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Effect of postoperative use of nasal oxygen catheter supplementation in wound healing following total knee arthroplasty

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OBJECTIVES: Healing is an event that is fundamental to the success of total knee arthroplasty. The aims of the present study were to compare the rates of complications related to wound healing between two groups of volunteers submitted to total knee arthroplasty and to evaluate the effects of postoperative oxygen supplementation by means of a nasal catheter.

METHOD: A total of 109 patients who underwent total knee arthroplasty were randomized into two groups, namely, groups that did and did not receive postoperative oxygen supplementation via a nasal catheter. The surgical wound was monitored every day during the hospital stay and on the 7th, 14th, 21st, 30th and 42nd postoperative days. Characteristics related to healing were observed, including hyperemia, dehiscence, necrosis, phlyctenules and deep and superficial infection.

RESULTS: There were no cases of deep infection. Hyperemia was statistically correlated with the total number of complications in the groups, with oxygen demonstrated to be a protective factor against hyperemia. Approximately 30% of the patients who exhibited hyperemia had other complications, independent of oxygen supplementation.

CONCLUSION: Oxygen supplementation following total knee arthroplasty was shown to be effective in diminishing hyperemia around the operative wound. The development of hyperemia was a precursor to other complications, irrespective of whether oxygen supplementation was used.

KEYWORDS: Arthroplasty; Knee Prosthesis; Wound Infection; Oxygen Inhalation Therapy; Postoperative Complications.

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INTRODUCTION

Total knee arthroplasty (TKA) is a procedure used to treat degenerative pathological conditions of the knee that yields excellent results (1). Because of the aging of the population and the significant increase in the number of TKA procedures performed worldwide, the number of complications inherent to this procedure is also increasing (2,3). Complications related to operative wounds have high morbidity rates and can rapidly evolve into local infectious processes that are difficult to treat (4-6). These complications may be local or systemic and depend on many factors related to the patient, the environment and the surgical technique (7).

Good postoperative healing is a factor that is fundamental for the success of this procedure. Disturbances of the healing process frequently lead to additional surgeries, prolonged hospital stays, impaired functional rehabilitation and higher costs (8-12). The classical measures for preventing complications related to the operative wound involve knowledge of the vascular anatomy of the knee, assessment and control of patient risk factors, biomechanical considerations and surgical technique optimization (10).

Certain other alternatives for such preventive measures have been cited in the literature, such as oxygen supplementation during the postoperative period (13). Although it has been established that certain elements of tissue repair are dependent on oxygen, the importance of oxygen in the healing process and infection prevention has not been

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universally accepted in clinical practice among a wide variety of specialties (14-16). Oxygen has been reported to increase fibroblast migration and replication, increase the rate of collagen production and the tensile strength of collagen fibers, stimulate angiogenesis, promote macrophage chemotaxis and enhance the antibacterial activities of leukocytes. Therefore, it is not surprising that increased oxygen delivery to wounds has been reported to improve wound healing and tissue repair (17).

The aims of the present study were to compare the rates of complications related to wound healing between two groups of volunteers submitted to TKA and to evaluate the effects of postoperative oxygen supplementation by means of a nasal catheter.

MATERIALS AND METHODS

In this study, 109 patients who underwent TKA between January 2007 and October 2012 were prospectively evaluated. The study was reviewed and approved by the institutional ethics committee (CAPPesq – Comissão de Ética para Análise de Projetos de Pesquisa - n° 1345/06). These patients were randomized into two groups (group 1: supplementation and group 2: control) and underwent TKA in accordance with the technique described below.

Inclusion criteria

- Diagnosis of primary knee osteoarthrosis with surgical indication;
- Age between 50 and 80 years;
- No previous surgery on the knee that was to be operated on;
- Absence of the following preoperative diagnoses: diabetes mellitus, chronic inflammatory disease, occlusive arterial disease, malignant tumors of any nature, chronic obstructive pulmonary disease, severe obesity (BMI>35 kg/m^2), immunodeficiency (due to transplantation, acquired immunodeficiency syndrome [AIDS], neoplasms, or the use of immunosuppressant drugs), hydro-electrolytic disorders, kidney failure, nutritional deficiency, smoking, hypothyroidism and alcoholism (18);
- Acceptance of participation in the study by filling out an informed consent form.

Exclusion criteria

- Return for outpatient follow-up outside of the date stipulated;
- Development of systemic infections unrelated to the surgical procedure;
- Need for admission to the intensive care unit during the immediate postoperative period.

Procedure

All of the patients underwent cemented TKA with replacement of the posterior cruciate ligament by means of a median access route and joint access via a transquadriceps and medial parapatellar approach. The incision extended from the anterior tuberosity of the tibia to approximately 4 cm proximal to the upper pole of the patella. During the surgical procedure, precautions involving the use of spacers were taken to avoid skin distress. All procedures were performed by one senior orthopedic surgeon with knee expertise who was assisted by two orthopedic residents.

A pneumatic tourniquet was used at the root of the thigh with a standard pressure of 300 mmHg. The tourniquet was inflated immediately before making the skin incision and was deflated and removed after the arthroplasty components had been cemented to achieve hemostasis. The length of the tourniquet used was documented. Both groups received perioperative antimicrobial prophylaxis consisting of 1.5 g of cefuroxime intravenously every 12 hours over the first 24 hours, in accordance with the protocol predefined by the Hospital Infection Committee of Orthopaedic and Traumatology Institute, Hospital das Clínicas, University of São Paulo School of Medicine. Spinal block anesthesia was the anesthetic technique used in all patients and all patients received oxygen supplementation during the procedure by means of a nasal catheter with a mean flow of 3-5 L/min, in accordance with the Anesthesia Department of this institution.

A continuous intra-articular vacuum suction drain was used, with its exit through the skin in the lateral suprapatellar region. The drain was kept in place for 48 hours.

Randomization

A simple randomization method was used to form the groups. To avoid any bias from the surgeon, the patients were allocated to the group with or without oxygen by means of a simple drawing performed immediately after the surgical procedure was complete. The simple drawing was always accomplished by randomly choosing one of two sealed envelopes, each containing a card previously labeled as group 1 or group 2.

Postoperative follow-up:

During the postoperative period, the patients in group 1 received oxygen supplementation by means of a nasal catheter with a mean flow of 3-5 L/min over the first 24 hours and at night for another two days (18,19). The patients were monitored during this period, with the aim of maintaining the peripheral oxygen saturation higher than 99% (measured by means of a pulse oximeter). Group 2 did not receive oxygen supplementation during the postoperative period. Throughout the hospital stay and at the subsequent outpatient return visits on the 7th, 14th, 21st, 30th and 42nd postoperative days, the operative wounds of the patients were monitored. The dressing was first changed 48 hours after the surgical procedure and was then changed every day thereafter. The patients were instructed to only clean around the dressing using 0.9% physiological serum until the stitches were removed.

The skin sutures were removed on the 21st day after the surgery. The rehabilitation protocol, which started on the first postoperative day, consisted of physiotherapy to increase the knee range of motion from 0 to 90 degrees and gait training with partial weight bearing, with the aid of a walking frame.

All of the patients received prophylaxis against venous thromboembolism, which consisted of enoxaparin (40 mg) for 30 days after the surgical procedure (20).

The following parameters related to healing were evaluated: hyperemia around the operative wound, which was taken into consideration when it comprised an area of more than 2 mm lateral or medial to the incision, as evaluated under white light; border necrosis of any size around the incision; dehiscence of the suture of any size;

and the presence of phlyctenules. To avoid bias, patient evaluations were conducted by an examiner who was unaware of the group to which each patient had been allocated and who had not participated in patient care during the study period. Thus, in this study, only the examiner was blinded during the outpatient return visits, given that the patient knew whether he/she had received oxygen (single blinding).

During the clinical follow-up, cases that evolved into infection were identified by means of wound observation, systemic parameter measurements, laboratory tests of inflammatory markers (C-reactive protein and erythrocyte sedimentation rate), and, possibly, by means of joint puncture, in accordance with the criteria used at our institution (4,21).

Statistical analysis

The data obtained were statistically evaluated using Fisher's exact test, the chi-square test and the Mann-Whitney test. Significance was indicated by $p<0.05$. The power of the study was also calculated for all variables. The sample size calculation was performed based on a pilot study of 40 cases, yielding a minimum power of 80%, in which the primary outcome was chosen to be the presence of any complication related to the operative wound. Thus, a minimum sample size of 100 cases was calculated for the study.

■ RESULTS

A total of 120 patients were included in the study. Eleven patients (9.2%) were excluded during postoperative follow-up for the following reasons: eight because they returned for their outpatient follow-up on days that were outside of the assessment routine and three because of clinical complications that were not directly related to the surgical procedure. Regarding the three patients with unrelated complications, two were excluded due to medication allergies and one was excluded due to pneumonia. The patients with medication allergies presented a diffuse cutaneous rash in the immediate postoperative period secondary to medication use (one patient was allocated to group 1 but only received oxygen supplementation for 1-2 h until the allergy was diagnosed). The patient with pneumonia required non-invasive ventilation in the intensive care unit and antibiotic therapy for 2 weeks. The data of these 3 patients were not used in the analyses because the patients were excluded as soon as the intervention was initiated and/or because other treatment directly related to the intervention was necessary. Of the remaining 109 patients (90.8%), 74 were female and 35 were male, with a mean age of 62.3 years. The patient demographic data are shown in Table 1. During the intraoperative period, there were no cases of blood transfusion in either group. The patients were randomly distributed into the two groups during the intervention; 52 patients were assigned to group 1 (supplementation) and 57 patients were assigned to group 2 (control).

Among the patients in both groups, there were no significant differences regarding the following complication rates: border necrosis, dehiscence, phlyctenules and superficial infection. Superficial infection was successfully treated with oral antibiotic therapy and daily dressing changes. There were no cases of deep infection in either group during the study period. There were no cases of hypoxemia ($SpO_2<90\%$) during the postoperative period that required oxygen supplementation in the control group. There was a significant difference between the groups with respect to the rate of hyperemia and the total number of complications (Table 2).

All of the patients with complications initially exhibited hyperemia around the operative wound. Excluding patients who exhibited hyperemia as the only adverse effect, seven patients (13.4%) in group 1 and 14 (24.5%) patients in group 2 presented other complications as well.

Of the patients who exhibited hyperemia, seven of the 19 patients in group 1 (36.8%) and 14 of the 42 patients in group 2 (33.3%) developed other complications. Overall, a total of 21 of the 61 patients (34.4%) developed some type of skin complication after initially exhibiting hyperemia around the incision site.

Both the number of patients with complications and the absolute number of complications were significantly greater in the group that did not receive oxygen therapy.

Separate evaluations of the variables studied revealed that only hyperemia around the operative wound presented a statistical correlation with the use or non-use of oxygen therapy during the postoperative period ($p<0.05$). Although group 1 presented a smaller absolute number of complications, such as dehiscence of the suture, border necrosis and presence of phlyctenules, there were no statistically significant correlation. Similarly, there was no correlation between the groups.

Evaluation of the duration of tourniquet use did not reveal a significant difference between the groups studied.

■ DISCUSSION

Total knee arthroplasty (TKA) has been extremely successful in elderly patients with degenerative pathological conditions but is not free from complications. A significant proportion of local infection processes following TKA occur as a result of primary wound healing failure. The management of such infections is difficult and the functional outcome is poor. The ability of a wound to heal is dependent

Table 1 - Patient demographic data.

	Group 1 (n = 52)	Group 2 (n = 57)	*p*
Gender (male/female)	*16/36*	*19/38*	*NS*
Mean age (years)	*60.6±9.4*	*63.8±8.3*	*NS*
Mean weight (kg)	*68.4±11.8*	*71.2±10.6*	*NS*
Mean BMI (body mass index)	*26.6±5.2*	*27.9±4.1*	*NS*
Mean procedure duration (min)	*110±35.2*	*115±30.5*	*NS*
Crystalloid administration (mL)	*2176.4±525.2*	*2017.3±517.4*	*NS*

NS: Not significant.

Table 2 - Complications related to the operative wound.

	Group 1 (n = 52)	Group 2 (n = 57)	*p*	1-beta(power)
Hyperemia	*19*	*42*	***<0.001***	*0.99*
Border necrosis	*0*	*3*	*0.245*	*0.68*
Dehiscence	*3*	*7*	*0.326*	*0.38*
Phlyctenules	*2*	*4*	*0.681*	*0.18*
Superficial infection	*4*	*4*	*0.999*	*0.05*
Patients with complications	*19*	*42*	***<0.001***	*0.99*
Duration of tourniquet use (*mean in minutes*)	*99.1*	*99.8*	*0.793*	
Total number of complications	*28*	*60*	***0.001***	

on factors such as the orientation of the skin incision, the wound tension and the viability of the wound edges, as assessed by skin oxygen tension estimations (22).

With regard to anatomical aspects of the vascular irrigation of the knee, there is greater vascularization of the medial border of surgical incisions when an anterior longitudinal approach to the knee is used and the oxygen tension on the lateral border is low when a medial parapatellar incision is used (10,22-24). For this reason, choosing a more lateral approach is recommended in patients with multiple incisions in the knee.

The skin flap needs to be deeply elevated to preserve the blood supply, particularly in areas without musculature, such as the regions of the patella, patellar tendon and tibial tuberosity. The infrapatellar fat should be preserved if possible (10).

The risk factors for these patients include obesity, diabetes, smoking, peripheral vascular disease, chronic use of corticosteroids, infection, previous healing problems and malnutrition (10,18,25,26). As inclusion criteria, the absence of some preoperative diagnoses was used with the aim of reducing the number of confounding variables. However, the use of this technique certainly reduces the generalizability of these data.

The operative incision causes tissue hypoxia, particularly on the first postoperative day, with a 67% diminution of oxygen tension. Oxygen tension then remains below normal (decreased by 16%) until the end of the first week post-surgery. Oxygen supplementation through the nose (24% oxygen) increases the skin tissue oxygenation to preoperative levels after only five minutes of application (6). O'Connor (10) recommended postoperative oxygen supplementation for several days following TKA in patients with a high risk of healing problems. Alternatively, Vince et al. (18) believed that 24 to 48 hours of supplementation is sufficient. Both of these authors added that early mobilization and the use of continuous passive mobilization also diminished the oxygen tension at the lateral border of the wound and should be avoided in high-risk patients.

With regard to the surgical technique, cauterization of the superior genicular vessels diminishes the oxygen tension at the lateral border of the incision and tourniquet use increases tissue hypoxia. Tourniquet use should be avoided in high-risk patients and the pressure should not be raised to more than 100 mmHg above the systolic pressure of the patient (10,27).

The mean oxygen tension in the surgical wound and its influence on the healing process and the prevention of infection have been the subjects of several studies. The formation of granulation tissue and connective tissue is dependent on the formation and the extent of new blood vessels in the wound (28,29). The inhaled oxygen causes hyperoxia at the border of the incision and increases the oxygen gradient in the wound. This gradient increase stimulates angiogenesis (via the increased release of angiogenic factors), which improves healing and diminishes the risk of infection via increased phagocytic function (30-35). Anoxia or severe hypoxia decreases phagocytic function and cell division (36).

The present study demonstrated that the group that received postoperative oxygen supplementation presented fewer complications related to the operative wound. Most studies that evaluated skin complications following knee arthroplasty only took major complications requiring surgical intervention into consideration. Thus, the number of skin complications in our study can be considered to be high; however, samples that also considered minor complications have shown adverse event rates reaching up to 35% (37).

Hyperemia was the most frequent event and the only single event with a statistical correlation favoring oxygen therapy. In the cases in which hyperemia was observed in isolation, the patients did not present major complications. Nevertheless, hyperemia should potentially be considered to represent initial skin distress and should be considered a predisposing factor for other adverse events, given that all patients who presented any skin complication initially had hyperemia at the borders of the incision. Hyperemia is also considered to be an initial event leading to possible superficial infection of the surgical site by the Centers for Disease Control (CDC), thus emphasizing its importance as an adverse event worldwide (38).

The use of oxygen was a protective factor against the development of hyperemia around the wound. However, among the patients in both groups who presented hyperemia, the development of other skin complications was similar (approximately 30%).

Although separate analyses of the other variables showed that there were lower absolute values in the group that received oxygen therapy, there were no statistical correlations. The total number of complications and the number of patients with a complication were statistically correlated, with oxygen serving as a protective factor.

Because none of the patients analyzed in this study had any clinical comorbidities that could have negatively influenced operative wound healing, the incidence of complications was lower than would be expected in a population without initial exclusion criteria that further diminished the incidence of less common adverse events.

One variable that may have introduced bias into this study was the duration of tourniquet use and length of surgery, but no significant differences in these variables were present between the groups. Another factor that could have interfered with the results was the method of oxygen therapy administration. Previous studies used a mask that precisely controlled the percentage of inhaled oxygen (10,13); however, this method was not used in the present study. We chose to use a more widely available form of oxygen supplementation so it would be possible to reproduce the procedure in any hospital, including those with fewer resources available.

Further studies on populations with a higher risk of skin complications should be conducted to assess the real benefits of oxygen in this group.

Oxygen supplementation was shown to be efficient in diminishing hyperemia around the operative wound subsequent to TKA. The development of hyperemia was a precursor of other complications, irrespective of whether oxygen supplementation was used.

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AUTHOR CONTRIBUTIONS

Helito CP project and wrote the manuscript. Junqueira JJ conducted bibliographic research and wrote the manuscript. Gobbi RG, Rezende MU and Tírico LE conducted the surgical procedures and clinical follow-up of patients and wrote the manuscript. Demange MK and Albuquerque RF analyzed the results, reviewed the manuscript and conducted the surgical procedures. Pécora JR and Camanho GL reviewed the manuscript and supervised the project.

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