OXYGEN AS A FACILITATOR IN THE REDUCTION OF SURGICAL SITE INFECTIONS

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ABSTRACT:

Globally surgical site infections (SSIs) are one of the most common nosocomial infections. Oxygen acts as a facilitator in the reduction of surgical site infections particularly in colorectal and abdominal surgery. During surgery the normal flora present in large intestine have also been eradicated which are the potential source of post operative infections. Supplemental oxygen aids in the eradication of pathogenic bacteria by oxidative killing. The oxidative killing not only heals the wounds but also enhances the activity of immune system by forming superoxide radicals. High fraction of inspired oxygen facilitate in reduction in the frequency of postoperative nausea and vomiting. Polymorphnuclear leukocytes also participate in the eradication of bacteria by oxidative killing. Free radicals of oxygen activate vascular endothelial growth and help in vasoconstriction. Hypoxia is one of the major problems encountered by anesthetist. Oxygen is used in combination with other gases to enhance the analgesic and anesthetic activity. Oxygen also reduces the chances of post-operative infection, nausea, and vomiting. High supplemental inspiration helps in the prevention of pneumonia. Oxygen is involved in a number of metabolic reactions. The size of the lesions and infections is reduced by an increase in the level of tissue oxygenation.

Keywords: Oxygen; Atelectasis; Oxidative killing; Tissue oxygenation; Immune system; Phagocytosis

INTRODUCTION:

Surgical Site Infections (SSIs) are the most common nosocomial infection all over the world. According to CDC (1997), about 27 million operations are held in USA annually. SSI is the major cause of morbidity and mortality and is mainly associated with overstay in the hospitals which increase the expenditure on the patient’s pocket. Coello with his colleagues estimated the extra stay in hospital increases 11.4 days with an extra expenditure of £ 3,500 (Coello et al., 2005). Thus, it is important to reduce or prevent the chance of SSIs by several precautionary measurements such as transfusion of blood, shaving, hypovolumia, hypothermia, hyperglycemia, malnutrition, oxygen supply, preoperative stay, antiseptic solutions, ultra clean room, gown, gloves, and duration and technique of operation (Mangram et al., 1999). Hypothermia decreases tissue oxygen tension and perfusion (Rabkin and Hunt 1987). Several studies have been conducted to show importance of administration of supplemental oxygen during surgeries (Pryor et al., 2004; Mayzler et al., 2005). The most SSIs occur in colorectal surgeries mainly due to the presence of anaerobes. Perioperative supplemental oxygen helps in the eradication of anaerobes which constitute normal flora in large intestine.
ADVANTAGES OF SUPPLEMENTAL OXYGEN:

WHO recommends the proper supply of oxygen according to the need of the patient during operation (WHO, 2009). It has been found that high a fraction of inspired oxygen has advantages like reduction in the frequency of postoperative nausea and vomiting (Greif et al., 1999; Turan et al., 2006), healing of colorectal anastomosis (Garcia-Botello et al., 2006) and above all reduction in the rate of SSIs (Belda et al., 2005). Hyperoxia may help in the prevention of pneumonia (Hohn et al., 1976).

RISK ASSOCIATED WITH SUPPLEMENTAL OXYGEN:

Pulmonary immune defense can be weakened by supplemental oxygen or mechanical ventilation (Kotani et al., 2000). Supplemental oxygen might lead to insufficient regulation of blood glucose level (Bandali et al., 2003). Supplemental oxygen may change in cardiac index (Carpagnano et al., 2004). Hyperoxia has been related to unfavorable effects such as an increased risk of airway irritation (Harten et al., 2003). Its excess use for prolong period may cause pulmonary inflammation and atelactesis (Akca et al., 1999; Kotani et al., 2000).

ATELECTASIS:

Akca et al. (1999) found that high level of inspire oxygen might lead to respiratory complications like pulmonary atelectasis that can be identified by computed tomography (CT) scan. This may collapse the alveoli and create difficulty in breathing due to gaseous exchange. Large area of atelectasis is caused by exposure to air for 5 minutes with 100% oxygen as compared to ventilation with lower oxygen concentration (Edmark et al., 2003). Pulmonary atelectasis is mainly caused by shorter period of oxygen administration (Lindberg et al., 1992). Supplemental oxygen may cause risk of fire because of laser instruments and heated surgical instruments (Barnes and Frantz, 2000; de Richemond and Bruley 2000). Hyperoxia also cause lung and myocardial injury especially in cardiopulmonary bypass (Donat and Levy, 1998; Rubertsson et al., 1998).

SUPPLY OF OXYGEN:

WHO recommends the presence of liquid oxygen cylinders in the hospitals. Oxygen helps in ignition of flammable material. Hudson mask, nasal catheters, endotracheal intubation, nasal prongs, orotracheal intubation, face mask ventilation, supraglottic airway ventilation, fiber-optic intubation, and many other devices are used for the proper supply of oxygen in different condition to patient. Endotracheal intubation proves 100% supply of supplemental oxygen while external devices like masks and reservoir bags supply 70% oxygen (WHO, 2009). For orotracheal intubation, skillful staff is needed to uphold the supply of oxygen ≥ 90% (Murphy and Doyle 2008). The quantity of oxygen in blood and tissue is determined by pulse oximetry (WHO, 2009). The oxygen partial pressure can be measured by microelectrodes (Silver, 1978).

ANESTHESIA:

Hypoxia is one of the most dreadful conditions for anesthetist (WHO, 2009). For general anesthesia, supplemental oxygen is necessary to ensure the proper supply of oxygen and the prevention of the patient to undergo hypoxia. It has been found that analgesics and anesthesia influence on respiratory function and may lead to hypoxia which may produce persistent effect up to five days especially at night (Wilkinson et al., 2000).

REASONS OF HYPOXIA:

It has been found that neuromuscular blocking agent benzodiazepines and opioids suppress ventilation. Prolonged operation and reoperation enhances the loss of blood which may cause hypoxia (Haridas and Malangoni, 2008). Oxygen delivery to tissues is impaired by coronary obstructive pulmonary disease which may reduce the oxidative killing (Henry and Garner 2003). Myocardial ischemia, thrombosis, and vascular surgery reduce
Oxygen as a Facilitator in the Reduction

Oxygen tension in tissues and may lead to hypoxia (Gill et al., 1992). Hypoxia is common after operation caused by weakening of ventilatory and gas exchange.

**Body Mass Index:**

If the body mass index is 35 kg/m$^2$, it increases the chances of SSIs by impaired oxygen supply due to poorly vascularised adipose tissues and decrease in the immune system which may enhance the chances of SSIs. Obesity decreases blood circulation by which oxygen supply is also decreased (Hopf et al., 1997). Pryor with his colleagues found that if BMI exceed 30 kg/m$^2$ the supply of 80% oxygen to patient is increased (Pryor et al., 2004). It may complex and extends the surgery like cardiac, spinal and cesarean section (Olsen et al. 2003; Abboud et al., 2004; Olsen et al., 2008).

**Smoking:**

Several studies (Ridderstolpe et al., 2001; Neumayer et al., 2007; Gravante et al., 2008) found that smoking increases the chances of SSIs. Smoking may causes vasoconstriction and reduces tissue oxygenation. Gravante with his co-workers have been that nonsmokers have less chance of SSIs as compared to permanent smokers 37.2% (Gravante et al., 2008). Smoking decreases tissue oxygenation for an hour which may cause hurdle in tissue healing (Jensen et al., 1991). Fleischmann et al. (2006) suggested that hypercarbia enhances tissue oxygenation and help in the reduction of SSIs by supplemental supply of oxygen.

**Combination of Gases:**

Oxygen is always used in combination with nitrous oxide in anesthesia and as analgesic gas (WHO, 2009). It has been established by studies that nitrous oxide helps in the control or reduction of SSIs (Myles et al., 2004; Pryor et al., 2004). By the use of nitrous oxide irreversely inhibition of vitamin B12 which main impaires the immune system and wound healing (Parbrook, 1967; Nunn, 1987). In a study it has been found that no SSIs occur in 2 groups when 65% nitrous oxide and same amount of nitrogen is mixed with oxygen (Parbrook, 1967).

**Oxidative Killing:**

Pathogenic bacteria can be eradicated by oxidative killing. Oxidative killing helps in the reduction of SSIs by increasing the oxygen tension in the tissues (Hopf et al., 1997). Oxidative killing helps in the healing of wounds by epitheliazation, decrease initiation of collagen formation and neovascularization (Hopf and Holm 2008). Oxidative killing enhances the immune defense system by making of superoxide radicals from oxygen, due to NADPH linked oxygenase which act as a catalyst (Babior, 1978; Allen et al., 1997). For healing of wounds lysyl and prolyl hydroxylase are catalyzed by oxygen, which help in the hydroxylation of lysine and proline respectively (Prockop et al., 1979).

**Tissue Oxygenation:**

Tissue oxygenation is dependent on circulating haemoglobin in tissues, level of oxygen in plasma and tissue blood flow (NICE, 2008). Oxygen partial pressure in tissue is enhanced by perioperative supplemental oxygen administration. Oxidative killing helps in the reduction of SSIs by increasing the oxygen tension in the tissues (Hopf et al., 1997). Tissue oxygenation depends upon smoking, fluid management, temperature of patient, anemia, pain (Sessler, 2006). The level of oxygenation in tissue is often low in wounds and colorectal anastomoses and reduces tissue healing by oxidative killing and also decreases neovascularization, epitheliazation and initiation of collagen formation (Niinikoski et al., 1973; Babior, 1978; Hopf and Holm, 2008).

**Radicals Formation:**

Oxidative killing depends upon the production of bactericidal superoxide radicals from oxygen. By the increased supply of oxygen the formation of unstable oxygen intermediates and hydrogen peroxide increases which boost up the phagocytic
activity of neutrophils (Allen et al., 1997). Oxidative pathway inhibitors like cyanide and hypoxia greatly impair killing of ingested organisms (Cheson et al., 1977). Vascular endothelial growth factor is activated by oxygen free radicals. Peripheral vasoconstriction is caused by hypoxia which impaired cardiac output and slight bradycardia, disturbance of cardiac rhythm (Hohn, 1977; Lodato and Jubran, 1993).

Neutrophils need glucose for energy and molecular oxygen for production of bacterial killing free radicals of oxygen and hydrogen peroxide (Hohn, 1977). The energy production by glucose and oxygen intermediate free radicals is hampered by some bacteria.

**IMMUNE SYSTEM:**

Polymorphonuclear leukocytes help in the reduction of bacterial count due to oxidative killing. Thus, high amount of oxygen for shorter exposure of time effectively decreases bacterial count and reduces the size of lesions. Silver found mainly oxygen is consumed by phagocytes in infection area (Silver, 1978). Around 0-150 mmHg oxygen needs for oxidative killing of pathogenic bacteria (Togawa et al., 1976). Mandell found in anaerobic condition some bacteria are efficiently killed by phagocytosis but some are not killed (Mandell, 1974). If the host immune system is better then the destruction of lymphatic and microvasculature is reversible with the span of time and vice versa with nécrosis in uncontrolled infection. The size of lesion increases in hypoxia. Knighton et al. (1984) observed that exposure of 45% and 12% oxygen for 1.5 and 46.5 hours respectively, the wound size is decreased by 36%.

**PHAGOCYTOSIS:**

The environmental oxygen plays a vital role in infection. Phagocytes utilizing more oxygen help in the reduction of tissue edema and the eventual occlusion of the microvasculature. During phagocytosis neutrophils are activated by a number of metabolic reactions with consequence raise in oxygen utilization (Klebanoff, 1980). Phagocytes can be contributed by product of oxygen metabolism. Triggered neutrophils increase oxygen consumption resulting in lower oxygen level in tissue and injured tissue cell by hydrogen peroxide, superoxide anions, hydroxyl radicals and others (result of neutrophil respiratory explode) may lethal to tissue (Knighton et al., 1986). Mandell (1974) observed that certain bacteria were killed by phagocytes in anaerobic condition whereas some other bacteria are not killed in anaerobic condition. Oxygen is needed for neutrophil killing of *Serratia marcescens*, *S aureus*, *E. coli* and *Klebsiella* and *Proteus* species (Mandell, 1974).

**TISSUE PARTIAL PRESSURE (PO2)/FRACTION OF INSPIRED OXYGEN (FiO2):**

Tissue partial pressure (PO2) is mainly dependent upon sufficient amount of oxygen that is provided to the blood. Hohn et al. found that if the level of oxygen is raised to 5 mmHg, the killing rate is 58% while if the level increases to 30 mmHg the bactericidal activity is 70%. Oxygen enhances the activity of leukocytes to kill microbes. The bactericidal activity of of neutrophils against *Staphylococcus aureus* is reduced if the level of tissue partial pressure (PO2) is below 15 mmHg (NICE, 2008). Knighton et al. (1984) found in his animal experimentas that pathogenic bacteria like *E coli*, *S aureus*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Salmonella typhimurium* and *Proteus vulgaris* are effectively killed by phagocytosis in aerobic condition. There is a minor change in killing efficacy if the tissue partial pressure (PO2) increases upto 150 mmHg13. Knighton with colleagues (1984) observed in their animal model experiments that after inclusion of bacteria phagocytosis is more during first four hours with approximately 30 mmHg and may alter fraction of inspired oxygen (FiO2) which may effect on tissue partial pressure (PO2). It has found that if oxygen saturation in major surgery is more than 95% it helps in the recovery (NICE, 2008). Tissue partial pressure of oxygen in infected and normal tissue is changed; the reduction in partial pressure is from 60 mmHg in normal tissue to...
0-10 mmHg in infected tissue (Silver, 1978). It has been observed that the rate of SSIs decreases if the fraction of inspired oxygen is high (Belda et al., 2005; Greif et al., 2000). If the fraction of inspired oxygen (FiO2) is 45%, the tissue partial pressure (PO2) is 40 mm Hg but if the fraction of inspired oxygen falls to 20%, the partial pressure may be reduced to 20 mm Hg. This change may provide minute changes in oxygen content in blood but huge changes in tissue oxygenation. The changes in fraction of inspired oxygen (FiO2) in the tissue between capillaries are effected in partial pressure changes to 10-15 mmHg. Tissue partial pressure (PO2) is low in infected tissue. If the fraction of inspired oxygen (FiO2) is 12%, (PO2) would derive to level zero but in the case with FiO2 to 45% tissue partial pressure (PO2) rise from 10-40 mm Hg (Silver, 1969). Supplemental oxygen helps to increase the level of fraction of inspired oxygen (FiO2), which help in the prevention of weakening of neutrophil killing, tissue necrosis, and aid in the proliferation of bacteria and death of local tissues and cells. Decreased oxygen delivery due to a decreased Fio2 results in local tissue anoxia, impaired neutrophil killing, and delayed bacterial clearance, which favor bacterial proliferation and skin and connective-tissue cell death. The result is a larger area of infectious necrosis. Administration of antibiotic with increased level of fraction of inspired oxygen (FiO2), produce efficient bacterioidal activity. If there is delayed administration of antibiotics, it may increase the size of lesion. Knighton et al. (1984) found by the exposure of 21% oxygen there is 56% reduction in injury size while if the exposure increases to 45% the reduction in lesion area around 63%.

PERCENTAGES OF OXYGEN:

Belda et al. (2005) with his colleagues found that 15% of patients, administered 80% oxygen as compared to who receive 30% oxygen supply suffers from 24% SSIs. Greif with his colleagues (2000) found that 5.2% patient suffers from SSIs who receive 80% oxygen in contrast to patient who receive 30% oxygen suffer 11.2% from SSIs (Greif et al., 2000). It is supported by another study in which 15.2% SSIs found in 30-35% oxygen supply and 11.5% in patient receiving 60% oxygen (Dellinger, 2005). Mayzler et al. (2005) found less SSIs reported in case with patient receive 80% oxygen supply. In another study.

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