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Original Article

Effects of oxygen concentration and active warming on surgical site infections in pediatric appendectomy: A prospective randomized study

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Abstract

Objectives: We aimed to evaluate the potential effects of postoperative active warming and oxygen support on the incidence of surgical site infections (SSIs) in pediatric patients who underwent surgery for acute appendicitis.

Patients and methods: Between March 2011 and September 2011, a total of 80 pediatric patients (49 males, 31 females; mean age: 129.63 ± 44.39 months; range: 39 to 220 months) who underwent surgery for acute appendicitis were prospectively enrolled in this randomized clinical study. Patients were sequentially allocated into four groups according to perioperative oxygen concentration and postoperative thermal bed use. All patients were warmed with a thermal bed during the operation. Group A (n = 22) received 40% oxygen without thermal bed support; Group B (n = 18) received 40% oxygen with postoperative thermal bed application; Group C (n = 20) received 100% oxygen without thermal bed support; and Group D (n = 20) received 100% oxygen with postoperative thermal bed application. Each group was planned to include 22 patients, and sequential randomization was used to ensure balanced group allocation.

Results: Among the pediatric patients included in the study, acute non-complicated appendicitis was the most common diagnosis (63.8%). No statistically significant difference was observed among groups regarding age ($p = 0.497$), sex ($p = 0.093$), or diagnosis ($p = 0.340$). Surgical site infection occurred in 13.8% of patients, significantly more in Groups A (31.8%) and C (20.0%) ($p = 0.005$). No differences were observed in infection type ($p = 0.545$) or culture positivity ($p = 0.120$). Fever ≥ 37.5°C within 48 h postoperatively was present in all patients with SSI (100%) and in 56.5% without SSI, showing a strong association ($p = 0.006$). The mean number of febrile days was higher in infected patients (10.73 *vs.* 7.31, $p = 0.153$). Abdominal ultrasonography in deep SSI cases (n = 3) showed only fascia inflammation. No free fluid or abscess in the abdomen.

Conclusion: Active warming significantly reduced the incidence of SSIs in pediatric appendectomy patients, regardless of perioperative oxygen concentration.

Keywords: Appendicitis, hypothermia, oxygen, surgical site infection.

Surgical site infections (SSIs) are one of the most prevalent and clinically significant surgical complications.[1] In recent years, SSIs have emerged as the leading type of hospital-acquired infection, representing approximately 20% of all nosocomial infections.[2] The effect of SSIs extends far beyond mere incidence; the infections are associated with significant morbidity, increased healthcare utilization, and a tremendous amount of economic cost. Patients who develop SSIs also have a more extended hospital stay, usually several days longer than those who are not infected. Surgical site infections have also been observed to increase

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mortality risk 2- to 11-fold.[2,3] While most infected patients eventually recover with no long-term complications, a considerable proportion of patients experience devastating consequences: up to 77% of the deaths that occur in patients with SSIs are directly due to the infection itself.[3,4]

Surgical site infections, including deep organ infections, substantially increase health care costs due to extended hospitalizations in both pediatric and adult populations. In addition to physical morbidity, SSIs can induce psychological dysfunction, such as depression and anxiety, in vulnerable people. The prevention of SSI is a crucial aspect of perioperative care due to its extensive effects on physical and mental health.[1-4]

Complicated appendicitis is common in children, and its prevalence rate varies from 20% to 76%, rising in a reverse ratio with age.[5,6] In children below five years of age, prevalence approximates 82%, whereas in infants less than one year of age, it approximates 100%.[3,7,8] In dirty and contaminated wound classes such as complicated appendicitis, SSI is the most frequent postoperative morbidity, although mortality is below 1%.[9] Recently, three perioperative strategies were emphasized to reduce SSI risk to a minimum: normoglycemia preservation, adequate thermal regulation, and sufficient peri- and intraoperative oxygenation.

Previous studies have demonstrated that maintaining blood glucose concentrations at < 110 mg/dL, maintaining normal body temperature intra- and postoperatively, and administering high-concentration oxygen (e.g., 80% fraction of inspired oxygen [FiO_2]) significantly reduce the incidence of. Intraoperative hypothermia and tissue hypoxia have been shown to decrease immunity, whereas systemic or local warming, and augmented delivery of oxygen increase tissue oxygenation and reduce infections.[1-3] Therefore, in this study, we aimed to investigate the potential effects of intraoperative and postoperative active warming and oxygen support on the incidence of SSIs in pediatric patients who underwent surgery for acute appendicitis.

PATIENTS AND METHODS

This prospective randomized clinical study was conducted at the Department of Pediatric Surgery, İstanbul Medeniyet University Göztepe Training and Research Hospital, between March 2011 and September 2011. A total of 80 pediatric patients (49 males, 31 females; mean age: 129.63 ± 44.39 months; range: 39 to 220 months) who underwent surgery for acute appendicitis were included in the study and randomized into four groups: Group A (n = 22), Group B (n = 18), Group C (n = 20), and Group D (n = 20). Pediatric patients undergoing surgery for acute appendicitis were eligible for inclusion in the study. Patients were excluded if they had previously undergone abdominal surgery for complicated or non-complicated appendicitis; had conditions precluding the application of active warming or had a body temperature ≥ 37.5°C in the early postoperative period; required oxygen concentrations other than the target levels due to comorbidities, congenital anomalies, or intraoperative problems; if legal guardians declined or withdrew consent; or if histopathological examination did not confirm the diagnosis of acute or perforated appendicitis. All patients and their parents were informed about the nature of the study, and written informed consent was obtained from the parents or legal guardians prior to enrollment. The study protocol was approved by the Local Ethics Committee of İstanbul Medeniyet University Göztepe Training and Research Hospital (Date: 01.03.2011, Approval No: 10/A). The study was conducted in accordance with the principles of the Declaration of Helsinki and the Good Clinical Practice and Good Laboratory Practice guidelines issued by the Turkish Ministry of Health.

Randomization

In this study, pediatric patients scheduled for surgery due to acute appendicitis were randomly assigned to one of four treatment groups. The study initially planned to recruit 22 patients per group. Randomization was performed by a sequential assignment method: the first enrolled patient was assigned to Group A, and subsequent patients were consecutively allocated to Groups B, C, and D. The cycle was replicated throughout the enrollment period to provide balanced group distribution. In the early postoperative period, patients presenting with a body temperature ≥ 37.5°C did not receive a heated bed. During follow-up, within 2 h postoperatively, fever ≥ 37.5°C was observed in 15 patients; therefore, these patients were not included in Groups B and D, which received postoperative heat support. Additionally, some patients were withdrawn due to failure to attend long-term follow-ups. Consequently, the final group sizes were as follows: Group A (n = 22), Group B (n = 18), Group C (n = 20, and Group D (n = 20).

Study groups and perioperative interventions

Group A: Received 40% oxygen during the perioperative period (via endotracheal tube during surgery and via mask for 6 h postoperatively). This group was not placed on a thermal bed in the postoperative period.

Group B: Received 40% oxygen via endotracheal tube during the surgery. Postoperatively, this group was placed on a thermal bed maintained at 36°C for 24 h.

Group C: Received 100% oxygen during the perioperative period (including both the surgical and recovery phases) via endotracheal tube, followed by 80% oxygen at a flow rate of 3 L/min via mask for 6 h after awakening. This group was not placed on a thermal bed postoperatively.

Group D: Received 100% oxygen during the perioperative period (surgery and recovery) via endotracheal tube, followed by 80% oxygen at a flow rate of 3 L/min via mask for 6 h after awakening. This group was placed on a thermal bed maintained at 36°C for 24 h postoperatively.

Classification and diagnostic criteria for surgical site infections

The surgical wound classification developed by the National Academy of Sciences/National Research Council was used for the preoperative determination of SSI risk. Surgical site infections were defined according to the diagnostic criteria of the Centers for Disease Control and Prevention and the National Nosocomial Infections Surveillance (NNIS) system. According to these classifications, acute non-complicated appendicitis was classified as a contaminated wound, whereas perforated or complicated appendicitis was classified as a dirty wound.[1,3,10]

According to the NNIS criteria, superficial incisional SSIs were defined as the presence of at least one sign of local infection, i.e., localized pain, tenderness, swelling, erythema, or warmth, or intentional reopening of the incision by the surgeon in the absence of a negative culture result, together with the clinical judgment of the clinician or surgeon. For diagnosing deep incisional SSIs, the following additional NNIS criteria were utilized. These include purulent drainage from the fascial layers, reopening of the wound by the surgeon for fever, localized pain, or tenderness; intraoperative or histopathology/radiology evidence of infection or abscess; and the surgeon's clinical decision to confirm the diagnosis of a deep SSI.[1,3]

Statistical analysis

For statistical analyses, the Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software (Utah, USA) were used. In the evaluation of study data, descriptive statistical methods (mean, standard deviation, median, frequency, and percentage) were employed. For comparisons between groups of normally distributed parameters, the one-way ANOVA test was used, and the Tukey's Honestly Significant Difference (HSD) test was applied to determine which group caused the significant difference. For non-normally distributed parameters, intergroup comparisons were performed using the Kruskal-Wallis test and the Mann-Whitney U test. Intragroup comparisons of normally distributed parameters were analyzed using the paired samples t-test, while the Wilcoxon signed-rank test was used for non-normally distributed parameters. For comparisons of categorical variables, the chi-square test and Fisher's exact test were used. Results were evaluated within a 95% confidence interval, and statistical significance was set at $p < 0.05$.

RESULTS

Among the pediatric patients included in the study, the most common diagnosis was acute non-complicated appendicitis (63.8%), followed by perforated complicated appendicitis with localized peritonitis (18.7%) and generalized peritonitis (17.5%). Patients were evenly distributed among four treatment groups: Group A (27.5%), Group B (22.5%), Group C (25%), and Group D (25%). Surgical site infection was observed in 11 (13.8%) patients, whereas 69 (86.2%) patients had no signs of postoperative infection, as shown in Table 1.

There were no statistically significant differences among the groups in terms of age ($p = 0.497$), sex distribution ($p = 0.093$), or diagnosis ($p = 0.340$).

TABLE 1
Patients' demographics

	n	%
Sex		
Female	31	38.8
Male	49	61.2
Diagnosis		
Acute non-complicated appendicitis	51	63.8
Perforated appendicitis + localized peritonitis	15	18.7
Perforated appendicitis + generalized peritonitis	14	17.5
Group		
A	22	27.5
B	18	22.5
C	20	25
D	20	25
Infection		
Present	11	13.8
Absent	69	86.2

The mean age ranged from 115.72 to 135.70 months across the groups. The female ratio increased across groups. Acute appendicitis was the most common diagnosis, followed by localized and generalized perforated appendicitis in all groups, as shown in Table 2.

Surgical site infection rates differed significantly among the groups ($p = 0.005$), with infections observed only in Groups A (31.8%) and C (20.0%). Superficial and deep infections were more frequent in Group A. No statistically significant differences were observed in infection type ($p = 0.545$) or culture positivity ($p = 0.120$), although positive cultures were more common in Groups A, C, and D, as shown in Table 3. Abdominal ultrasonography was performed during postoperative follow-up in two patients from Group A and one patient from Group C who were diagnosed with deep SSI. As a result, inflammation was detected in the fascia tissues, while no intra-abdominal collection or abscess was identified.

During the postoperative 48-h follow-up period, there was no statistically significant difference in fever monitoring among the groups ($p > 0.05$). All patients who developed SSI (n = 11) had a body temperature of 37.5°C or higher within the first 48 h postoperatively. Among these, six patients were originally assigned to receive active warming, but due to high perioperative temperatures, they were monitored without heat

TABLE 2
Evaluation of age, sex, and diagnoses by groups

	Group A (n = 22)			Group B (n = 18)			Group C (n = 20)			Group D (n = 20)			
	n	%	Mean ± SD	n	%	Mean ± SD	n	%	Mean ± SD	n	%	Mean ± SD	*p*
Age (month)			134.55 ± 45.09			115.72 ± 43.69			135.70 ± 47.27			130.65 ± 41.87	0.497
Sex													0.093
Female	5	22.7		6	33.3		8	40.0		12	60.0		
Male	17	77.3		12	66.7		12	60.0		8	40.0		
Diagnosis													0.340
Acute appendicitis	13	59.1		15	83.3		10	50.0		13	65.0		
Perforated appendicitis with localized peritonitis	3	13.6		2	11.1		6	30.0		4	20.0		
Perforated appendicitis with generalized peritonitis	6	27.3		1	5.6		4	20.0		3	15.0		

SD, standard deviation.

TABLE 3
Distribution of surgical site infection, presence of infection, culture growth in intraoperative samples by groups

	Group A (n = 22)		Group B (n = 18)		Group C (n = 20)		Group D (n = 20)		
	n	%	n	%	n	%	n	%	*p*
Surgical site infection									0.005
Present	7	31.8	0	0	4	20.0	0	0	
Absent	15	68.2	18	100	16	80.0	20	100	
Type of infection									0.545
Superficial	4	57.1	0	0	1	25.0	0	0	
Deep	3	42.9	0	0	3	75.0	0	0	
Culture									0.120
Positive	10	45.5	2	11.1	7	35.0	8	40.0	
Negative	12	54.5	16	88.9	13	65.0	12	60.0	

TABLE 4
Relationship between surgical site infection and postoperative fever

	Infection present (n = 11)				Infection absent (n = 69)				
	n	%	Mean ± SD	Median	n	%	Mean ± SD	Median	*p*
Fever (≥ 37.5°C)									0.006
Present	11	100			39	56.5			
Absent	0	0			30	43.5			
Number of febrile days			10.73 ± 6.36	13			7.31 ± 6.40	5	0.153

SD, standard deviation.

support. Of these patients, two underwent surgery for acute appendicitis and four for perforated appendicitis. In the same period, 56.5% (n = 39) of patients who did not develop SSI also exhibited a temperature of 37.5°C or higher. A statistically highly significant difference was observed between the development of SSI and having a body temperature ≥ 37.5°C within the first 48 h postoperatively ($p < 0.01$), as shown in Table 4.

DISCUSSION

In this prospective randomized study, the effects of perioperative and postoperative oxygen concentration and active thermal support on the development of SSI in pediatric appendectomy patients were evaluated. The findings revealed that SSIs were more frequently observed in groups that did not receive active warming postoperatively, despite varying oxygen levels. All patients who developed SSIs experienced postoperative fever, suggesting a strong association between early postoperative fever and infection. However, no statistically significant differences were observed regarding the type of infection or the presence of microbial growth in cultures. Our results highlight the importance of thermal regulation in infection prevention.

Surgical site infections are defined as infections observed at the incision site or in the organs and areas manipulated during surgery within the first 30 days following the operation.[1] They account for one-fourth of all hospital-acquired infections and occur in approximately 1% to 5% of hospitalized patients.[9,10] They can prolong the length of hospital stay by up to 16 days (ranging from 7.4 to 16 days). Compared to patients who do not develop SSIs, those who do require intensive care 60% more frequently, have a fivefold higher likelihood of readmission, and face a 2- to 11-fold increased risk of death.[11-13] In addition to reduced quality of life and productivity in patients who develop SSI, healthcare costs increase significantly. In the United States, the additional cost per patient with SSI ranges between

$3,000 and $30,000.[14,15] Surgical site infection is one of the most common complications following appendectomy, with incidence rates reaching up to 11%.[16] Its occurrence is closely related to the degree of wound contamination. According to NNIS data and other literature, the incidence of SSI is reported as 1-3% for clean wounds, 3-10% for clean-contaminated wounds, 10-15% for contaminated wounds, and 15-40% for dirty wounds.[17-20] Acute appendicitis is classified as a contaminated wound, while perforated appendicitis falls under the dirty wound category, and in both clinical scenarios, the risk of SSI is high. In our study, SSI developed in one patient with acute appendicitis and six patients with perforated appendicitis in Group A, where neither active warming nor oxygen support was provided. In Group C, where oxygen support was provided but no active warming was given, SSI developed in one patient with acute appendicitis and three patients with perforated appendicitis. When SSI occurrence is evaluated in relation to the type of appendicitis, the results appear to be consistent with the data available in the literature.

Several factors, such as preoperative disinfection of the skin with cold antiseptics, prolonged exposure to a cold environment, and cold infusion fluids during surgery, and the negative effects of anesthetic agents on thermoregulation mechanisms, can lead to a decrease in core body temperature by 1 to 3°C. This effect may persist into the postoperative period.[21,22] In response to hypothermia, increased serum concentrations of catecholamines activate β-2 adrenergic receptors, which reduce nuclear translocation of nuclear factor kappa B and weaken the synthesis of pro-inflammatory cytokines, leading to anti-inflammatory responses. Furthermore, cortisol, one of the most important hormones involved in energy expenditure during hypothermia, is activated, contributing to susceptibility to infections through multiple mechanisms.[23,24] Hypothermia has been observed to increase SSI rates following clean-contaminated procedures such as cholecystectomy.[25] In addition, SSIs are more frequently observed after laparoscopic colorectal resections and radical nephrectomies performed under hypothermic conditions.[26] These findings indicate that hypothermia is a significant risk factor for SSIs in clean-contaminated and contaminated surgical procedures.[27] In another study focusing on hypothermic patients undergoing colorectal surgery, while no significant increase in superficial SSI was found, hypothermia was associated with a notable rise in organ/space SSIs, accompanied by intra-abdominal or pelvic abscesses.[28]

Perioperative hypothermia stimulates the sympathetic nervous system, increasing serum adrenaline and noradrenaline levels, leading to vasoconstriction. Vasoconstriction plays a key role in the development of perioperative hypothermia. It reduces tissue partial oxygen pressure, which negatively affects neutrophil oxygen-dependent oxidative immune functions, resulting in suppression of the immune system.[29,30] Hypothermia during surgery adversely affects the functions of immune-related cells such as T-cell-mediated antibody production, macrophage motility, granulocyte chemotaxis and phagocytosis activity, and natural killer cell activity. It also suppresses the production of immunomodulatory cytokines such as tumor necrosis factor-alpha and interleukin (IL)-6, reduces levels of chemotactic IL-8, and increases the levels of immunosuppressive IL-10.[30,31] Vasoconstriction resulting from hypothermia reduces tissue oxygen partial pressure. Consequently, dysfunction in oxygen-dependent enzymes impairs collagen and scar tissue formation, ultimately delaying wound healing and predisposing the patient to secondary infections.[30-32] In our study, no SSI was observed in Groups B and D, whose patients were protected from hypothermia using thermal beds in the postoperative period. In contrast, a total of 11 SSIs were detected in Groups A and C, which did not receive thermal bed support. This finding suggests that the prevention of hypothermia by using thermal beds during surgery and continuing their use in the postoperative period can prevent SSI in our routine practice.

This study has several limitations that should be acknowledged. The relatively small sample size may have limited the statistical power to detect differences between subgroups. The short follow-up period might have missed late-onset infections. Environmental factors and perioperative protocols not fully controlled, such as ambient temperature or anesthetic variations, could have influenced hypothermia outcomes. Additionally, due to ethical constraints, blinding was not possible in assigning thermal bed support, which may have introduced observer bias in SSI evaluation.

In conclusion, active warming significantly reduced the incidence of SSIs in pediatric appendectomy patients, regardless of perioperative oxygen concentration. Postoperative fever was strongly associated with infection. These findings highlight the critical role of maintaining normothermia during the perioperative period to prevent SSIs and improve surgical outcomes in children.

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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