

REVIEW

Ten tips and tricks for successful digestive tract decontamination

P.H.J. van der Voort^{1,2}, S. Buitinck¹, R.R. Jansen³, E.J.F. Franssen⁴, R.M. Determann¹

¹Department of Intensive Care, OLVG Hospital, Amsterdam, the Netherlands

²TIAS School for Business & Society, Tilburg University, Tilburg, the Netherlands

³Department of Clinical Microbiology, OLVG LAB, Amsterdam, the Netherlands

⁴Department of Pharmacy, OLVG hospital, Amsterdam, the Netherlands

Correspondence

P.H.J. van der Voort - p.h.j.vandervoort@olvg.nl

Keywords - selective digestive decontamination, SDD, decontamination, antimicrobial, infection

Abstract

In most intensive care units (ICUs) in the Netherlands, selective decontamination of the digestive tract (SDD) is currently a routine strategy to prevent secondary infection. The successfulness of infection prevention by SDD depends on whether decontamination is achieved or not. In addition, the rising rate of abnormal carriership with potential pathogenic and resistant microorganisms at the moment of ICU admission makes it sometimes difficult to obtain decontamination. It may be necessary to make adaptations to the standard antibiotic regime in SDD which is usually polymyxin, tobramycin and amphotericin B. Furthermore, persistent colonisation may need additional actions to enable the SDD regime to be successful. This article summarises tips and tricks to achieve successful decontamination of ICU patients, even in case of multi-resistant strains and persistent pathological carrier state.

Introduction

The infection prevention strategy for intensive care patients, selective decontamination of the digestive tract (SDD), was developed in the 1980s.^[1] The observation that patients who are admitted to the intensive care unit (ICU) relatively often acquire pneumonia due to bacteria that they did not have before their ICU admission initiated the development of a specific preventive strategy using hygiene, topical and systemic antimicrobials to eliminate abnormal carriership.^[2-4] Over the years, the discussion concerning SDD moved from clinical effectiveness to antimicrobial resistance. Nearly 70 randomised clinical trials have been performed and published. The effectiveness is evident with a reduction in respiratory tract infection and mortality rates.^[5-8] Evidence that SDD increases antimicrobial resistance rates is lacking.^[9,10] In contrast, several studies show a reduced incidence of resistant microbes in ICU patients when SDD is applied.^[11,12] The main goal of the SDD strategy is to

achieve decontamination of the digestive tract for potential pathological microorganisms. Usually, decontamination is reached within several days. However, clinical practice shows that some patients suffer from prolonged or repeated abnormal carriership. This article provides tips & tricks, evidence based or not practice based, to achieve decontamination.

Basic concept

The baseline hypothesis of SDD is that a sequence of events occurs in intensive care patients when they are not decontaminated. First, acquisition and second, subsequent colonisation of potentially pathogenic microorganisms (PPMs) at the hospital occurs or patients are colonised beforehand (abnormal carriership).^[3] Third, due to selective pressure, overgrowth occurs. When, in general, more than 1000 colonies per ml faeces or other body fluid are present (overgrowth), the risk for the fourth event, infection, will increase. Acquisition of PPMs rapidly occurs in hospitalised critically ill patients due to several reasons, such as the colonisation pressure in the ICU, the immunosuppression inherent to severe disease or treatment and the instrumentation, which breaks through defence lines (e.g. central lines, tubes and tracheostomy).

SDD is designed to intervene in this sequence of events. This implies that SDD is a preventive and not a treatment strategy for infection in ICU patients. In case of active infection, the addition of intravenous antimicrobial agents next to topical application of antibiotics is indicated.^[5,13] The application of topical antibiotics in the oral cavity and digestive tract prevents colonisation, overgrowth and secondary endogenous infection. The components that have been studied most thoroughly are polymyxin B or polymyxin E (colistin), tobramycin and amphotericin B (PTA). These antimicrobials are chosen because they are generally not absorbed from the lumen of the digestive tract except in patients with increased digestive tract

mucosal permeability.^[14] Usually a sticky paste (e.g. Orabase®) with 2% PTA is applied on the oral mucosa 4 times daily. A 10 ml solution with 80 mg tobramycin, 100 mg (1,000,000 U) polymyxin B/E and 500 mg amphotericin B is administered into the gastric tube. This regimen is highly effective in achieving decontamination in cases when sensitive microbes are present but also in more resistant ones, such as extended spectrum beta-lactamase producing facultative aerobic gram-negative bacteria.^[12,15]

Primary endogenous infection is caused by PPMs that are already present on admission in normally sterile organs, in particular the respiratory tract. This colonisation and the infection that is already beginning cannot be prevented by oral and digestive decontamination and needs an intravenous antimicrobial agent, usually cefotaxime, as an early treatment.^[13] When the admission culture of sputum is free of PPMs, the cefotaxime can be stopped unless another invasive infection needs this therapy. Exogenous infections are caused by directly introducing PPMs into sterile organs, e.g. by unsterile suction of the respiratory tract. These infections can be prevented by a high level of hygiene.

The fourth pillar of the SDD regimen, next to (1) hygiene, (2) the short intravenous course of cefotaxime and (3) the application of topical antibiotics in the digestive tract, is (4) surveillance. Twice weekly surveillance cultures of the oral cavity, rectum, sputum and wounds is mandatory to evaluate the decontamination strategy and to guide adaptations when necessary.^[3] When these surveillance cultures show decontamination failure or a renewed abnormal carrier state, the tips and tricks outlined below will help to get back on track.

Tips & tricks for successful decontamination

A. Stay in line with the concept

1. The normal indigenous flora consists almost completely of anaerobic *Lactobacilli*, anaerobic *Streptococci* and anaerobic *Bacteroides*.^[16,17] Less than 1% consists of coliform bacteria.^[16] These bacteria do not allow aerobic gram-negative bacteria and other PPMs to overgrow.^[16,18] This is called colonisation resistance, which in essence has nothing to do with antimicrobial resistance.^[18] Antibiotics such as penicillins affect the colonisation resistance by reducing the number of *Enterococci* and anaerobes.^[19] In general, antibiotics that enter the digestive tract via bile or mucosa or oral intake may reduce colonisation resistance. As a consequence, an important tool for clinicians is to choose antimicrobials that do not affect the normal, indigenous, flora. Therefore, penicillins, such as penicillin G, flucloxacillin, piperacillin, and amoxicillin should be avoided.^[19] If they cannot be avoided, intravenous administration is less harmful than oral intake. For instance, intravenous amoxicillin has limited effects on colonisation resistance.^[20] Metronidazole as an oral therapy should be

avoided for the same reason and, when given intravenously, should be limited to a short course of, for example, five days. Treatment of *Clostridium difficile* infection with either metronidazole or vancomycin orally is disastrous for the indigenous intestinal flora.^[21] However, during a well-executed SDD regime *Clostridium* infections seldom occur.^[22]

B. Improve practical execution

2. Decontamination of the digestive tract can only be achieved if the topical antibiotics reach all parts of the bowel. This implies that a discontinuous digestive tract because of surgery with stomata needs additional interventions. Suppositories with 2% PTA can be prepared by the local hospital pharmacy and applied into the rectum or into stomata. Patients with a post-pyloric tube should be given PTA suspension in this tube. In our setting, we usually divide the 10 ml PTA suspension and give 5 ml into the gastric tube and 5 ml into the duodenal or jejunal tube. In patients with reduced bowel movement and constipation early and appropriate laxation regimens are needed. We usually start polyethylene glycol laxation on the second day after the start of SDD and when stools do not appear on the 4th day, treatment with intravenous neostigmine is started (0.3-0.7 mg/h continuous infusion).^[23,24] In some patients a continuous nasogastric drip of macrogol (Klean-prep®) therapy is needed.^[24]
3. Persistent rectal colonisation is sometimes seen with aerobic gram-negative bacteria or candida. Firstly, laxative therapy is needed as described above to allow the SDD suspension to reach the rectum. When this is the case and colonisation persists, foreign bodies such as a Flexi-seal® might be the cause. In our ICU, the rule of thumb is that a Flexi-seal® can only be applied when decontamination has been achieved. Increasing the dose of the PTA suspension is never needed nor is it ever the solution.^[25] In addition, a higher dose of PTA might increase the absorption of PTA.^[26,27] The tobramycin level can, for this reason, be monitored in patients undergoing a prolonged stay in the ICU. Sometimes a low-grade *Candida* colonisation persists, for instance 15-100 colonies per ml faeces. Clinically this is not a problem and will not lead to infection. In general, the more sites that show *Candida* colonisation, the higher the chance that candidaemia occurs.^[28,29]
4. Wounds are sometimes difficult to decontaminate. Small wounds can be decontaminated by applying Orabase® paste with 2% PTA twice daily. The larger wounds, e.g. abdominal or after surgery for soft tissue infection, might be treated with vacuum therapy and/or local treatment with a sterile taurolidine solution. Special attention is needed for tracheostomies. The discontinuity of the skin can easily lead to local overgrowth of PPMs and secondary respiratory infection. Application of the sticky paste that is used for

oral decontamination (i.e. Orabase® with 2% PTA) around the tracheostomy will prevent pneumonia.^[30,31] In addition, routine changing of the cannula, e.g. once a week, will help to achieve and retain decontamination.

5. Hygiene is one of the cornerstones of SDD. However, due to high colonisation pressure in the ICU, strict adherence to hygienic measures alone cannot completely prevent secondary endogenous and exogenous infection. The combination of hygienic measures with SDD will be able to prevent these infections.^[2,4] In particular exogenous infection cannot, by definition, be prevented by SDD but only by application with strict hygiene during instrumentation and daily care. Notably, hygienic measures when performing endobronchial suction are essential. We use sterile gloves for handling a suction catheter. Closed suction systems should only be used if decontamination has been reached as otherwise the plastic suction tube will retain the tracheal contamination.

C. Provide additional measures when needed

6. Additional topical therapy is needed in case of abnormal colonisation of the respiratory tract. Aerosolised tobramycin or polymyxin B or colistin has to be applied in those cases. We prefer ultrasonic aerosol therapy when available. Nebulisation of 40 mg tobramycin 4 times daily and/or 80 mg colistin nebulisation 4 times daily is sufficient for susceptible PPMs. In case of *Staphylococcus aureus* tobramycin can be nebulised or a first-generation cephalosporin such as cephazolin (500 mg 4 times daily) can be used. In exceptional cases aerosolised therapy with amikacin can be used.^[32]
7. Additional topical therapy for colonisation of the bladder is usually only needed for *Candida*. This is combined with the renewal of the Foley catheter as *Candida* sticks to the catheter. A high colonisation index for *Candida* can lead to infection which is prevented by appropriate decontamination.^[28,29] Urinary tract infection on admission is effectively treated with the short course of cefotaxime or might need an additional intravenous antibiotic, for instance ciprofloxacin. *Candida* colonisation needs amphotericin B bladder irrigation.^[33] A 100 ml solution containing 50 mg of amphotericin B can be instilled twice daily and left in the bladder for one hour. After the first irrigation the urinary catheter should be changed for a new one. Usually four bladder instillations with one catheter renewal are effective to eliminate pathological *Candida* colonisation.
8. Persistent oral colonisation with PPMs such as Enterobacteriaceae or *Candida* can be treated with extra application of the sticky paste (e.g. Orabase® with 2% PTA) up to 8 times daily until decontamination has been reached. It is important to check whether prostheses or false teeth are present. Toothbrushes and other personal care products

might be the cause of persistent colonisation. These items should be removed, cleaned and left out. Also, renewal of the gastric tube is needed to get the patient transformed from the abnormal to the normal carrier state. Occasionally, the endotracheal tube also needs to be replaced.

9. Colonisation with polymyxin/colistin and tobramycin resistant gram-negatives might be a challenge. In case of co-trimoxazole sensitive PPMs such as non-fermenting Enterobacteriaceae, the pharmacist can add 2% co-trimoxazole to the sticky paste for oral decontamination and/or in the suppositories. Twice daily co-trimoxazole 960 mg into the gastric tube will generally be enough to eliminate these PPMs from the digestive tract. In case of combined resistance for polymyxin/colistin, tobramycin and co-trimoxazole an alternative regimen should be applied. These regimens are less well studied. The intravenous preparation of amikacin can be used at a dose of 500 mg 4 times daily into the gastric tube. This intravenous formulation cannot be added to the sticky oral paste but the intravenous formulation can be applied by an oral swab onto the oral mucosa 4 times daily.^[34] In exceptional cases topical application of fosfomycin, paromomycin or temocillin might be considered. These strategies should only be used in extraordinary situations and should be combined with intensive monitoring of rectal and oral cultures.
10. In case of methicillin resistant *Staphylococcus aureus* (MRSA) an alternative decontamination strategy can be applied.^[35-37] This consists of the normal PTA containing paste and suspension with the addition of vancomycin. The oral paste can be enriched with 2% vancomycin, which can be prepared by the hospital pharmacy. To decontaminate the digestive tract, 500 mg of vancomycin 4 times daily can be given into the gastric tube (the intravenous formulation can be used).^[36-37] Infections should concomitantly be treated with vancomycin intravenously. Nasal carriage should be eliminated by local application of mupirocin. MRSA infection can be treated with vancomycin or ceftaroline.

Conclusion

Decontamination of the digestive tract and other normally sterile sites in the body must be achieved to prevent secondary endogenous infections in ICU patients. Active involvement of intensivists and extensive education and training of the nursing team is obligatory to achieve this in all patients. Usually the standard SDD regimen is sufficient. However, when the surveillance cultures show an abnormal carrier state or persistent colonisation additional measures are needed. This article has summarised the necessary routine measures to obtain successful decontamination. In addition, measures needed in specific circumstances, such as in case of highly resistant organisms, are summarised as well.

Disclosures

All authors declare no conflict of interest. No funding or financial support was received.

References

- Stoutenbeek CP, van Saene HKF, Miranda DR, Zandstra DF. The effect of selective decontamination of the digestive tract on colonisation and infection rate in multiple trauma patients. *Intensive Care Med.* 1984;10:185-92.
- Van Saene HKF, Petros AJ, Ramsay G, Baxby D. All great truths are iconoclastic: selective decontamination of the digestive tract moves from heresy to level 1 truth. *Intensive Care Med.* 2003;29:677-90.
- van Saene HKF, Ramos B, Langer M. Surveillance samples and selective digestive decontamination in the intensive care unit. *Minerva Anestesiologica.* 2015;81:809-15
- Silvestri L, Petros AJ, Sarginson RE, de la Cal MA, Murray AE, van Saene HKF. Handwashing in the intensive care unit: a big measure with modest effects. *J Hosp Inf.* 2005;59:172-9
- de Smet AM, Kluytmans JA, Cooper BS, et al. Decontamination of the digestive tract and oropharynx in ICU patients. *New Engl J Med.* 2009;360:20-31.
- Plantinga NL, de Smet AMG, Oostdijk EA, et al. Selective Digestive and Oropharyngeal Decontamination in medical and surgical ICU-patients; an individual patient data meta-analysis. *Clin Microbiol Infect.* 2018;24:505-13.
- D'Amico R, Pifferi S, Torri V, Brazzi L, Parmelli E, Liberati A. Antibiotic prophylaxis to reduce respiratory tract infections and mortality in adults receiving intensive care (Review). *Cochrane Library.* 2013, Issue 2. DOI: 10.1002/14651858.CD000022.pub3
- Silvestri L, van Saene HKF, Milanese M, Gregori D, Gullo A. Selective decontamination of the digestive tract reduces bacterial bloodstream infection and mortality in critically ill patients. Systematic review of randomized, controlled trials. *J Hosp Inf* 2007;65:187-203.
- Daneman N, Sarwar S, Fowler RA, Cuthbertson BH. Effect of selective decontamination on antimicrobial resistance in intensive care units: a systematic review and meta-analysis. *Lancet Infect Dis.* 2013;13:328-41.
- Plantinga NL, Bonten MJM. Selective decontamination and antibiotic resistance in ICUs. *Crit Care.* 2015;19:259.
- Houben AJ, Oostdijk EA, van der Voort PHJ, Monen JC, Bonten MJ, van der Bij AK. Selective decontamination of the oropharynx and the digestive tract, and antimicrobial resistance: a 4 year ecological study in 38 intensive care units in the Netherlands. *J Antimicrob Chemother.* 2014;69:797-804.
- Oostdijk EA, de Smet AM, Kesecioglu J, Bonten MJ, Dutch SOD-SDD Trialists Group. Decontamination of cephalosporin-resistant Enterobacteriaceae during selective digestive tract decontamination in intensive care units. *J Antimicrob Chemother.* 2012;67:2250-3.
- D'Amico R, Pifferi S, Leonetti C, Torri V, Tinazzi A, Liberati A. Effectiveness of antibiotic prophylaxis in critically ill adult patients: systematic review of randomized controlled trials. *BMJ.* 1998;316:1275-85.
- Oudemans-van Straaten HM, Endeman H, Bosman RJ, et al. Presence of tobramycin in blood and urine during selective decontamination of the digestive tract in critically ill patients, a prospective cohort study. *Crit Care.* 2011;15:R240.
- de Smet AM, Kluytmans JA, Blok HE, et al. Selective digestive tract decontamination and selective oropharyngeal decontamination and antibiotic resistance in patients in intensive-care units: an open-label, clustered group-randomised, crossover study. *Lancet Infect Dis.* 2011;11:372-80.
- Dubos RJ, Savage DC, Schaedler RW. The indigenous flora of the gastrointestinal tract. *Dis Colon Rectum.* 1967;10:23-34.
- Sghir A, Gramet G, Suau A, Rochet V, Pochart P, Dore J. Quantification of bacterial groups within human fecal flora by oligonucleotide probe hybridization. *Environ Microbiol.* 2000;66:2263-6.
- van der Waaij, Berghuis-de Vries JM, Lekkerkerk- van der Wees JEC. Colonization resistance of the digestive tract in conventional and antibiotic-treated mice. *J Hyg Camb.* 1971;69:405-11.
- Wieggersma N, Jansen G, van der Waaij D. Effect of twelve antimicrobial drugs on the colonization resistance of the digestive tract of mice and on endogenous potentially pathogenic bacteria. *J Hyg Camb.* 1982;88:221-30.
- Zhang L, Huang Y, Zhou Y, Buckley T, Wang HH. Antibiotic administration routes significantly influence the levels of antibiotic resistance in gut microbiota. *Antimicrob Agents Chemother.* 2013;57:3659-66.
- Lewis, BB, Buffie CG, Carter RA, et al. Loss of Microbiota-Mediated Colonization Resistance to Clostridium difficile Infection With Oral Vancomycin Compared With Metronidazole. *J Infect Dis.* 2015;212,1656-65.
- Selective Digestive tract Decontamination in intensive care medicine. A practical guide to controlling infection. van der Voort PHJ, van Saene HKF (eds). Springer-Verlag Milano 2008.
- van der Spoel JI, Oudemans-van Straaten HM, Stoutenbeek CP, Bosman RJ, Zandstra DF. Neostigmine resolves critical illness-related colonic ileus in intensive care patients with multiple organ failure – a prospective, double-blind, placebo controlled trial. *Intensive Care Med.* 2001;27:822-7.
- van der Spoel JI, Oudemans-van Straaten HM, Kuiper MA, van Roon EN, Zandstra DF, van der Voort PHJ. Laxation of critically ill patients with lactulose or polyethylene glycol: A two center randomized, double-blind, placebo-controlled trial. *Crit Care Med.* 2007;35:2726-31.
- Pieterse JM, dos Reis Miranda D, Rietdijk W, Bakker J. Increasing intensity of selective digestive decontamination dosing does not result in improved clinical outcomes. *Minerva Anestesiologica.* 2017;83:529-30.
- Mol M, van Kan HJM, Schultz MJ, de Jonge E. Systemic tobramycin concentrations during selective decontamination of the digestive tract in intensive care unit patients on continuous venovenous hemofiltration. *Intensive Care Med.* 2008;34:903-6.
- Oudemans van Straaten HM, Endeman H, Bosman RJ, et al. Presence of tobramycin in blood and urine during selective decontamination of the digestive tract in critically ill patients, a prospective cohort study. *Crit Care.* 2011;15:R240.
- Silvestri L, van Saene HKF, Milanese M, Gregori D. Impact of selective decontamination of the digestive tract on fungal carriage and infection: systematic review of randomized controlled trials. *Intensive Care Med.* 2005;31:898-910.
- Eggimann P, Pittet D. Candida colonization index and subsequent infection in critically ill surgical patients: 20 years later. *Intensive Care Med.* 2014;40:1429-48.
- Morar P, Makura Z, Jones A, et al. Topical antibiotics on tracheostoma prevents exogenous colonization and infection of lower airways in children. *Chest.* 2000;117:513-8.
- van der Voort PHJ, Zandstra DF. Kolonisatie van de lage luchtwegen na minitracheostomie tijdens selectieve darmdecontaminatie. *Intensive Care Review.* 1996;11:213-7.
- Hassan NA, Awdallah FF, Abbassi MM, Sabry NA. Nebulized Versus IV Amikacin as Adjunctive antibiotic for hospital and ventilator-acquired pneumonia postcardiac surgery: A randomized controlled trial. *Crit Care Med.* 2018;46:45-52.
- Sullivan KA, Caylor MM, Lin FC, Campbell-Bright S. Comparison of Amphotericin B bladder irrigations versus fluconazole for the treatment of candiduria in intensive care unit patients. *J Pharm Pract.* 2017;30:347-52.
- Nahar J, Buitinck S, Jansen R, et al. Use of enteral amikacin to eliminate carriage with multidrug resistant Enterobacteriaceae *J Infect* 2019; in press.
- Silvestri L, van Saene HKF, Milanese M, et al. Prevention of MRSA pneumonia by oral vancomycin decontamination: a randomised trial. *Eur Respir J.* 2004;23:921-6.
- Cerdá E, Abella A, de la Cal MA, et al. Enteral Vancomycin Controls Methicillin-resistant Staphylococcus Aureus Endemicity in an Intensive Care Burn Unit. A 9-Year Prospective Study. *Ann Surg.* 2007;245:397-407.
- de la Cal MA, Cerdá E, van Saene HKF, et al. Effectiveness and safety of enteral vancomycin to control endemicity of methicillin-resistant Staphylococcus aureus in a medical/surgical intensive care unit. *J Hosp Inf.* 2004;56:175-83.