Clinical Study

Supplemental Perioperative Oxygen (80% FIO$_2$) for the Prevention of Surgical Site Infection after Emergency Cesarean Section

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Objective. Cesarean section can be a lifesaving procedure. However, as with many surgeries, it is not exempt of complications. Surgical site infections generate higher costs, serious morbidity, and mortality. This study evaluates the benefits of perioperative oxygen to prevent surgical site infections. *Methods*. We conducted a randomized controlled trial to assess the effects of perioperative oxygen to prevent surgical site infection after emergency cesarean section. Patients were randomized to receive either oxygen (80% FIO$_2$) during cesarean section plus two hours postsurgery or no supplemental oxygen. A sample of 326 patients was calculated for the primary outcome (163 in each group) and they were evaluated daily before leaving the hospital, at days 15 and 30. *Results*. Initially, 360 patients were enrolled, from which 17 were excluded (sample size: 343 (179 patients in the air group and 164 in the oxygen group)). We found no significant difference in the incidence of surgical site infection between these two groups at any of the evaluation times. *Conclusion*. In this study of patients with emergency cesarean section, we showed that the use of supplemental oxygen does not reduce the incidence of surgical site infection. This trial is registeres with ClinicalTrials.gov NCT01340534.

1. Introduction

There are many indications for performing a cesarean section, but being a surgical procedure can be associated with several complications. One of the most importants is surgical site infection (SSI) which can be managed in an outpatient setting but sometimes requires hospitalization due to extension, concomitant bacteremia, or developing sepsis.

The Center for Disease Control (CDC) and the National Nosocomial Infections Surveillance (NNIS) reports a pooled mean rate of SSI after cesarean section of 15% [1] in the United States. Other studies report SSI rates ranging from 3% to 15% [2] with many cases being diagnosed before leaving the hospital. The number of SSI that develops afterwards is sometimes unknown, unless an adequate surveillance system is implemented.

The role of oxygen as a fundamental factor in the healing process of any wound has been discussed. Vascular disruption and increased cell metabolism produce a hypoxic wound [3].

Although hypoxia could act as a stimulus for tissue repair by creating a gradient between the injury and the unbroken tissue [4], the supplemental use of oxygen at high levels during surgery could allow the correction of hypoxemia on the surgical wound so that a normal growth and regeneration of injured tissues can occur.

Our purpose is to evaluate a simple method to prevent SSI that has proven to be of some use in other studies. To supplement the mother with 80% oxygen during and two hours after surgery. If our hypothesis is correct, the benefits (costs, health, and personal satisfaction) would be considerable.

2. Material and Methods

We conducted a prospective, randomized, controlled trial between October 2011 and November 2011. Women with singleton pregnancies of 37 or more weeks' gestation who

were admitted to the hospital for labor and delivery were eligible for the study. Once the decision was made to perform an emergency cesarean section for maternal or obstetrics reasons, written informed consent was obtained by one of the investigators. Exclusion criteria were elective cesarean sections, multiple pregnancies, immunocompromised patients (AIDS, cancer, systemic lupus erythematosus), chorioamnionitis, presence of fever upon admittance, acute fetal distress that required general anesthesia, acute or chronic maternal lung diseases and all pathologies that contraindicated the use of regional anesthesia. Patients were in stable condition (no evidence of maternal hemodynamic instability) before randomization and their management afterwards followed the standards accepted in our country and established in the national guidelines for the management of any patient after cesarean section.

For the sample size calculation, we decided to use the previous mentioned SSI rate of 15% from the NNIS. We considered the reduction to a third as of clinical relevance (from 15% to 5%). With an α error rate of 5% and a power of 85%, the calculated sample size was 318 (159 for group). A total of 370 patients (185 per group) were deemed necessary to account for dropouts or other problems.

After signing the informed consent, the surgeon in charge of the case opened a sealed, opaque envelope numbered sequentially containing a computer generated code randomizing the patient into one of the two groups. One group received oxygen 80% FIO_2 during surgery and 2 hours after the procedure. For this purpose an oxygen mask with reservoir was used (to guarantee the supply of 80% oxygen during and after surgery). Most studies done on the subject used this particular FIO_2, so we decided to use it as well. The other group received no supplemental oxygen.

All patients received antibiotic prophylaxis before surgery and the procedure was performed in a similar fashion in all cases (abdominal preparation, surgical steps, and sutures). The patients were evaluated for evidence of surgical site infection (fever, suppurative secretion through the wound, or cutaneous changes compatible with infection) before leaving the hospital and then, in outpatient setting, at days 15 and 30 after surgery. These evaluations were done by their primary physicians (gynecologist/obstetrician), so their evaluations were blinded to the procedure used.

The primary outcome of the study was the presence of surgical site infection at any time during one of the evaluations. Secondary outcome was the presence of a respiratory complication (persistent cough, fever, dyspnea, atelectatic rales, or wheezing) after surgery and before leaving the hospital.

Statistical analysis was performed using EpiInfo version 3.5.3 (Centers for Disease Control and Prevention, Atlanta GA, USA). Differences in continuous variables were analyzed using the Mann-Whitney U test and noncontinuous variables were analyzed using the chi-square test. Statistical significance was set at $P < 0.05$. The study was approved by the National Bioethics Committee (approval number: 1750/CNBI/ICGES/11) and registered in a public database (ClinicalTrials.gov NCT01340534).

TABLE 1: Baseline characteristics of the study population.

	Air (n: 179)	Oxygen (n: 164)	P value
Age (years)	25.67 (6.64)	25.13 (6.00)	0.60
Gestational age (weeks)	38.86 (1.37)	38.7 (1.40)	0.36
Parity	1.00 (1.04)	1.18 (1.24)	0.17
Body mass index	29.77 (5.48)	29.90 (5.20)	0.69
Hours in labour before cesarean section	8.90 (4.22)	8.20 (4.49)	0.16

Values presented as mean (standard deviation).

TABLE 2: Primary Outcomes.

	Air (n: 179)	Oxygen (n: 164)	P value
Surgical site infection (before day 15)	13 (7.26)	9 (5.48)	0.33
Outpatient management	11 (6.14)	6 (3.66)	0.21
Hospitalization	2 (1.12)	3 (1.82)	0.45

Values presented as number (percentage).

3. Results

Initially 370 patients were screened, but two were removed before randomization due to twin pregnancies and eight declined to participate. Of the 360 remaining patients, two were not able to receive the allocated intervention (due to temporary lack of oxygen mask with reservoir for delivering 80% FIO_2) and 15 were lost to followup. Therefore, our sample was made of 343 patients who underwent intrapartum cesarean delivery (179 in the air group and 164 in the oxygen group) (Figure 1) fulfilling our initial calculations.

Both groups were similar according to the general characteristics analyzed. There were no statistical differences in regard to age, gestational age, parity, body mass index and hours in labor before cesarean section (Table 1). Also, there was no difference in surgery time or hospital stay afterwards.

In the analysis of the primary outcome (rate of surgical site infections at any time during the followup), we found no statistical differences between the groups (13 patients in the air group and 9 in the oxygen group). There were no differences either in the outpatient management or the hospitalization rates between groups (Table 2). All cases of surgical site infection were diagnosed before or at day 15. No cases were recorded at day 30.

Our secondary outcome was the presence of a respiratory complication after surgery and before leaving the hospital. There were no cases reported of either of these complications in any of the two groups.

Although it was not part of the study, 6 cases of neonatal complications were reported in the air group and 5 in the oxygen group. All of them were related to malformations diagnosed postpartum.

4. Discussion

Surgical site infections are a frequent cause of morbidity and mortality around the world. They represent 25% of all

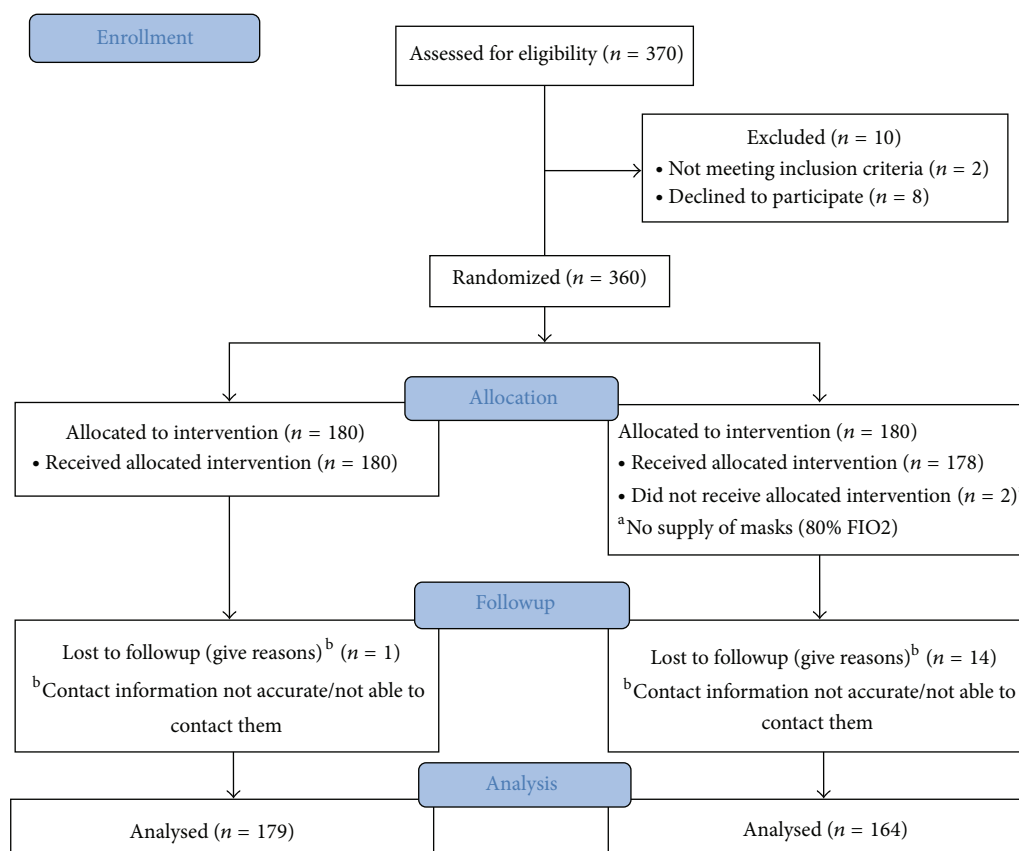Trial profile of participant recruitment and randomization

FIGURE 1: Trial profile of participant recruitment and randomization.

nosocomial infections and are the most common adverse event after a surgery, even though many cases of SSI are diagnosed after the patient leaves the hospital. According to a recent study in the UK, 9.6% of women developed a post-surgical infection and 0.6% were readmitted for treatment of the infection [5]. Younger women and body mass index ($>25\,kg/m^2$) were found to be risk factors for the development of SSI. Considering the number of cesarean sections performed around the world every day, the associated costs (clinical, economic, and social) [6], any measure that proves useful in reducing SSI, should be investigated as a public health issue.

Thomas Hunt was one of the pioneers in the discovery of the different mechanisms involving cicatrization and oxygen [7]. Hypoxemia, caused by vascular disruption, is a critical factor in this process [8]. It is well known that the central region of a wound is highly hypoxic (pO_2 between 0 and $10\,mmHg$) when compared with the borders (pO_2 around $60\,mmHg$) and arterial blood (pO_2 around $100\,mmHg$). Considering this evidence, a proper cicatrization requires an adequate supply of oxygen for tissue growth and regeneration.

Angiogenesis is also important and it has been shown that the use of supplemental oxygen accelerates the growth of blood vessels [9], increases the levels of vascular endothelial growth factor [10], and helps to differentiate fibroblasts into myofibroblasts, cells responsible for the contraction phase of a wound [11].

When oxygen is increased inside a wound above the levels found in normal conditions, maximum effects are obtained in terms of collagen deposit and tensile strength. The use of supplemental oxygen during surgery and the optimization of wound perfusion have proven to be useful in reducing SSI [12].

In a study by Greif et al. using 500 patients who underwent elective open colorectal resection, they compared the use of supplemental oxygen during surgery and two hours afterwards. One group received oxygen FIO_2 80% and the other FIO_2 30%. They showed a reduction in SSI rate in the FIO_2 80% (13 patients (5.2%; 95% CI: 2.4%–8.0%) as compared with 28 of the 250 patients given FIO_2 30% (11.2%; 95%: 7.3%–15.1%) $P = 0.01$) [13].

Sessler and Akça reviewed two factors associated with a reduced incidence of SSI. Maintenance of perioperative normothermia and provision of supplemental perioperative oxygen. Their data showed that the use of supplemental oxygen improves results with little or no risk [14].

A randomized double blind controlled study by Pryor et al. evaluated 165 patients after a major intra-abdominal surgical procedure. They were divided into two groups (FIO_2

80% versus FIO_2 35%). Their results showed a higher rate of SSI in the first 14 days after receiving oxygen FIO_2 80% (25% versus 11.3%; $P = 0.02$). This result remains constant even after multivariate regression analysis ($P = 0.03$). Their conclusion was that the use of supplemental oxygen does not reduce the rate of SSI and that surgical patients should receive it only in cases of cardiorespiratory dysfunction [15].

Palacio et al. evaluated the use of supplemental oxygen during cesarean section and their neonatal effects in 130 patients. They were divided into two groups (no oxygen supplement or oxygen FIO_2 40%). No difference in neonatal wellbeing was found [16].

As far as maternal complications, the use of supplemental oxygen has been associated with atelectasis and pulmonary fibrosis. Oxygen toxicity is not a real risk when used for short periods of time (<24 hours) and is negligible when used as a supplement in the operating room [17].

Our data showed that the use of oxygen (FIO_2 80%) during and for two hours after surgery does not reduce the rate of SSI when compared with no oxygen supplement at all. Many cases appeared after the patient leaves the hospital but, in our case, all were diagnosed before day 15. An appropriate surveillance system is invaluable in order to detect these cases. However, the use of supplemental oxygen does not help to reduce SSI after emergency cesarean section within the parameters established in our protocol.

Conflict of Interests

The authors of this study state no conflict of interests.

Acknowledgments

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