgical procedures were 4 after SC, as compared to 11.8 after SOD and 8 after SDD ($p = 0.04$ when comparing SC to SDD and SOD combined). Among the 26 patients with SSI in both post-intervention groups, 18 were diagnosed with superficial infections (15 patients not cultured or with a negative culture) and in 7 patients *Staphylococcus aureus* was documented as the cause of SSI.

Hospital mortality was 7.6% (22 patients) in the SC group, 5.2% (15 patients) in the SOD group and 7.1% (21 patients) in the SDD group. Hospital mortality among

Table 1 Patients' characteristics

	Standard care	SOD	SDD
No. of patients	289	286	296
Sex (male/female)	187/102	181/105	180/116
Age			
Mean (median)	56.7 (59)	57.9 (61)	57.0 (60)
SD	18	17.1	17.5
Range	16–93	12–87	16–87
APACHE II at ICU admission			
Mean (median)	18.9 (18)	19.8 (19)	20.1 (19)
SD	7.85	7.86	7.98
Range	4–48	4–45	0–45
LOS in ICU			
Mean (median)	13.6 (8)	12.6 (8)	14.2 (9)
SD	15	11.8	15.1
Range	1–141	1–93	1–121
Mechanical ventilation in ICU			
Yes (%)	243 (84)*	274 (96)*	279 (94)*
No	46	12	17
Specialty			
Cardiology	9	15	10
Cardiothoracic surgery	13	27	16
Surgery	109	94	117
Medical	61	54	61
Pulmonology	8	8	7
Neurosurgery	38	49	43
Neurology	28	26	23
Other	23	13	19
No. of surgical patients	126	127	137

LOS Length of stay

* Standard care versus SOD and SDD significantly different ($p = 0.000$), no difference between SOD and SDD

Table 2 Infections, time until diagnosis and mortality

	Standard care ($N = 289$)	SOD ($N = 286$)	SDD ($N = 296$)
Number of patients with HAI	23	34	34
Number of HAI	26	39	37
Incidence of HAI/1,000 days at risk	8.3	12.9	11.2
RR standard care versus intervention	–	1.49	1.44
CI_{95}		0.9–2.47	0.87–2.39
Proportion of patients (%)with HAI	8	12	11
CI_{95}	5–12	8–16	8–16
Specialty of patients with HAI			
Cardiology	1	2	–
Cardiothoracic surgery	–	2	–
Surgery	12	14	19
Medical	2	7	4
Pulmonology	–	–	–
Neurosurgery	3	3	6
Neurology	2	4	3
Other	3	2	2
Mortality: no. of patients (%)	22 (7.6)	15 (5.2)	21 (7.1)
Mortality of patients with HAI: no. of patients (%)	2 (8.7)	3 (8.8)	3 (8.8)
Mean LOS in surveillance on ward (days)	10.1	10.0	11.0
Median; range	13; 1–14	14; 1–14	14; 1–14
No. of RTI	16	18	18
Mean time until diagnosis (days)	4.6	5.0	4.7
Median; range	4.5; 1–9	4.5; 1–13	3.5; 1–12
No. of BSI	5	5	8
Mean time until diagnosis (days)	4.8	5.6	9.0
Median; range	4.0; 1–8	5; 2–12	10; 1–12
No. of SSI	5	15	11
Incidence/100 surgical procedures	4.0	11.8	8.0

Differences in times until diagnosis are not significant between the three groups or between the standard care group versus SOD and SDD combined

HAI Hospital acquired infections, *RR* relative risk, *LOS* length of stay, *RTI* respiratory tract infection, *BSI* blood stream infection, *SSI* surgical site infection

The proportion of patients with HAI in the standard care period versus SOD and SDD combined (RR 1.47, CI_{95} 0.935–2.305) is not significantly different

patients that developed HAI was 8.7% ($n = 2$), 8.8% ($n = 3$) and 8.8% ($n = 3$).

Discussion

Incidences of HAI in general wards tended to be higher in patients that had received either SDD or SOD during ICU-stay, but it seems unlikely that these infections have an important effect on hospital mortality rates. Of note, the observed differences in relative risks only approached statistical significance.

To the best of our knowledge this is the first study that has quantified timing and incidences of infections in general wards after ICU discharge related to antimicrobial infection prevention measures in the ICU. Strengths include the prospective monitoring of infections performed by a limited number ($n = 3$) of trained and experienced infection control professionals. The open study design in the ICU was an unavoidable limitation of the present analysis. By using objective, and internationally accepted, criteria we aimed to minimize information bias. The fact that the study was performed in only two tertiary care centers may reduce the generalizability of our findings.

The observed tendency towards a higher infection rate after an antibiotic intervention in ICU might be related to differences in patient risk factors or to changes in the colonization status between the intervention groups and the patients that received standard care. Indeed, at the time of ICU admission, a higher proportion of patients in the standard group did not receive mechanical ventilation. Yet, there were no significant differences in age, APACHE II score at the time of ICU admission or the lengths of stay in ICU or on mechanical ventilation, or in distribution of medial specialties. We therefore assume that the risk profile at the time of ICU discharge was similar for the three patient populations.

Both SDD and SOD aim to modulate the colonization status of patients, which resulted in lower colonization rates with Gram negative bacteria in the respiratory and intestinal tract [6]. After discontinuation of the prophylactic regimens, though, patients may acquire colonization with typical hospital pathogens or suppressed colonization with such bacteria may reemerge. If these phenomena are relevant, and whether they are responsible for our observations, remains to be determined.

Our study was motivated by the observation of a tendency towards higher mortality rates after ICU discharge among patients that had received SDD in a previous study [4]. In the current study, 58 patients (7%) succumbed in the hospital after ICU discharge, and eight (14%) of these patients had been diagnosed with a HAI in the first 14 days after ICU discharge. Overall mortality rates were comparable between the three study groups and the numbers of patients that died after developing a HAI was two in the standard care period and three in both the SDD and SOD period. Considering the low rates of infection, the overall low mortality rates after ICU discharge and the low prevalence of infections among those that succumbed after ICU discharge, we reject the hypothesis that an increased infection rate after ICU discharge affects the clinical outcome of patients that have received SDD or SOD in ICU, in spite of a tendency of more infections, especially superficial SSIs, in these patients after ICU discharge.

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