Effect of Hyperoxygenation During Surgery on Surgical Site Infection in Colorectal Surgery

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Purpose: Despite the use of different surgical methods, surgical site infection is still an important cause of mortality and morbidity in patients and imposes a considerable cost on the healthcare system. Administration of supplemental oxygen during surgery has been reported to reduce surgical site infection (SSI); however, that result is still controversial. This study was performed to evaluate the effect of hyperoxygenation during colorectal surgery on the incidence of wound infection.

Methods: This study was a prospective double-blind case-control study. The main aim of the study was to evaluate the effect of hyperoxygenation during colorectal surgery on the incidence of SSI. Also, secondary outcomes, such as atelectasis, pneumonia, respiratory failure, length of hospital stay, and required hospitalization in the intensive care unit were evaluated.

Results: SSI was recorded in 2 patients (2 of 40, 5%) in the hyperoxygenation group (FiO_2 80%) and 6 patients (6 of 40, 15%) in the control group (FiO_2 30%) ($P < 0.05$). Time of hospitalization was 6 ± 6.4 days in the hyperoxygenation group and 9.2 ± 2.4 days in the control group ($P < 0.05$).

Conclusion: This study showed a positive effect of hyperoxygenation in reducing SSI in colorectal surgery, especially surgery in an emergency setting. When the low risk, low cost, and effectiveness of this method in patients undergoing a laparotomy are considered, it is recommended for all patients undergoing colorectal surgery.

Keywords: *Surgery; Wound infection; Hyperoxygenation; Anesthesia*

INTRODUCTION

Surgical site infection (SSI) is one of the most common postoperative complications and is estimated to account for up to 29% of all hospital infections. The incidence of SSI in colorectal surgery is about 4% to 27% according to the literature [1-3]. Several risk factors make surgical sites prone to infection, and independent risk factors for SSI include time of surgery, the use of prophylactic antibiotics, and wound contamination. Dependent risk factors include age, malnutrition, smoking, immunosuppression, infection in other parts of the body, body temperature, and hypovolemia during surgery [4-6].

The first hours after bacterial contamination are critical for SSI. Tissue oxygen is important for wound healing and preventing SSI, and the body's defense against infection depends on the partial pressure of oxygen in tissue. In recent studies, the effect of hyperoxygenation during surgery on SSI was evaluated. Although in some studies on patients who underwent appendectomies or colorectal surgeries hyperoxygenation reduced the incidence of SSIs [7-10], in other studies, hyperoxygenation had no effect on the SSI rate for gastrointestinal (GI) and ovarian surgeries [11]. Because the effects of hyperoxygenation on the SSI rate are still controversial, in this study, we evaluated the effects of hyperoxygenation in reducing the SSI rate for emergency and elective

Annals of
Coloproctology

Effect of Hyperoxygenation During Surgery on Surgical Site Infection in Colorectal Surgery
Mina Alvandipour, et al.

colorectal surgeries.

METHODS

This was a prospective, double-blinded, case-controlled study. Its main purpose was evaluating the effect of hyperoxygenation during colorectal surgeries on the SSI rate at Emam hospital in Sari, Iran. Other outcomes that were evaluated during this study included atelectasis, pneumonia, respiratory failure and intensive care unit (ICU) admission. All patients who were candidates for emergency or elective colorectal surgeries were entered in the study after they had completed the form required by the hospital's ethics committee. Patients with chronic diseases, such as chronic obstructive pulmonary disease or pneumonia, body mass index (BMI) >35 kg/m^2, severe malnutrition (albumin <3), leukopenia (white blood cell <4,000 g/dL), surgery within the previous 30 days and O_2 saturation < 90%, as measured using a pulse oximeter, were excluded from the study.

The GI track was prepped mechanically the day before surgery in the selected candidates. Prophylactic antibiotics (ceftriaxone 1 g and metronidazole 500 mg) were given intravenously to all patients prior to surgery. All assignments were based on computer-generated random numbers and were kept in opaque, sealed, sequentially numbered envelopes until shortly before surgery. Laboratory tests, such as tests for hemoglobin and blood glucose, were completed perioperatively. The time for the administration of general anesthesia, the duration of surgery, the core temperature during and after surgery, and vital signs during and after surgery was recorded.

All subjects were given 100% oxygen during anesthesia induction and emergence. After induction of anesthesia and tracheal intubation, a mixture of 80% oxygen and 20% N_2O was administered to patients in the first group (group 1, hyperoxygenation group), and a mixture of 30% oxygen and 70% N_2O was administered to patients in the second group (group 2, control group). These mixtures were administered during the surgery and during the first hour postoperatively in the recovery room. The anesthesiologist was allowed to increase FiO_2 to maintain a pulse oximeter saturation (SpO_2) ≥95% to ensure patient safety. Patients were returned to the defined FiO_2 as tolerated. Intraoperative crystalloids were generally given at a rate of 6 to10 mL/kg/hr, based on actual body weight, even if obese, which is considered a moderate approach. Intraoperative core temperature was maintained near 36°C by using forced-air warmers and fluid warmers as per the attending anesthesiologist's request throughout the intraoperative period. In all cases, at the end of the surgery, the peritoneum and fascia were sutured continuously, followed by interrupted skin sutures at the end of the surgery. All surgeries were performed by one colorectal surgeon. The surgeon and the assistant surgeons were blinded to the kind of anesthesia and the patients' O_2 saturation.

During hospitalization, all patients were examined daily by a surgeon who was unaware of the patient's group assignment. Primary and second outcomes was measured and recorded. Blood replacement was done in order to achieve hemoglobin above 10 g/dL in patients with ischemic heart disease and above 8 in patients without coronary artery disease. Wound characteristics were evaluated at each visit according to the ASEPSIS wound scoring system. a wound scoring method, ASEPSIS, make assessment of wound sepsis more objective and reproducible by allotting points both for the appearance of the wound in the first week and for the clinical consequences of infection. ASEPSIS scores were between 0 and 70, and a score above 20 was considered to indicate wound infection [12].

Attending surgeons made hospital discharge decisions. Discharge timing was based on routine surgical considerations, including return of bowel function, control of infections (if any), adequate healing of the incision, and overall recovery during the postoperative period. After discharge from the hospital, all patients were seen weekly in the clinic by a surgeon not involved in the study for 1 month following discharge from the hospital. Data analyses were performed by using the t-test and the chi-square test with IBM SPSS Statistics ver. 19.0 (IBM Co., Armonk, NY, USA). A P-value < 0.05 was considered significant.

RESULTS

Eighty-five patients were enrolled in the study and randomly divided into 2 groups. Five patients died postoperatively in the hospital because of cardiopulmonary failure or sepsis, so 80 patients remained in the study at its conclusion. The mean ages of patients in the hyperoxygenation and the control groups were 58.4 ± 8.1 and 59.2 ± 9.2 years, respectively (P > 0.05). Gender showed no statistically significant difference between the 2 groups (P > 0.05); neither was there a significant difference in BMI between the 2 groups: 26.2 ± 8.1 in the former and 25.9 ± 6.8 in the latter (P > 0.05). Patient's characteristics and results of laboratory tests are recorded in Table 1. Among the 80 patients, 54 patients underwent elective surgery (28 patients in the hyperoxygenation group and 26 patients in the control group) and 26 patients underwent an emergency laparotomy (12 patients in the hyperoxygenation group and 14 patients in the control group) (P > 0.05). Patients were classified on the basis of the cause of the laparotomy, as shown in Table 2.

SSI was observed in 8 patients (2 patients in the hyperoxygenation group and 6 patients in the control group). Similarly, anastomotic leakage was observed in 3 patients, who were all in control group with FiO_2 30% (Table 3). The 2 patients with SSIs in the hyperoxygenation group underwent surgery in an emergency setting; thus, of the 12 patients in the hyperoxygenation group who underwent an emergency laparotomy, the SSI rate was 16% (2 of 12). Among the 6 patients with SSIs in the control group, 4 underwent surgery in an emergency setting; thus, of the 14 patients in the control group who underwent emergency surgery, the SSI rate was 29% (4 of 14) (Fig. 1). Eight patients in the hyperoxygen-

Table 1. Characteristic of the patients

Characteristic	Hyperoxygenation group	Control group	P-value
Age (yr)	58.4 ± 8.1	59.2 ± 9.2	>0.05
Body mass index (kg/m^2)	26.2 ± 8.1	25.9 ± 6.8	>0.05
Male sex	26	23	>0.05
Ischemic heart disease	4 (10)	4 (10)	>0.05
Hypertension	4 (10)	3 (7.5)	>0.05
Diabetes	5 (12.5)	4 (10)	>0.05
Smoker	9 (22)	8 (20)	>0.05
Hemoglobin (g/dL)	12.45 ± 2.07	11.8 ± 2.8	>0.05
White blood cell (g/dL)	7,900 ± 4,850	8,540 ± 5,340	>0.05
Albumin	3.5 ± 1.4	3.7 ± 2.1	>0.05
Opium addiction	5 (12.5)	7 (17.5)	>0.05
Chemotherapy	6 (15)	6 (15)	>0.05
Radiotherapy	4 (10)	3 (7.5)	>0.05
Colon cancer	17 (42)	20 (35)	>0.05
Right hemicolectomy	10 (25)	11 (27)	>0.05
Left hemicolectomy	7 (17)	9 (22)	>0.05
Rectal operation	7 (17)	8 (20)	>0.05
Preoperative O$_2$ saturation	98.1	97.8	>0.05

Values are presented as mean ± standard deviation or number (%).

Table 2. Etiology of the laparotomy in the 2 groups

Variable	Hyperoxygenation group	Control group	P-value
Colorectal cancer	24	28	>0.05
Diverticulitis	8	6	>0.05
Obstruction	8	6	>0.05

Table 3. Surgical site infection between the 2 groups

Variable	Hyperoxygenation group	Control group	P-value
Surgical site infection	2 (5)	6 (15)	<0.05
Anastomosis leakage	-	3 (7.5)	>0.05
Postop hospitalization days	6 ± 6.4	9.2 ± 2.49	<0.05
Asepsis score	10 ± 5	15 ± 5	<0.05
During operation O$_2$ saturation	98.5	97.5	>0.05
Postoperative O$_2$ saturation	98.1	97.5	>0.05

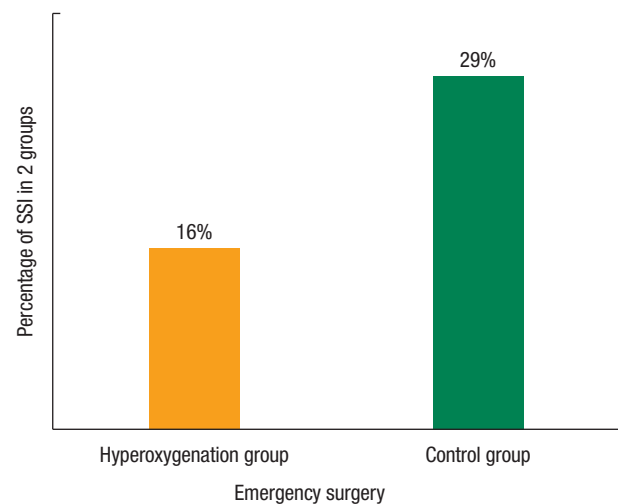Values are presented as number (%) or mean ± standard deviation.

Fig. 1. Comparison of surgical site infection (SSI) in emergency surgery between the hyperoxygenation and the control groups.

ation group (8 of 40, 20%) and 9 patients in the control group (9 of 40, 23%) had nausea or vomiting (P > 0.05); totally, 21% of all patients (17 of 80) experienced nausea and vomiting. Two patients postoperatively had atelectasis (1 patient in the hyperoxygenation group and 1 patient in the control group).

DISCUSSION

A SSI is defined as an infection of a surgical site and leads to prolong hospital admission and increase morbidity and mortality. Therefore, SSIs increase the cost of treatment [12, 13]. The first hours after bacterial contamination are critical for wound infection. Oxygen is vital for wound healing and for preventing SSIs. The presence of collagenases in tissue, which play important roles in determining the strength of a wound, depend on tissue oxygenation; also, angiogenesis, which is vital for wound healing, increases with increasing oxygen [14]. Oxygen tension at the end of surgery is often low, so bacterial eradication, which depends on oxidative killing with neutrophils, will be diminished. Thus, the oxygen free-radical level is correlated with the SSI rate [5, 15-17]. In colorectal surgeries, tissue oxygen levels are low at the anastomosis site and the skin. Therefore, hyperoxygenation can increase the tissue oxygen level and the number of oxygen free radicals at those sites and has a protective effect on anastomosis leakage [18, 19].

This study was designed to evaluate the effect of hyperoxygenation on the SSI rate after colorectal surgery. Our result showed that hyperoxygenation during surgery reduced the SSI rate, as well as the rate of anastomosis leakage. In this regard, some authors do not accept the effectiveness of supplemental oxygen [11, 20, 21], and some theories are used with respect to this controversy. The physiologic changes and interactions that occur after a substantial increase in the PaO$_2$ are multiple, complex, and difficult to study *in vivo*. A high oxygen partial pressure will increase the production of a number of derived reactive oxygen species, including the superoxide anion, hydroperoxyl radical, and hydrogen peroxide. A number of the reactions involving these reactive oxygen species are components of bactericidal host defenses [22-

Annals of
Coloproctology

Effect of Hyperoxygenation During Surgery on Surgical Site Infection in Colorectal Surgery
Mina Alvandipour, et al.

24]. However, reactive oxygen species are also involved in several processes that produce tissue injury and inhibit antibacterial mechanisms. Reactive oxygen species cause cellular dysfunction through damage to DNA and proteins, and can increased lipid peroxidation, so they can induce tissue cell death through apoptosis or necrosis. Additionally, the actions of hyperoxia on actin cause endothelial cell damage and impair the antibacterial function of macrophages [25-28].

The balance of beneficial and deleterious effects may depend on tissue factors that can vary greatly in a heterogeneous surgical population [11]. In fact, certain subgroups of patients may experience benefit or harm through this intervention, but no clear pattern was established in previous studies. In fact, tissue oxygenation, which reflects local perfusion and arterial oxygen partial pressure (PaO_2), is enhanced by cardiac output, pain control, supplemental fluids and management of carbon dioxide [29, 30]. Meyhoff et al. [17] gave their patients much less fluid than the researchers in other studies did, which might have compromised peripheral perfusion and oxygen delivery even in patients given supplemental oxygen. Therefore, in this study, crystalloid serum was generally given at a rate of 6 to 10 mL/kg/hr to improve tissue perfusion. With adequate tissue perfusion, supplemental oxygen can increase tissue oxygen tension. In the present study, the risk of a SSI was higher in patients that underwent an emergency laparotomy or had peritonitis with dehydration and inadequate tissue perfusion than it was in patients who underwent elective surgery.

Kurz et al. [20] in a clinical trial study said that despite subjects with lower PaO_2 having higher SSI rates up to a PaO_2 level of about 100 mmHg, that higher supplemental oxygen did not reduce the SSI rate when PaO_2 exceeded this level was intriguing. This may be partly attributable to impaired lung function, such as atelectasis, preventing higher oxygen delivery to wound tissue. In the present study, we excluded patients with severe pulmonary disease. Also, postoperatively, atelectasis was not higher in the hyperoxygenation group. While we cannot be certain that wound oxygen tension was not increased in the other negative trials, we also cannot be certain that it was because in most cases, wound tissue oxygen tension was not directly measured. This fact may explain inconsistencies between the results of different studies. In this study, the increase in oxygen tension in tissues and at anastomosis sites caused by receiving 70% oxygen seems to have played the main role in decreasing the SSI rate in hyperoxygenation patients, so O_2 saturation was higher in hyperoxygenation patients, although this result was not statistically significant. O_2 saturation varies with the PaO_2 in a nonlinear relationship. Above 90 mmHg of PaO_2, the curve becomes almost flat, so only a small rise in O_2 saturation is seen in spite of a large increase in PaO_2 [31]. Due to the sigmoidal shape of the oxy-hemoglobin dissociation curve, although the differences between 97% and 98% O_2 saturation is statistically not significant, the PaO_2 differences is significant.

In the emergency laparotomy setting, the risk of anastomosis leakage and SSI is higher because of hemodynamic instability, dehydration, and lack of mechanical prep of the GI track [18]; therefore, in this study, patients were matched with this variable to reach an accurate result. Among patients in the hyperoxygenation group who underwent an emergency laparotomy, the SSI rate was 16% (2 of 12) as compared to 29% (4 of 14) among the patients in the control group who underwent an emergency laparotomy; this means that hyperoxygenation had a great effect in reducing the SSI rate in emergency colorectal surgeries.

Colon cancer as an immune suppressor factor may have a great role in the SSI rate. Also, perioperative chemotherapy has a similar result. In this study, 65% of the patients had colorectal cancer. The SSI rate was higher in this group as compared to patients with other pathologies, although the differences were not statistically significant. The risks of peritoneal bacterial contamination and a SSI are higher in rectal surgery than in colon surgery. Also, peritoneal contamination, anastomotic leakage and wound infection are higher in left colon surgeries than they are in right colon surgeries. In this study, the distributions of patients by site of the colorectal surgery were not different, so the results of our study indicate that surgical site is not a factor affecting the SSI rate.

Although patients with supplemental oxygen had less nausea and vomiting in some studies [32, 33], in our study, no differences in nausea and vomiting were observed between the 2 groups. Also, hyperoxygenation can induced airway inflammation, blood glucose mismanagement, and change in cardiac index [34, 35]. Fortunately, in this study, no signs of these complications were observed.

In this study, patients were matched in 2 groups according to some variables like site of GI surgery, presence of malignancy, and administration of chemotherapy. They were also classified according to whether they underwent emergency or elective surgery. Thus, the results of this study should be more accurate and consequential. Therefore, based on these results, we conclude that hyperoxygenation with FiO_2 80% during surgery reduces the SSI rate in colorectal surgeries, as well as the duration of hospitalization. We recommend the use of supplemental oxygen during all colorectal surgeries because it is effective and has a cost benefit with negligible complications.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Annals of
Coloproctology

Effect of Hyperoxygenation During Surgery on Surgical Site Infection in Colorectal Surgery
Mina Alvandipour, et al.

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