Background

Ventilator Associated pneumonia (VAP) contributes substantially to mortality, morbidity and ICU length of stay (LOS) in critically ill patients. These infections are thought to be caused by oropharyngeal and intestinal colonization with gram negative aerobic bacteria (GNAB) and fungi. Using antibiotic combinations to prevent such colonization (Selective Digestive Decontamination, SDD) may decrease the incidence of nosocomial infections and improve ICU mortality, morbidity and LOS. The CDC published in 2005 some guidelines for the use of such intervention.3

Selective Oral Decontamination (SOD): SOD refers to the use of an oral paste of nonabsorbable antibiotic combination (2% gentamycin, 2% colistin and 2% vancomycin) applied with the gloved finger every 6 hours to the buccal mucosa of ventilated ICU patients.4,5 This therapy is continued until the patient is extubated. By eradicating most aerobic bacteria and Candida from the mouth, this regimen has been associated with a decrease in the incidence of Hospital Acquired Pneumonia (HAP) by 60% and in ICU mortality by 23%.4

SDD: SDD was introduced into critical care practice in 19846 and consists of three components: 1) Oral decontamination using an oral paste similar to the one described above (2% polymyxin E, 2% tobramycin, and 2% amphotericin q 6 h). 2) Gastro-intestinal decontamination using a 10 mL solution of 100 mg polymyxin E, 80 mg tobramycin, and 500 mg amphotericin via NGT q 6 h. 3) A systemic antibiotic (e.g. intravenous cefuroxime, 1.5 grams q 8 h or cefotaxime, 1g q 6 h) given in the 1st 4 days of therapy to prevent early nosocomial infections until the bowel regimen is fully effective at 1 week.5 SDD is continued until the patient is discharged from ICU. It is considered selective as it eradicates the GNAB and fungi from the oropharynx, stomach and bowel but spares the normal flora. SDD was found to reduce the incidence of VAP and also UTIs and catheter-related sepsis.7 A systematic review of over 10 randomised controlled trials evaluating SDD showed a combined relative risk reduction of ICU-acquired infections of around 40%.8 Despite that, there have remained two nagging concerns that have hindered the wide adoption of SDD in the ICU: (1) skepticism about the impact on mortality and (2) fear of promoting antimicrobial resistance. Each of these concerns was addressed by the study under discussion.
Critique of Article

Patients and Methods: This trial is an unblinded, prospective, randomized, controlled trial conducted over a 2-year period, ending in Dec, 2001. Patients were assigned to either one of two separate MSICUs in The Academic Medical Centre in Amsterdam, where one ICU was used as an intervention (SDD) unit and the other as a control unit to prevent cross-colonization. The two units were similar in terms of the case mix and practice pattern. 1090 eligible patients were recruited and 934 patients gave consent. 466 patients were assigned to the SDD unit and 468 patients were assigned to the control unit, with comparable baseline characteristics. Patients in the SDD unit received the standard SDD regimen described above with the addition of antibiotic paste for tracheostomy sites and antibiotic suppositories for blind-bowel loops, if applicable. They were also treated with nebulized polymyxin E or amphotericin B if there was a documented colonization of the tracheobronchial tree. Patients in the control unit were managed in the standard way with the use of antibiotics only if clinically indicated. Selective cultures for resistant micro-organisms were taken from the patients (sputum, throat, rectum, axilla, and wounds) and from sinks in both units.

Results: The primary end-points of the trial were ICU and hospital mortality and the acquisition of resistant bacteria. The secondary end-points were the length-of-stay in the ICU and the total costs of antibiotic treatment. This trial showed a significant reduction in all of these outcomes in the SDD group compared to the control as shown in the following table.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>SDD</th>
<th>Controls</th>
<th>RRR</th>
<th>ARR</th>
<th>NNT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU mortality</td>
<td>14.8%</td>
<td>22.9%</td>
<td>35%</td>
<td>8.1%</td>
<td>12</td>
<td>0.002</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>24.2%</td>
<td>31.2%</td>
<td>22%</td>
<td>7%</td>
<td>14</td>
<td>0.02</td>
</tr>
<tr>
<td>Acquisition of resistant GNAB</td>
<td>16%</td>
<td>26%</td>
<td>39%</td>
<td>10%</td>
<td>10</td>
<td>0.001</td>
</tr>
<tr>
<td>Acquisition of VRE</td>
<td>1.1%</td>
<td>1.3%</td>
<td>20%</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition of MRSA</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median ICU LOS (days)</td>
<td>6.8</td>
<td>8.5</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Costs</td>
<td></td>
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</tbody>
</table>

Major results of the trial

Critical Appraisal: To date, this is the second largest trial evaluating outcomes after SDD and the first to show a significant overall mortality reduction in a mixed patient population. In addition, the reduction in the acquisition of resistant GNAB challenges one of the long-standing arguments against the widespread adoption of SDD. The favourable secondary outcome regarding antibiotic cost and ICU LOS may also support the use of the SDD strategy. Nevertheless, the study has limitations. First, it is not known if the results are sustainable beyond the 2-year follow-up period, particularly concerning the acquisition of antibiotic resistance. Second, the low prevalence of VRE and MRSA in the population under study limits the generalizability of this trial. Third, since this was an unblinded study, there may have been surveillance bias or a drift in practice or co-interventions which could have independently altered the outcome. A crossover design would not have been viable in this circumstance as the need for a protracted wash-out period would have made this untenable. Perhaps the most effective way to
have conducted this study would have been as a cluster-randomized trial but this would have been costly and fraught with difficulties related to low statistical power.†

Finally, despite the presence of evidence that supports the potential utility of SDD, there is significant lingering doubt about its effectiveness and this is compounded by a prevalent fear of propagation of antimicrobial resistance. Other barriers that contribute to the poor uptake of this intervention include its preparation time and the need for pharmacy expertise.

Abbreviations (Alphabetically arranged):

ARR: Absolute Risk Reduction; CDC: Centers for Disease Control; GNAB: Gram Negative Aerobic Bacteria; h: hour(s); HAP: Hospital Acquired Pneumonia; ICU: Intensive Care Unit; LOS: Length of Stay; MRSA: Methicillin-Resistant Staphylococcus Aureus; MSICU: Medical and Surgical Intensive Care Unit; NGT: Nasogastric Tube; NNT: Number Needed to Treat; RRR: Relative Risk Reduction; SDD: Selective Digestive Decontamination; SOD: Selective Oral Decontamination; UTI: Urinary Tract Infection; VAP: ventilator Associated Pneumonia; VRE: Vancomycin-Resistant Enterococci.

References:


† Published recently is a cluster randomized trial of 5939 patients from 13 ICUs that looked only at the effect of SDD & SOD on the short term mortality in critically ill patients. In this trial, the 28-day mortality was reduced by 3.5% in the SDD group & by 2.9% in the SOD group compared to placebo.†