Selective Decontamination of the Digestive Tract in Surgical Patients

A Systematic Review of the Evidence

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Objective: To determine the comparative efficacy of selective decontamination of the digestive tract in critically ill surgical and medical patients, and in selected subgroups of surgical patients with pancreatitis, major burn injury, and those undergoing major elective surgery and transplantation.

Data Sources: The MEDLINE database was searched from January 1966 to December 1996 using the terms “decontamination or prophylaxis,” “intensive care units,” and “antibiotics.” The search was limited to English-language studies evaluating the efficacy of selective decontamination of the digestive tract in human subjects.

Study Selection: The primary review was restricted to prospective randomized trials.

Data Extraction: End points of interest included rates of nosocomial pneumonia, bacteremia, urinary tract infection, wound infection, mortality, and length of intensive care unit stay. Methodologic quality of individual studies was assessed using a previously described model.

Data Synthesis: Odds ratios (ORs) together with their (95% confidence interval [CIs]) were reported and determined using the Mantel-Haenszel method. Mortality was significantly reduced with the use of selective decontamination of the digestive tract in critically ill surgical patients (OR, 0.7; 95% CI, 0.52-0.93), while no such effect was demonstrated in critically ill medical patients (OR, 0.91; 95% CI, 0.71-1.18). The greatest effect was demonstrated in studies where both the topical and systemic components of the regimen were used. Rates of pneumonia were reduced in both subsets of patients, while those of bacteremia were significantly reduced only in surgical patients.

Conclusions: Selective decontamination of the digestive tract notably reduces mortality in critically ill surgical patients, while critically ill medical patients derive no such benefit. These data suggest that the use of selective decontamination of the digestive tract should be limited to those populations in whom rates of nosocomial infection are high and in whom infection contributes notably to adverse outcome.


SELECTIVE decontamination of the digestive tract (SDD) is an infection prophylaxis regimen that employs topical and oral nonabsorbable antibiotics to eradicate pathogenic organisms from the gastrointestinal (GI) tract. The regimen was first used in patients with neutropenic leukemia undergoing induction therapy with promising results. In 1983, Stoutenbeek et al adapted the technique of SDD to patients in an intensive care unit (ICU) setting; the first clinical trial in a homogeneous group of multiple trauma patients was described the following year. Since then, at least 25 controlled clinical trials and 4 meta-analyses evaluating the technique have been reported; however, although SDD is widely used in European ICUs, it has not found favor in North America.

The microbiologic rationale for SDD derives from clinical and experimental studies on the normal GI tract flora and its changes in critical illness. The indigenous flora of the oropharynx and GI tract is remarkably constant over time. Mechanisms preventing overgrowth with potentially pathogenic organisms include saliva flow, gastric acidity, bile acids, secretory IgA, and peristalsis. In addition, obligate anaerobic bacteria contribute to the prevention of colonization of the digestive tract by facultative anaerobic and potentially pathogenic bacteria and yeasts, a phenomenon referred to as colonization resistance.

In the critically ill patient, the mechanisms limiting overgrowth of potentially pathogenic organisms are compromised by the underlying disease processes, instrumentation, and medication that result in
is the most plausible and readily demonstrable mecha-

nia. Aspiration of contaminated upper GI tract fluid
in the pathogenesis of ventilator-associated pneumo-
support, but do not confirm, a role for altered gastric flora
acidity is maintained by the use of cytoprotective agents
moniae include patients admitted to an ICU; the most common isolates
zation develops within days in more than two thirds of
the initiation of SDD. Cefotaxime treats early established infection by community-acquired pathogens, particu-
larly Streptococcus pneumoniae or Haemophilus influenzae, that may be aspirated during intubation, and tempo-
rizes until the enterally administered antibiotics have ade-
ately decontaminated the GI tract. Selective decontamina-
tion of the digestive tract is initiated as soon as possible following admission and is continued until cessa-
tion of mechanical ventilation or discharge from the ICU.

The disparate results of clinical trials in different pa-
tient populations suggest that the practice may benefit
select groups of patients. Its role in surgical patients has
not been explicitly evaluated, although surgical patients
might be anticipated to show particular benefit. Rates of
nosocomial pneumonia seem to be higher in critically ill
surgical patients than in patients admitted to a medical
ICU, and the mortality attributable to nosocomial pneu-
monia is notably greater in the surgical subpopulation.
On the other hand, concerns have been voiced that a
reduction in rates of pneumonia in SDD studies does
not seem to result in improved outcome and that wide-
spread adoption of the technique may contribute to the
emergence of antibiotic resistance.

To evaluate the utility of SDD in surgical patients,
we conducted a formal, systematic, English-literature re-
view using an evidence-based methodology that gen-
erates recommendations based on the strength of posi-
tive evidence provided by clinical studies. Grade A
recommendations are supported by level I evidence that
reflects statistically significant conclusions from ran-
donized, controlled trials and provides a strong argu-
ment for adopting the therapy evaluated. Grade B rec-
ommendations are supported by level II evidence; and
grade C recommendations, by level III, IV, or V evi-
dence. Grade B and C recommendations provide less con-
vincing evidence of therapeutic efficacy and justify ei-
ther adoption or withholding of the therapy in question.
Noteable differences in the response to SDD in surgical,
as compared with medical, ICU patients are evident, jus-
tifying a grade A recommendation in support of the use
of routine SDD prophylaxis in critically ill surgical pa-
tients. Selective decontamination of the digestive tract
shows evidence of clinical benefit in subpopulations of
surgeical patients as well, although the limited sample sizes
of published studies preclude definitive conclusions re-
garding its use in specific subgroups.

MATERIALS AND METHODS

The MEDLINE database from January 1966 to De-
cember 1996 was searched using the search terms “de-
contamination or prophylaxis,” “intensive care units,”
and “antibiotics.” Titles and abstracts were also
searched during this period for the term “decontami-
nation.” Additional citations were obtained from sev-

eral recent meta-analyses and through personal com-
munications from other investigators involved in
primary studies. The primary review was restricted
to prospective, randomized, or consecutive trials.
Studies using historic controls were reviewed only
in patient populations where limited data exist. Stud-
ies were considered to have enrolled surgical pa-
tients if at least 75% of the subjects evaluated had been
admitted following trauma or major surgery. Stud-
ies were considered to have enrolled medical pa-
tients when fewer than 25% of patients met this cri-
terion.

Methodologic quality of the studies selected for this
systematic review was evaluated using a model
previously described by Heyland et al.

Odds ratios (ORs) and pooled ORs together with their
95% confidence intervals (CIs) were reported and de-
termined using the Mantel-Haenszel method. An OR
of less than 1.0 suggests that SDD results in a reduc-
tion in the relative odds of dying or developing a noso-
comial infection.

impairment of salivary flow, gastric alkalization, cho-
estasis, and intestinal ileus. In addition, the use of broad-
spectrum antibiotics eradicates the anaerobic flora, lead-
ing to a loss of colonization resistance. The net result is
that within days of admission to an ICU, the relatively
avirulent indigenous flora is replaced by a variety of po-
tentially pathogenic species. Abnormal gastric coloni-

Many descriptive studies have shown an associ-
bation between pathologic, oropharyngeal, and gastric
colonization and the development of nosocomial infec-
tion. Interventional studies in which normal gastric
acidity is maintained by the use of cytoprotective agents
support, but do not confirm, a role for altered gastric flora
in the pathogenesis of ventilator-associated pneumo-
nia. Aspiration of contaminated upper GI tract fluid
is the most plausible and readily demonstrable mecha-
nism of infection with proximal gut organisms.
Alternatively, proximal GI tract colonization may lead to
translocation of viable organisms through an intact gut
wall. Although a well-established phenomenon in ani-
mal models, translocation has not been conclusively
demonstrated in humans.

The standard SDD regimen consists of 2 compo-
nents. Topical, nonabsorbed polymyxin E, tobramycin, and
ampotericin B, a combination active against essentially
all aerobic gram-negative bacteria and fungi. These
antibiotics have limited activity against the normal anaer-
obic flora and maintain normal colonization resistance.
In addition, intravenous cefotaxime sodium is adminis-
tered until surveillance cultures demonstrate adequate de-
contamination of the GI tract, generally 4 days following
the initiation of SDD. Cefotaxime treats early established infection by community-acquired pathogens, particu-
larly Streptococcus pneumoniae or Haemophilus influenzae, that may be aspirated during intubation, and tempo-
rizes until the enterally administered antibiotics have ade-
ately decontaminated the GI tract. Selective decontamina-
tion of the digestive tract is initiated as soon as possible following admission and is continued until cessa-
tion of mechanical ventilation or discharge from the ICU.

SDD IN CRITICALLY ILL SURGICAL PATIENTS

Eleven randomized prospective studies have been pub-
lished on the use of SDD in surgical ICU patients.
All of the available studies are limited in their sample
size, and thus have insufficient power to detect even

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modest reductions in mortality. The OR for mortality in patients treated with SDD was less than 1 in 8 of the 11 trials, with 1 demonstrating a significant reduction in mortality (Figure 1). The pooled OR for these 11 trials is 0.70, with CIs indicating at worst a 7% and at best a 48% reduction in the odds of death in surgical ICU patients treated with SDD (Table 2). Separate analysis of studies in which systemic antimicrobial therapy was administered compared with those with only the topical components of the regimen demonstrated the greatest survival benefit in the former group. The effect of SDD on rates of nosocomial infection in surgical patients is similarly evident. Nine of 10 assessable trials demonstrated a clear reduction in length of ICU stay, although there is a significant reduction in the pooled length of stay in these 8 studies (for control patients, 16.9 ± 13 days vs 15.2 ± 12.5 days for SDD patients; P < .05, t test). All values are expressed as mean ± SD.

### SDD IN CRITICALLY ILL MEDICAL PATIENTS

Ten prospective, randomized, controlled clinical trials of SDD have been carried out in critically ill medical patients. Similar to the trials in critically ill surgical patients, almost all of the studies lack sufficient power to detect a clinically significant reduction in mortality. Only 1 study (445 evaluable patients) had adequate power to detect a 25% reduction in mortality. This trial failed to demonstrate any notable survival benefit in patients receiving SDD. In contrast to most of the other studies, systemic antimicrobial therapy was not administered. The pooled OR for a reduction in mortality using SDD prophylaxis in medical patients is 0.91 with the upper limit of the CI being more than 1.0 (Figure 2). Even if the analysis is limited to studies in which systemic antimicrobials are administered, the effect on survival fails to reach statistical significance (Table 2). Selective decontamination of the digestive tract had a

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**Table 1. Criteria Used to Assess Methodologic Quality**

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Not randomized</td>
<td>Double blinded</td>
<td>Truly randomized</td>
</tr>
<tr>
<td>Blinding</td>
<td>Not blinded</td>
<td>Intention to treat</td>
<td></td>
</tr>
<tr>
<td>Analysis</td>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population</td>
<td>Selected patients or cannot tell</td>
<td>Consecutive eligible patients</td>
<td></td>
</tr>
<tr>
<td>Comparability of groups of baseline</td>
<td>No or not sure</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Extent of follow-up, %</td>
<td>&lt;100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>Poorly described</td>
<td>Reproducibly described</td>
<td></td>
</tr>
<tr>
<td>Cointerventions†</td>
<td>Not described</td>
<td>Described but not equal or not sure</td>
<td>Well described and equal</td>
</tr>
<tr>
<td>Crossovers, %</td>
<td>Not described</td>
<td>&gt;10</td>
<td></td>
</tr>
</tbody>
</table>

* Variables were dichotomous variables scored on a 3-point scale with no middle value. Ellipses indicate no middle value.
† From Heyland et al.

**Table 2. Efficacy on Mortality and Nosocomial Infection Rates of Selective Decontamination of the Digestive Tract, Surgical vs Medical Intensive Care Units**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Surgical</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>0.70 (0.52-0.93)</td>
<td>0.91 (0.71-1.18)</td>
</tr>
<tr>
<td>Topical and systemic</td>
<td>0.60 (0.41-0.88)</td>
<td>0.75 (0.53-1.06)</td>
</tr>
<tr>
<td>Topical only</td>
<td>0.86 (0.51-1.45)</td>
<td>1.14 (0.77-1.68)</td>
</tr>
<tr>
<td>Nosocomial Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.19 (0.15-0.26)</td>
<td>0.45 (0.33-0.62)</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>0.51 (0.34-0.75)</td>
<td>0.77 (0.43-1.36)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>0.51 (0.34-0.76)</td>
<td>0.51 (0.32-0.82)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>0.56 (0.23-1.37)</td>
<td>...</td>
</tr>
</tbody>
</table>

* CI indicates confidence interval; ellipses, no analysis performed.
significant effect in reducing episodes of nosocomial pneumonia and urinary tract infections in medical patients (Table 2); however, there was no reduction in the risk of bacteremia (OR, 0.77) or length of ICU stay (for controls patients, 16.7 ± 6 days vs 16.8 ± 13 days for SDD patients).

To rule out the possibility that differences in the methodologic quality of the clinical trials evaluating medical and surgical patients accounted for the differential benefit seen in surgical patients, a formalized assessment of the quality of the individual trials was performed as described in the “Materials and Methods” section. Methodologic quality scores were similar in medical (7.6 ± 1.9) and surgical trials (7.9 ± 2.3), suggesting that the conduct of the study did not account for the differential results observed.

Data from meta-analyses and from subset analysis of critically ill medical and surgical patients provide sufficient level I and II evidence for a grade A recommendation for the use of SDD in critically ill surgical patients as a prophylactic measure to reduce mortality. Topical antimicrobial therapy should be used in conjunction with a short course of systemic antibiotics.

**SDD IN TRANSPLANTATION**

Infection contributes to mortality in patients undergoing solid-organ transplantation. Selective decontamination of the digestive tract has only been formally evaluated in patients undergoing orthotopic liver transplantation. Case series and retrospective studies suggest a reduction in rates of infection when compared with historic controls. There are 3 randomized prospective studies of SDD in liver transplantation that show a reduction in rates of nosocomial infection and a modest improvement in survival. Support for the use of SDD in liver transplantation is based on level II evidence and is given a grade B recommendation. Further studies are required in both liver transplant and other solid-organ recipients to provide adequate power to determine whether a true survival benefit exists.

**SDD IN MAJOR ELECTIVE SURGERY**

Selective decontamination of the digestive tract has been most extensively studied in cardiac surgical patients, a homogeneous group of patients undergoing major elective surgery. Randomized trials show a reduction in rates of infection, but not mortality, in a group of patients with a low baseline mortality rate (2% vs 3%). The effectiveness of SDD in patients undergoing total gastrectomy and esophagojugal anastomosis has been evaluated in a designed prospective multicenter study. Selective decontamination of the digestive tract initiated the evening prior to the procedure resulted in a significant reduction in the rate of anastomotic leaks (10.9% vs 2.9%), pneumonia (22.3% vs 8.8%), and mortality (10.6% vs 4.9%).

Although SDD can reduce the incidence of postoperative infection in patients undergoing cardiac surgery, its routine use is probably unnecessary. Risk factors for

### Table 3. Randomized Trials of Selective Decontamination of the Digestive Tract (SDD) in Liver Transplantation and Cardiac Surgery

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Mortality, Placebo</th>
<th>SDD</th>
<th>Pooled Odds Ratio (95% CI)</th>
<th>Infection, Placebo</th>
<th>SDD</th>
<th>Pooled Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver Transplantation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smith et al, 1993</td>
<td>17</td>
<td>11</td>
<td>[0.29 (0.06-1.47)]</td>
<td>61</td>
<td>17</td>
<td>0.44 (0.23-0.87)</td>
</tr>
<tr>
<td>Bion et al, 1994</td>
<td>16</td>
<td>0</td>
<td></td>
<td>39</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Arnow et al, 1996</td>
<td>.</td>
<td>.</td>
<td></td>
<td>42</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Cardiac Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zobel et al, 1991</td>
<td>8</td>
<td>12</td>
<td></td>
<td>36</td>
<td>8</td>
<td>0.28 (0.12-0.67)</td>
</tr>
<tr>
<td>Flaherty et al, 1990</td>
<td>2</td>
<td>0</td>
<td>0.68 (0.19-2.50)</td>
<td>27</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; ellipses, no analysis performed.*
infection and mortality in cardiac surgery have been clearly elucidated, and include Acute Physiology and Chronic Health Evaluation II scores greater than 19 in the first 24 hours,68 prolonged use of an intra-aortic balloon pump,69 and prolonged mechanical ventilation (>72 hours).67 It is recommended that SDD be considered for high-risk cardiac surgical patients. This is a grade B recommendation based on 4 level II clinical trials. The use of SDD as a method of infection prophylaxis in patients undergoing esophageal and gastric resection seems promising. Although these data cannot necessarily be extrapolated to all patients undergoing operations on the GI tract, it would seem that patients undergoing upper GI tract surgery derive benefit through a reduction in the risk of aspiration pneumonia. It is recommended that SDD be considered for patients undergoing upper GI tract surgery as a form of infection prophylaxis. This is a grade B recommendation based on level II data.

**SDD IN THERMAL INJURY**

The development of gram-negative bacteremia or nosocomial pneumonia following thermal injury is associated with an increased risk of death.68,69 To our knowledge, there are no prospective randomized studies evaluating the efficacy of SDD in burn patients. Mackie et al70 described a series of 31 consecutive patients with burns of greater than 30% of total body surface area who were treated with SDD, comparing them with a group of 33 historic controls. The incidence of respiratory tract infections (27.3% vs 6.5%) and bacteremias (24.2% vs 3.2%) was reduced, with a concomitant reduction in mortality (21.2% vs 3.2%); however, there was no reduction in length of hospital stay. Although promising, data on the role of SDD prophylaxis following thermal injury are retrospective and must be interpreted with due consideration. On the basis of level IV evidence, the use of SDD in patients with significant thermal injury is awarded a grade C recommendation. There is a need for well-designed prospective studies in this patient population.

**SDD IN ACUTE PANCREATITIS**

In a prospective randomized trial of SDD in acute pancreatitis, Luiten et al71 demonstrated a 50% reduction in the incidence of infected pancreatic necrosis (38% vs 18%). Patients receiving SDD required fewer laparotomies and had a significant reduction in mortality when stratified by Imrie score, with Imrie scores of 3 or higher obtaining the greatest survival benefit. A small, retrospective study72 of critically ill patients receiving mechanical ventilation examined the effects of SDD on patients with pancreatitis compared with historic controls. This study demonstrated a reduction in the incidence of bacteremia and nosocomial pneumonia in patients poorly matched for both Acute Physiology and Chronic Health Evaluation score and Ranson criteria. It is recommended that SDD be considered in patients with severe acute pancreatitis. This grade B recommendation is based on a single level I study.

The results of this meta-analysis show that the technique of SDD can benefit surgical patients. Selective decontamination of the digestive tract reduces rates of nosocomial pneumonia and bacteremia and nosocomial infections at remote sites. More importantly, it has a statistically significant effect on mortality. The best estimate for this effect is a 30% reduction in ICU mortality with CIs narrow enough to all but exclude the possibility of a type I error. This mortality effect is larger than that seen with other prophylactic modalities that have become standard care in surgical practice, including those that prevent deep venous thrombosis and pulmonary embolism or surgical wound infections.

Nonetheless, SDD has not been widely adopted as a prophylactic measure. There are several possible explanations for this. Pharmaceutical-grade preparations of polymyxin E and amphotericin B for topical use are not readily available. As a result, centers that have adopted the SDD technique have had to use intravenous preparations at substantially greater cost and local hospital pharmacies must prepare the SDD paste and suspension. The cost of SDD in the ICU setting has received only passing attention. In the 21 studies evaluating the efficacy of SDD in the ICU, 6 make no reference to overall antibiotic use,33,36,41,45,48,49 In 4 studies, overall antibiotic costs were higher in patients receiving SDD,34,42,43,50 in only 1 study was total antibiotic cost lower in the treatment group.50 Further, no attempt has been made to estimate costs related to microbiologic surveillance. With currently available data, it is not possible to conclude that SDD is a cost-effective, infection prevention strategy.

Although available data show no increase in the prevalence of resistant gram-negative organisms in patients managed with SDD (and indeed SDD has been promoted as a potential method of decontaminating patients with resistant gram-negative organisms49), its safety in centers where resistant gram-positive organisms are common has not been established. Several studies have documented an increase in rates of isolation of gram-positive organisms, particularly *Staphylococcus aureus*,34,42,43 coagulase-negative *Staphylococcus*, and *Enterococcus*34,37,38 when SDD is implemented. The spectrum of resistance is poorly reported. Gentamicin sulfate-resistant enterococci were prevalent in one study; however, surveillance cultures were not performed on the control group.34 In another study, a notable increase in methicillin-resistant *S aureus* colonization in patients receiving SDD compared with controls was documented.42 Resistant gram-negative organisms seem to be less of a concern; however, tobramycin-resistant, aerobic, gram-negative bacilli have been reported in 2 studies.34,35 Although notably overt infection with resistant organisms has not been reported with the use of SDD, this potential exists, and routine surveillance cultures may be necessary to allow for the early detection of antimicrobial resistance.

Meta-analyses show that SDD has a favorable effect on both nosocomial infection and ICU mortality when it is used as standard prophylactic therapy for critically ill surgical patients. Yet the technique is not widely employed
in North America but rather viewed with suspicion and skepticism by many. The appropriate resolution of such a state of clinical equipoise is a randomized, double-blind, placebo-controlled, clinical trial, and we believe it is important that such a trial be undertaken. This trial should evaluate a homogeneous group of patients at high risk for infection-related morbidity and mortality; for example, victims of multiple trauma or patients undergoing solid-organ transplantation. It must have an objective primary end point, namely, ICU mortality, and be adequately powered to include or exclude a clinically important mortality effect. It must also incorporate the microbiologic surveillance that will permit definitive conclusions regarding the effect of SDD on the microbial ecology and resistance patterns in patients undergoing cardiac surgery. Finally, the study should incorporate a control group of patients receiving systemic but not topical prophylaxis. A prospective, randomized trial of SDD in trauma patients showed comparable outcomes in a control group receiving systemic antimicrobial prophylaxis alone.

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REFERENCES


