dulatórios seriam os responsáveis pela predisposição à infecção da ferida cirúrgica [46]. Metanálise de estudos com distribuição aleatória dos pacientes sobre o assunto não demonstrou superioridade da leucorredução na diminuição de infecção; contudo, quando foram excluídos os pacientes que não necessitaram de transfusões, foi observada redução da IFC [50].

Koch e col. estudaram 6.002 pacientes submetidos a procedimentos cirúrgicos cardíacos que receberam transfusões sanguíneas, sendo que 2.872 pacientes receberam 8.802 unidades de sangue que estavam estocados por 14 dias ou menos e 3.130 pacientes receberam 10.782 unidades estocadas há mais de 14 dias. Não houve diferenças nas características demográficas dos grupos, nem na quantidade de sangue transfundido por paciente; entretanto, os pacientes que receberam o sangue estocado por mais de 14 dias apresentaram maiores complicações pós-operatórias como intubação prolongada, falência renal, sepse, falência de múltiplos órgãos, entre outras. Além disso, a taxa de sobrevivência nos primeiros seis meses também foi menor nesse grupo. Deve-se considerar ainda a transfusão com sangue autólogo, visto que o risco de infecção é menor quando comparado com o alogênico [51].

Medidas Básicas de Prevenção de Infecção

Além dos cuidados intraoperatórios, há medidas preventivas básicas e simples que devem ser rigorosamente respeitadas sob risco de perda de sentido das discussões anteriores. O anestesiologista, por estar em posição que permite a observação do ambiente em que trabalha, deverá, além de realizá-las, exigir sua realização pelos outros profissionais da equipe. As recomendações básicas para a prevenção da IFC dividem-se em cuidados com o paciente, com a equipe e com o ambiente.

Em relação ao paciente, o banho pré-operatório deve ser feito com antisséptico desgermante (clorexidina desgermante a 2% ou água e sabão), mesmo que seja um procedimento simples como, por exemplo, blefaroplastia. A área de tricotomia deve ser a menor possível, ser feita com tricotomizador elétrico com cuidado para não lesar a pele, sem umedecer os pelos e imediatamente antes de encaminhar o paciente ao centro cirúrgico. No centro cirúrgico, deverá ser feita a desgermação da pele do paciente com clorexidina desgermante a 2% ou PVPI desgermante a 10% e, após antissepsia com clorexidina alcoólica a 0,5% ou PVPI alcoólico a 10%, utilizar o mesmo princípio ativo do desgermante.

A equipe cirúrgica deve realizar escovação por cinco minutos com solução antisséptica desgermante (clorexidina desgermante a 2% ou PVPI desgermante a 10%), com escova estéril de cerdas macias e de uso individual. Deve-se utilizar gorro, máscara, avental, luvas estéreis e propés, este último para proteção individual de respingos de sangue, secreções ou excreções. Outros profissionais deverão utilizar máscara, gorro, roupa privativa e equipamento de proteção individual quando necessário. O anestesista que for inserir cateteres venosos centrais deverá vestir paramentação completa, realizar limpeza da pele da região da punção com desgermante, seguida de antissepsia com clorexidina alcoólica a 0,5% ou PVPI alcoólico a 10% e usar campos estéreis. Para a inserção de cateter vesical deverá ser utilizada clorexidina aquosa ou PVPI tópico a 10%.

A sala cirúrgica deve ficar fechada durante a intervenção com o objetivo de manter as condições de ventilação e troca de ar dentro das normas estipuladas, umidade e temperatura adequadas, pressão positiva dentro da sala em relação aos corredores e número mínimo de pessoas dentro da sala.

As Recomendações Podem Ser Resumidas em:

1. Observar o antibiótico administrado de acordo com o procedimento e a flora bacteriana hospitalar, administrando-o antes da incisão em tempo hábil para garantir níveis sanguíneos e teciduais, além da correta administração intervalar, respeitando as 24 horas de duração da antibioticoprofilaxia.
2. Utilizar calor irradiado para aquecer o paciente duas horas antes do procedimento cirúrgico, evitando a perda de calor central para a periferia devido à vasodilatação causada pelos anestésicos.
3. Controle glicêmico adequado e justo.
4. Evitar altas frações inspiradas de oxigênio, realizar manobras intraoperatórias de recrutamento alveolar, utilização de PEEP.
5. Manutenção da euvolemia baseada em parâmetros clínicos e precaução com reposição hídrica agressiva com cristaloides ou coloides, haja vista que não se conseguiu demonstrar que ocorre diminuição da infecção e pode diminuir a função pulmonar e levar a edema de alças intestinais, atrasando a recuperação de sua função.
6. Diminuir quando possível o gatilho transfusional, dar preferência a sangue estocado por menos de 14 dias e, quando possível, utilizar filtros de leucócitos ou sangue autólogo.
7. Respeitar e fiscalizar as normas básicas de prevenção de infecção do paciente, da equipe profissional e da sala de operação.

Ways the Anesthesiologist Can Contribute to the Prophylaxis of Infection in the Surgical Patient

Fabiana Aparecida Penachi Bosco Ferreira, TSA, M.D., Maria Ligia Gomes Marin, M.D., Tânia Mara V. Strabelli, M.D., Maria José Carvalho Carmona, TSA, M.D.

INTRODUCTION

Nosocomial infections represent one of the most common complications of hospitalized patients especially those with more severe conditions. Infection of the urogenital tract (associated with urinary catheterization), surgical wound infection (SWI), infection of the blood stream (associated with intravascular devices), and pneumonia (associated with the ventilator) are responsible for approximately 80% of all nosocomial infections. Infection of the urogenital tract is more common (35%), but it is associated with the lowest morbidity. Infection of the surgical wound is the second in frequency (20%), but the third in costs; infection of the blood stream and pneumonia are less common (15% each), but they are associated with high mortality rates and costs[1,2].

Besides the increase in the duration of hospitalization and the need of intensive care that cause an increase in hospital costs, the condition of surgical patients with infection can deteriorate, they might not recover their prior condition, or they can even evolve to death.

Several risk factors for infection in surgical patients such as obesity, smoking, diabetes mellitus, use of corticosteroids or other immunosuppressors, malnutrition, duration of preoperative hospitalization, severity of the disease, and nasal colonization by *Staphylococcus aureus* have been identified[3]. Besides patient-related risks, infection in the surgical patient also depends on the surgical procedure, surgeon, and hospital[3,4]. In 1990, the National Nosocomial Infections Surveillance (NNIS) proposed an index to predict the risk of SWI based on three of the many risk factors: duration of the surgery (longer than predicted), surgical field (contaminated), and physical status according to the American Society of Anesthesiologists (ASA P3, P4, P5), which facilitated studies and comparisons on the incidence of infection in this group of patients[5,6].

The American Society of Anesthesiologists has educational recommendations on the control of nosocomial infections, such as disinfection of the equipment used in anesthesia aiming mainly at preventing mechanical ventilation-related infections, prevention of infection during insertion and maintenance of catheters, recommendations for the protection of immunosuppressed patients, and for prevention of drug contamination.

Special attention should be given to the storage and manipulation of propofol. Several reports have linked systemic infections to the injection of this drug whose active ingredient, 2,6-diisopropylphenol, is formulated in a sterile emulsion of soy oil, glycerol, and egg lecithin that unlike other intravenous drugs that are not lipid-based, allow fast bacterial growth at room temperature[7]. Those recommendations include disinfection of the vials with alcohol before opening them, use of syringes for a single patient, and the infusion should begin within six hours after opening the syringe and completed within 12 hours[8]. Those directives are also followed by ANVISA (Agência Nacional de Vigilância Sanitária - the Brazilian equivalent of the American FDA).

Besides the interventions proposed, standardization of intraoperative prevention measures is fundamental since the first few hours after bacterial contamination represent a very important window for the establishment of infection, and the anesthesiologist has a fundamental role during this period: optimization of the surgical patient for the prevention of infections. The objective of this review was to discuss those intraoperative medical measures.

Antibiotic Prophylaxis

Although it has been proven that adequate antibiotic prophylaxis, i.e., the administration of proper antibiotics with regular intervals and at the exact moment to guarantee blood and tissue levels above the minimum inhibitory concentration (MIC) of pathogens that might be encountered during medical procedures, is simple and effective, often times it is not done properly losing its effectiveness in the prevention of SWI, and it might even select resistant microorganisms. However, since the incidence of infection is associated with multiple risk factors, it rarely is associated with the improper administration of antibiotics[9-11].

The first clinical study, undertaken in 1969, demonstrated that preoperative antibiotic prophylaxis in patients undergoing intestinal surgeries reduced infection of the surgical field and the development of sepsis, which was not observed in patients who only received antibiotics in the postoperative period. Directives based on retrospective studies determined that tissue and blood levels should be above the MIC at the moment of the surgical incision. Thus, the administration should be instituted accordingly, usually 30 minutes to one hour before the incision, to promote adequate serum and tissue concentrations[12]. If a tourniquet is to be used during the procedure, antibiotic infusion should finish before insufflation[11].

The choice of the ideal antibiotic for the procedure is focused on fighting the most frequent microorganisms. For most surgeries not affecting chronically colonized organs, the most frequent microorganisms are those found in the skin: species of *Staphylococcus* and *Enterococcus*, and first generations cephalosporins have good cost-benefit ratio. On the other hand, surgeries of the gastrointestinal tract require coverage for Gram negative and anaerobes[10].

The use of vancomycin for prophylaxis is controversial since it is the antibiotic of choice in mediastinitis due to methicillin-resistant strains of *Staphylococcus aureus*, or infection of the incision with methicillin-resistant coagulase-negative *Staphylococci*, or in institutions with a high incidence of those infections[10].

In surgical procedures with cardiopulmonary bypass (ECC), cefuroxime, a second-generation cephalosporin, has been used for prophylaxis in different dosing schedules, ranging from a total dose of 3 to 6 g in 24 or 48 hours with different administration intervals, and often associated with an extra dose of 750 mg after ECC[13,14]. Nascimento et al., studying the pharmacokinetics of this antibiotic in patients undergoing surgical myocardial revascularization with ECC observed a plasma peak with a sudden, fast reduction when three 1.5-g doses administered every 12 hours were used. This characteristic proved to be inadequate for antibiotic prophylaxis, since plasma levels of cefuroxime six hours after each bolus were lower than 16 µg.mL^{-1} (4 x MIC, adequate bactericidal level). Besides, according to the decay curves of concentration over time, levels of cefuroxime were below required at the lowest point for most administrations (approximately 4 µg.mL^{-1} around the ninth hour, and approximately 1 µg.mL^{-1} on the 12th hour after the administration)[14]. This low drug concentration especially in the immediate postoperative period can be a risk factor for the surgical patient, contributing for the development of nosocomial infections and strains of bacteria resistant to cefuroxime and other β-lactam antibiotics[15].

Prevention and Treatment of Hypothermia

Moderate hypothermia, i.e., body temperature between 34 and 36° C, is frequently observed in surgical patients, and among its complications we find increased duration of hospitalization, intraoperative bleeding, and the need of transfusion of blood products, the presence of tremors, increased oxygen consumption, and discomfort. All those factors can predispose surgical patients to infections[9,16].

A randomized, double-blind study with 400 patients undergoing colorectal surgery separated into two groups: hypothermia (34.4 ± 0.4° C) or normothermia (37 ± 0.3° C), followed up for two weeks postoperatively, was interrupted with 200 patients because the hypothermia group had an 18.8% incidence of infection of the surgical wound versus 5.8% in the other group. Normothermic patients had more collagen in the surgical wound, sutures were removed one day earlier, patients had eaten earlier, and the incidence of vasoconstriction was lower, 6% versus 74%. This study showed that hypothermia is a risk factor for SWI. Although patients in the hypothermia group had greater need of transfusions, this was not an independent contributing factor according to multivariate regression analysis[17]. Excluding patients who required transfusions, Flores-Maldonado et al. demonstrated an 11.5% incidence of SWI in hypothermic patients versus 2% in normothermic patients[18]. Other authors also associated hypothermia with an increased incidence of SWI[19].

Hypothermia causes vasoconstriction, decreases subcutaneous tissue perfusion and, consequently, decreases the oxygen tension in the surgical wound. Patients with oxygen tension of 90 mmHg did not develop infection. Hypothermia can also decrease the inflow of polymorphonuclear cells into the incision, thus hindering bacterial destruction, induces the production of interleukins X and II, similar to the inflammatory status of patients with severe burn, increases the loss of nitrogen, and decreases collagen production[9,16,20,21].

Blood Glucose Control

The role of diabetes mellitus as one of the risk factors for the development of infection in surgical patients is well-established and, even in non-diabetic patients, hyperglycemia is associated with an increase in morbidity and mortality. Several recent studies have demonstrated this correlation between hyperglycemia and SWI[9,22-24].

The increase in glucose in healthy volunteers reduced transiently the total number of lymphocytes and inactivated immunoglobulins by non-enzymatic glycosylation and glycosylation of C3 complement, blocking its binding to bacteria. It has been demonstrated that neutrophil chemotaxis, phagocytosis, and bactericidal function are decreased in diabetic patients. It has also been demonstrated the recovery of those functions in nomoglycemic environments *in vitro*[25].

Van den Berghe et al. observed in severely ill patients treated with insulin infusions to maintain blood glucose levels below 110 mg.dL^{-1} a reduction in mortality from 8.4% to 4.6% regardless of whether they were diabetics or not. Mortality was decreased due to a reduction in multiple organ dysfunction secondary to sepsis[22].

To extrapolate those data for surgical patients, two series of cases in the same institution analyzed the effects of continuous infusion of insulin to maintain blood glucose levels below 200 mg.dL^{-1}, and observed a 66% reduction in the incidence of mediastinitis in those patients; the infusions were maintained postoperatively[26].

Although randomized clinical studies are necessary to define the need for rigid intraoperative control of blood glucose levels, evidence support this conduct: intraoperative blood glucose levels above 200 mg.dL^{-1} are not appropriate.

Strategies for Intraoperative Pulmonary Ventilation

Postoperative pulmonary complications represent a significant cause of morbidity and mortality. Some type of pulmonary complication develops in approximately 25% of large-sized surgeries. Atelectasis and the consequent hypoxemia, and abundant hydration with positive water balance and the consequent loss of pulmonary function can increase mechanical ventilation time and, therefore, the risk factors for infection[27].

The concept of intraoperative atelectasis was first reported by Bendixen et al in 1963. They also reported that consecutive pulmonary insufflations during anesthesia were capable of restoring arterial oxygenation and pulmonary compliance[28]. That same year, Bergman reported that general anesthesia was responsible for the reduction in functional residual capacity. It is currently known that atelectasis have an incidence of 50 to 90% in adult patients undergoing general anesthesia with spontaneous or controlled ventilation. The causes of this complication include mechanical compression of the lung parenchyma, absorption of gas contents, and surfactant dysfunction, and the latter is associated with cardiopulmonary bypass. This concept is controversial since it has a turnover of 14 hours[29].

Regarding mechanical compression, general anesthesia by relaxing the diaphragm causes the cephalad dislocation of this muscle and consequent reduction in transpulmonary pressure in more dependent and caudal portions of the lungs, which is exacerbated in obese patients. Supine position by itself causes a 500-mL reduction in residual functional capacity. The heart and mediastinal organs or the hands of the surgeon can also cause direct compression[30].

The use of high oxygen fractions has been described as a factor for pulmonary collapse. Rothen et al. reported an increase in pulmonary shunt from 0.3% to 2.1-6,5% with increases in the fraction of inspired oxygen from 30% to 100%, and increased in atelectasis[31].

On the other hand, two randomized double-blind studies with 800 patients undergoing colorectal surgery assessed the effects of intraoperative fractions of inspired oxygen of 80% versus 30% two (500 patients) and six (300) hours after the surgery. Both reported a significant reduction in the incidence of SWI in the 80% group[32,33]. Those results were not supported by a randomized study by Pryor et al.[34] with 160 patients; this study was criticized by the smaller number of patients, lack of strictly double-blindness, infections were evaluated retrospectively, and the groups compared were not homogenous. None of the studies mentioned evaluated pulmonary function[35].

High fractions of inspired oxygen are also associated with lower incidence of nausea or vomiting and increased antimicrobial activity of alveolar macrophages; however, they can also hinder postoperative reversion of atelectasis. Thus, caution should be used when increasing the fraction of inspired oxygen intraoperatively[36,37].

Strategies to avoid perioperative pulmonary complications due to infections secondary to intraoperative atelectasis include alveolar recruitment maneuvers; opening collapsed territories depends on high pressures and the time necessary to overcome the opening pressure (40 cmH_2O for 30 seconds expands areas of atelectasis of a normal lung under general anesthesia), followed by the institution of adequate levels of positive end-expiratory pressure (PEEP) as long as the patient remains intubated during general anesthesia, and the use of lower fractions of inspired oxygen avoiding the development of new atelectasis[27,37]. The need of successive recruitment maneuvers might be an indication that the level of PEEP is not enough to prevent pulmonary collapse. Those maneuvers reduce mechanical ventilation-induced pulmonary damage, the time for extubation, the incidence of pneumonia, and consequently hospital costs. They should always be performed in patients with balanced hemodynamic parameters. Besides, by improving the use of a specific fraction of inspired oxygen, characterized by an increase in the arterial pressure of oxygen, one can achieve the benefits of high inspired fraction mentioned[38,39].

Volume Replacement

The objectives of intraoperative hydration include replacement of losses due to fasting, to third space, blood loss, and to maintain cardiac output, blood pressure, and urinary volume. Patients with adequate intravascular volume also maintain adequate oxygen tension in the subcutaneous tissue, and increasing the intravascular volume improves oxygen tension in patients with poor perfusion. On the other hand, mild to moderate hypovolemia can be tolerated in healthy adults since the fluid accumulated in the interstitial space moves into the intravascular space restoring the hemodynamic balance[40].

A double-blind randomized study with 56 patients undergoing colon surgeries proposed two types of hydration: 8 to 10 $mL.kg^{-1}.h^{-1}$ followed by 16 to 18 $mL.kg^{-1}.h^{-1}$ up to one hour postoperatively; and blood was replaced at a proportion of 3:1 to maintain urine output greater than 1 $mL.kg^{-1}.h^{-1}$ and blood pressure at 70% of baseline values. Although patients with lower hydration presented better oxygen tension in the subcutaneous tissue, the incidence of SWI was not decreased[41].

Lange et al. demonstrated that the use of hydroxyethyl starch decreases the need of crystalloids to maintain hemodynamic stability and urine output, with an increase in oxygen tension in the subcutaneous tissue (54% versus 29%)[42].

On the other hand, a randomized study that restricted hydration during surgeries of the gastrointestinal tract demonstrated lower incidence of complications, with a fast return of the intestinal transit, decreasing hospitalization by one day[43].

Blood Transfusions

Intra- and postoperative anemia is a risk factor for the development of infection in surgical patients, which has been demonstrated by several studies, some of them limited by the number of patients or for the retrospective nature of the study. On the other hand, some of those studies were well-designed and it is currently proven the association between transfusions and infections in patients undergoing cardiac, orthopedic, trauma, and colorectal surgeries, as well as the reduction of postoperative infection with autologous blood transfusion[44-48].

Another multicenter study in 11 Canadian centers with 1,349 patients undergoing colorectal surgeries demonstrated greater incidence of SWI and sepsis from abdominal sources in patients who received blood transfusions[49].

Some authors have suggested that leukocytes with their immunomodulatory effects in the blood transfused would be responsible for the predisposition for surgical wound infection[46]. A metanalysis of randomized studies on the subject did not demonstrate superiority of leukoreduction in the prevention of infections; however, when patients who did not require blood transfusions were excluded, a reduction in SWI was observed[50].

Koch et al. studied 6,002 patients undergoing cardiac surgeries who received blood transfusions; 2,872 of those patients received 8,802 units of blood that had been in storage for 14 days or less, and 3,130 patients received 10,782 units in storage for more than 14 days. Groups did not differ regarding demographic characteristics and the volume of blood transfused per patient; however, patients who received blood that had been in storage for more than 14 days had a higher incidence of postoperative complications, such as prolonged intubation, renal failure, sepsis, and multiple organ failure among others. The rate of survival in the first six months was also lower in this group. One should also consider transfusion with autologous blood, since the risk of infection is lower when compared to allogeneic blood transfusions[51].

Basic Measures for the Prevention of Infections

Besides intraoperative care, some basic and simple preventive measures should be strictly followed or the previous discussion could have been useless. Since the anesthesiologist is in a position that allows observation of the work place, besides following them, he should demand the observance of those measures by the other health care workers in the surgical team. Basic recommendations for the prevention of SWI are divided in patient care, team care, and environmental care.

Regarding the patient, degerming antiseptics (2% chlorhexidine or water and soap) should be used in the preoprative bath even in simple procedures such as blepharoplasty. The smallest possible skin area should be carefully shaved with an electric razor to avoid damaging the skin, the hair should be dry, and it should be done immediately before transferring the patient to the operating room. In the operating room, the skin of the patient should be cleaned once more with 2% chlorhexidine or 10% PVP-iodine, followed by 0.5% chlorhexidine in alcohol or 10% PVP-iodine alcohol, always using the same active principle of the water-based degerming solution. The surgical team should scrub for five minutes with degerming antiseptic solution (2% water-based chlorhexidine or 10% PVP-iodine with a soft single-use sterile brush. The surgical team should wear sterile cap, mask, gown, gloves, and surgical shoe covers, the latter for individual protection of spilled blood, secretions, or excretions. Other professionals should wear mask, cap, surgical scrubs, and individual protection equipment whenever necessary. The anesthesiologist inserting central venous catheters should wear the complete set of sterile clothing, clean the puncture area with a degerming solution followed by 0.5 chlorhexidine in alcohol or 10% PVP-iodine alcohol, and use sterile fields. For insertion of the urinary catheter, aqueous solution of chlorhexidine or topical 10% PVP-iodine should be used.

The operating room should remain closed during the surgery to maintain ventilation and change of air within recommended standards, as well as adequate humidity and temperature, positive pressure inside the operating room relative to the hallways, and the minimum number possible of people inside the room.

Recommendations Can be Summarized as:

1. The antibiotic used should follow the procedures of the institution, adequate to the bacterial flora of the hospital, and it should be administered long enough before the incision to guarantee proper blood and tissue levels, as well as observing the correct interval between doses, respecting the 24 hours of antibiotic prophylaxis.
2. Irradiated heat should be used two hours before the procedure to keep the patient warm, avoiding peripheral loss of central heat due to anesthetic-induced vasodilation.
3. Adequate glycemic control.
4. Avoid high fractions of inspired oxygen, and intraoperative alveolar recruiting maneuvers and PEEP should be used.
5. Maintenance of normal blood volume based on clinical parameters, being careful to aggressive fluid replacement with crystalloids or colloids since it has not been demonstrated that it reduces the incidence of infection and it can decrease pulmonary function and cause intestinal edema, delaying recovery of its function.
6. Whenever possible reduce the transfusion trigger, use blood stored for less than 14 days, use leukocyte filter, or promote the use of autologous blood.
7. Respect and supervise basic infection prevention norms related to the patient, the surgical team, and the operating room.

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RESUMEN
Ferreira FAPB, Marin MLG, Strabelli TMV, Carmona MJC - Cómo el Anestesiólogo Puede Contribuir para la Prevención de Infección en el Paciente Quirúrgico.

JUSTIFICATIVA Y OBJETIVOS*: El paciente quirúrgico con infección hospitalaria, además de aumentar los costes hospitalarios, puede que no recupere su condición previa e incluso muera. Además de los riesgos individuales ya establecidos, el desarrollo de la infección postoperatoria depende del procedimiento a que será sometido, de las condiciones hospitalarias y del cirujano. A pesar de haber muchas medidas para controlar la infección, falta una estandarización de las intervenciones intraoperatorias para optimizar ese paciente. Esta revisión tuvo el objetivo de discutir algunas de esas intervenciones que son eficaces y necesarias, alertando al anestesiólogo sobre su importancia en la prevención de la infección hospitalaria.*

CONTENIDO*: En esta revisión, fueron abordadas las causas de infección en el paciente quirúrgico, y se discutió también como una adecuada administración de antibióticos, el control térmico y glucémico y las estrategias de ventilación mecánica, hidratación y transfusión, pueden reducir los niveles de infección en el paciente quirúrgico.*

CONCLUSIONES*: El anestesiólogo es el profesional que debe intervenir en el intraoperatorio con medidas sencillas para optimizar la atención del paciente quirúrgico y reducir sus indicadores de infección.*