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# Antibiotic therapy and infection complications in paediatric burn injuries*

## Antybiotykoterapia a powikłania infekcyjne w oparzeniach u dzieci

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## Summary

**Aim:** Each year, nearly 1% of the population suffers from burn injuries. Infections are the main cause of complications and death after thermal injury. Excessive use of antibiotics affects the children treated for burns and can have negative effects. Therefore, specifying the recommendations for antibiotic therapy in patients after thermal injury seems to be of importance.

**Material/Methods:** An evaluation of 310 paediatric patients hospitalized for burn injuries was performed. The first part of the evaluation consisted of a retrospective analysis of treatment with particular focus on infection complications and administered antibiotics. This was followed by a prospective evaluation of the effectiveness of the principles of antibiotic therapy specified at the earlier stage.

**Results:** In 2010–2016, antibiotics were systemically administered to 53.4% of children treated for thermal injury, and in 87.1% of these cases it was introduced as a prophylactic measure. Infection of a burn wound was recorded in 4.7% of cases. The most frequently isolated bacterium (57.1%) was *Staphylococcus aureus* MSSA. Administration of antibiotics failed to reduce the number of infection complications or burn wound infections. The studies formed the basis for the specification of the internal antibiotic therapy criteria, the effectiveness of which was then evaluated. In 2017, an antibiotic was administered to 37.1% of patients. Reducing antibiotic therapy did not increase the risk of infection complications or the frequency of wound infections.

**Conclusions:** Routine antibiotic prophylaxis in burn injuries has no effect on the risk of infection complications and does not reduce the treatment time. It should be limited to perioperative prophylaxis in the case of skin grafts and to the patients with progressing symptoms of burn disease or with concomitant infections.

**Keywords:** burn •child •antibiotic therapy •infection •procalcitonin

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## INTRODUCTION

Each year, nearly 1% of the population suffers from burn injuries, with the vast majority of such cases occurring in children. Thermal injuries and related complications are the third most frequent cause of accident-related death in patients below eighteen years of age. The essential therapeutic difficulties and deaths are most frequently caused by infections leading to sepsis and multiple organ failure. Therefore, counteracting the infections and their immediate and effective management, in particular in children, is of significance. The above is associated with an adequate local therapy and wound management as well as with systemic antibiotic therapy.

Excessive use of antibiotics affects the children treated for burns and can have negative effects. Due to the increased risk of drug-resistant bacteria strains forming, such use also has a negative impact on the population. Therefore, specifying the recommendations for antibiotic therapy in patients after thermal injury seems to be of importance. It would enable the reduction of administered antibiotics, which are overused in this group of patients.

## MATERIAL AND METHODS

The study was performed on a group of 310 paediatric patients hospitalized for burn injuries in the Department of Paediatric Surgery, Traumatology and Urology of Poznan University of Medical Sciences in 2010-2017. The median age in this group was 18 months (minimum: 2 months, maximum: 219 months), with 72.9% of patients being below 3 years of age. Girls accounted for 33.2% of the population. Thermal injuries of the upper body were dominant, covering at least two body surface areas in more than half of the cases. All wounds were of mosaic nature and covered approximately 10.0% of the total body surface area (TBSA) on average. The first stage involved a retrospective analysis of 275 patients treated in 2010–2016. The effectiveness of antibiotic therapy, in particular prophylactic, and its impact on the recovery of paediatric patients with burn injuries were evaluated in detail. Recommendations for antibiotic supply after thermal injury were specified. In the second part of the study carried out in 2017, a prospective analysis of the effectiveness of antibiotic therapy principles specified at the earlier stage was performed. Upon admission to hospital, the following concentrations were determined: blood leukocyte (WBC), C-reactive protein (CRP) and procalcitonin (PCT). In addition, blood WBC level was determined after 24 hours of hospitalization. All patients (up to 18 years of age) treated for isolated burn injuries were enrolled in the studies – both prospective and retrospective. No other exclusion criteria were applied. There were no differences in age and sex structure, burn injury extension and management method (local and systemic) between the retrospective and prospective groups of patients. The obtained data were analyzed using the descriptive statistics methods and tools, adopting the significance level of $p<0.05$. The consent for performing the studies was issued by the Bioethical Committee at Poznan University of Medical Sciences (no. 175/17).

## RESULTS

In 2010-2016, antibiotics were administered systemically to 53.4% of children treated for thermal injuries, and in 87.1% of these cases it was introduced as a prophylactic measure. The most frequently administered drug was cefuroxime (84.5%) and amoxicillin with clavulanic acid (9.0%). These antibiotics were administered intravenously, usually from the first day of hospitalization (92.3% of patients). The average time of antibiotics supplementation was 5 days. In the case of cefuroxime, the dosage was 30mg/kg b.w. three times daily. Amoxicillin with clavulanic acid was administered at a dose of 30+5mg/kg b.w. every 8 hours. The other antibiotics were used sporadically – primarily as targeted therapy on the basis of the obtained culture in the case of wound infection (Figure 1). Wound infection was recorded in 4.7% of the cases, with the most commonly isolated bacteria (57.1%) being *Saphylococcus aureus* MSSA. The other detected pathogens included: *Staphylococcus epidermidis* MRSE, *Streptococcus pyogenes*, *Serratia marcescens* ESBL+, *Klebsiella pneumoniae* and *Escherichia coli* AmpC+.

The patients with introduced antibiotic prophylaxis (AP) were compared within the first 24 hours of hospitalization with the patients receiving no such treatment (N–AP). Upon admission to hospital, both groups were identical in terms of blood WBC ($p = 0.1212$) and CRP ($p = 0.1786$) levels. Frequencies of infection complications during hospitalization were also corresponding ($p = 1.0000$) and accounted for 4.8% of AP and 4.6% of N–AP, respectively. In addition, the length of stay to burnt surface area ratio (LOS/%TBSA) in the patients receiving no antibiotic prophylaxis proved to be significantly lower ($p = 0.0131$) compared to the patients receiving antibiotic prophylaxis (Table 1).

The obtained results prompted the authors of this publication to specify recommendations for antibiotic therapy in children with burn injuries. These guidelines, supposed to reduce excessive use of antibiotics, were validated in the prospective part of the study on the group of 35 paediatric patients treated for thermal injuries. The recommendations assumed antibiotic supplementation in only the following cases: increased procalcitonin level exceeding 0.5ng/ml at the start of therapy, fever or systemic symptoms of burn disease, wound infection or any other

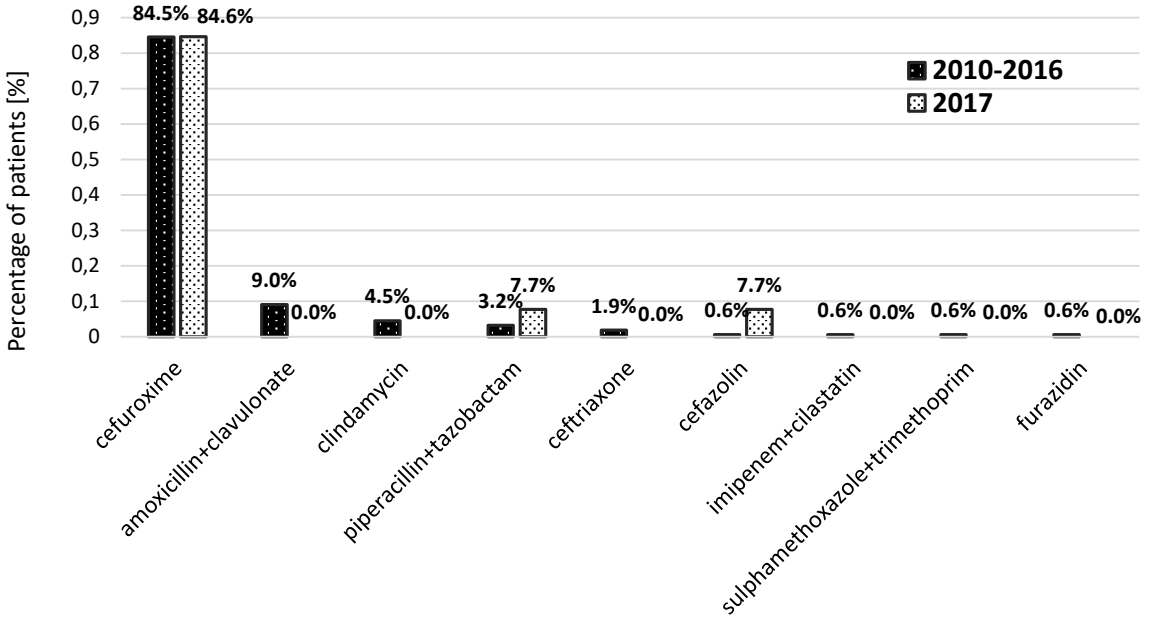


**Fig. 1.** Comparison of antibiotics used in 2010–2016 and in 2017

infection and perioperatively in autologous intermediate thickness skin graft. Introduction of antibiotic therapy was recorded, along with statement of reasons, in the individual treatment evaluation record of a paediatric patient with burn injury.

In 2017, antibiotics were administered to 37.1% of patients with thermal injuries, which enabled a significant reduction, i.e. by more than fifteen percent, of supplementation of these drugs compared to the previous years ($p = 0.0463$). In most cases, antibiotic therapy was introduced in the treatment of burn disease symptoms and was primarily associated with burns exceeding 10.0% of TBSA (Figure 2). It was less commonly applied in children with wound infections, provided that nearly half of infections were diagnosed on admission to hospital. The most frequently administered antibiotics included first and second generation cephalosporins (Figure 1). They were administered intravenously only. For cefuroxime, the dosage was 30mg/kg b.w. per dose. Cefazolin was administered at a dose of 25mg/kg b.w. for the application. Despite antibiotic therapy reduction, no significant increase in the frequency of burn wound infections or any other infections during hospitalization was observed ($p = 0.4049$). Also, the LOS/%TBSA ratio was similar, both when compared to the previous years ($p = 0.1980$) and between the patients receiving and not receiving antibiotics in 2017 ($p = 0.9592$). Both of these groups were identical in terms of blood WBC, CRP and PCT levels on admission to the surgery department as well as in terms of WBC values after 24 hours of hospitalization (Table 2). At the same time, a positive correlation between the adopted recommendations for antibiotic therapy and CRP concentration ($p = 0.0297$) was observed. A similar regularity was not recorded for WBC ($p = 0.3428$) and PCT ($p = 0.0876$). Increase in procalcitonin concentration was observed only in a single case – in the patient with burn wound infection covering nearly 20% of the body surface area and progressing burn disease.

**Table 1.** Comparison of the group receiving [AP] and not receiving [N-AP] antibiotics prophylactically in 2010–2016 (mean)

| | AP | N-AP | P value |
|---|---|---|---|
| WBC on admission | 13.2±5.0G/l | 12.3±4.3G/l | 0.1212 |
| CRP on admission | 0.78±2.25mg/dl | 0.51±1.21mg/dl | 0.1786 |
| Frequency of infection | 4.8% | 4.6% | 1.0000 |
| LOS/%TBSA | 1.9 | 1.3 | 0.0131 |

## DISCUSSION

Thermal injuries, particularly in children, are associated with the increased risk of infection. It can be limited to wound infection or skin graft (approximately half of the case), urinary or respiratory tract infections (more than one fourth of the case) or sepsis. According to Ramirez-Blanco et al., these infections are predominantly caused by bacteria (88.5%). This results in a common administration, frequently without any recommendations for antibiotic prophylaxis in this group of patients. Chahed et al. emphasize, however, that the appropriate and optimal burn treatment requires only adequate local therapy combined with wound management. Antibiotics should be administered only after infection. Ergün et al. and Sheridan et al. demonstrate that routine antibiotic prophylaxis fails to decrease the risk of local infection. According to the studies by Davies et al., the considerable majority of paediatric burn treatment centers implements no antibiotic therapy guidelines. These centers, however, do not apply antibiotic prophylaxis. On the other hand, the personnel of the hospitals with implemented internal standards demonstrate their insufficient knowledge. Therefore, establishing common and uniform guidelines regulating the use of antibiotics in burn management seems to be necessary, which is also emphasized by the authors of this publication [1, 3, 5, 11, 15].

The overuse of antibiotics as prevention has been observed; this can be significantly reduced by detailed control over the supplementation of these drugs and establishing of the internal guidelines tailored to the needs of a given burn treatment center. Such procedure would to a large extent eliminate redundant antibiotic therapy. As demonstrated in this study, such a reduction causes no increase in the frequency of wound infections or any other infections and is safe for the patients. Also, it is necessary to identify and diagnose the agents increasing the risk of infection in the patients. According to Fadeyibi et al., any delay in arriving to the burn treatment center and extended hospitalization length correlate with more frequent burn wound infection, while Rosanova et al. state that the risk of infection in children with burns increases in the case of central venous access, skin graft and routine antibiotic prophylaxis, which is also confirmed by the results presented in this study (LOS/%BSA significantly higher in children receiving antibiotic prophylaxis in 2010–2016). Ramos et al. demonstrate that prophylactic antibiotic supplementation is recommended in autologous intermediate thickness skin grafts. Such supplementation decreases the risk of postoperative wound infection and at the same time significantly contributes to successful graft healing [6, 12, 13].

There is high variability in the profiles of the most common pathogens causing the infections in patients with burn injuries. On the one hand, it is associated with environmental differences and different locations of the centers performing these studies. On the other hand, according to the study by Yali et al., there are differences in bacteria isolated in the burn intensive care units (dominating bacteria

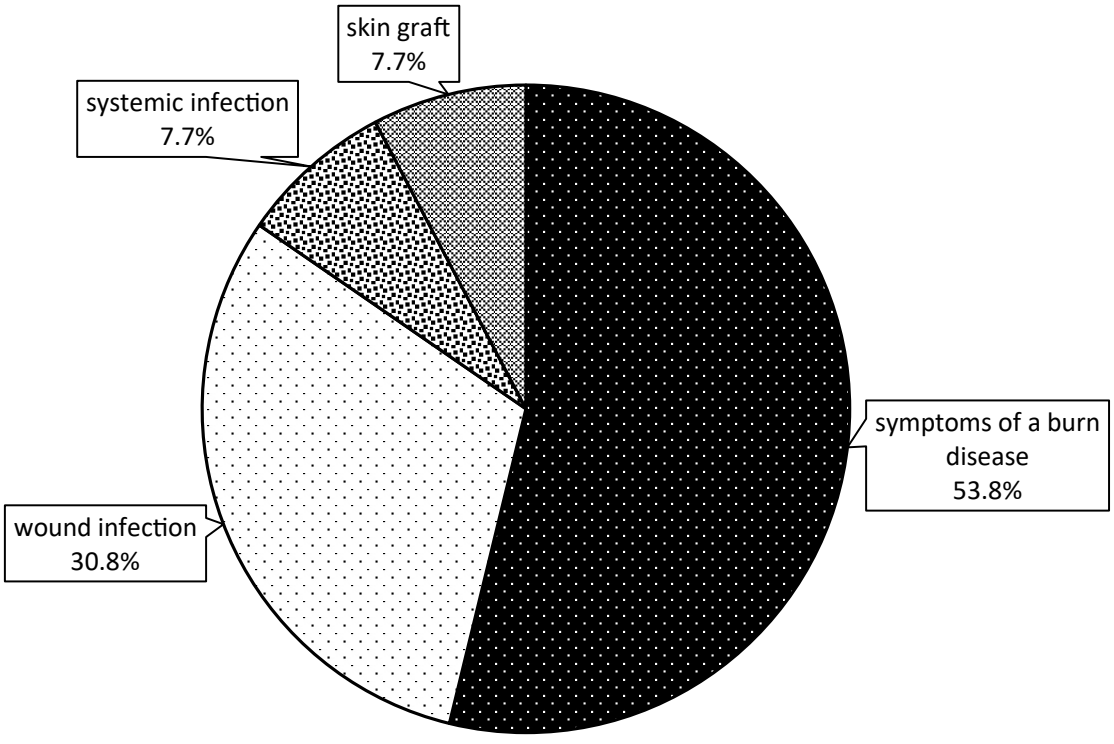


**Fig. 2**. Indications for antibiotic therapy in burned children in 2017

**Table 2.** Comparison of the group receiving [AP] and not receiving [N–AP] antibiotics prophylactically in 2017 (mean)

| | AP | N–AP | P value |
|---|---|---|---|
| WBC on admission | 13.1±7.6 G/l | 11.4±2.8 G/l | 0.3428 |
| WBC after 24h | 10.0±5.6 G/l | 9.7±2.5 G/l | 0.7573 |
| CRP on admission | 0.87±1.08mg/dl | 0.29±0.19mg/dl | 0.3050 |
| PCT on admission | 0.61±1.25ng/dl | 0.06±0.04ng/dl | 0.6303 |
| LOS/%TBSA | 1.6 | 1.8 | 0.9592 |

in descending order): *Acinetobacter baumani, Pseudomonas aeruginosa, Staphylococcus aureus* and *Klebsiella pneumoniae*) and in standard burn treatment units (dominating bacteria in descending order: *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Escherichia coli*), with pathogens isolated in the burn intensive care units manifesting higher antibiotic resistance. According to Gang et al., the most frequent cause of septic complications in patients with burn injuries is the infection with *Staphylococcus aureus,* the main source of which is wound contamination. The risk of sepsis is not reduced by antibiotic prophylaxis. In the retrospective population of patients treated with cefuroxime or amoxicillin with clavulanic acid, *Staphylococcus aureus* wound infections resulted mainly from the too late inclusion of antibiotic prophylaxis (not on the first day after the injury). DiMuzio et al. describe the variability of dominating bacteria over the years, accompanied with differences in drug resistance and the need to modify the recommended antibiotic therapy. Collier et al. demonstrate that there are no noticeable resistance schemes among the pathogens causing burn wound infections. Therefore, it is recommended that tests and examinations be performed that take into account genetic engineering methods in order to select adequate antibiotic therapy [2, 4, 7, 16].

It is postulated that inflammatory markers be used to specify recommendations for antibiotic therapy in burn management – primarily PCT and CRP. Kim et al. suggest that the PCT concentration equal or greater than 2ng/ml is an independent prognostic factor and correlates with a significant risk of septic complications. Rosanova et al. demonstrate that PCT and CRP are of low prognostic value and believe that none of these markers is capable of predicting the infection or risk of death. Matuszczak et al. state that the evaluation of proteasome 20S activity in plasma can act as an additional tissue damage biomarker in children with burns and influence the decision to introduce antibiotic therapy [8, 10, 14].

The issue of specifying the recommendations for antibiotic prophylaxis in paediatric burn management remains ongoing. These guidelines should be consistent and, as far as possible, uniform. However, they should also be tailored to the needs of the individual burn treatment centers. Inclusion of antibiotic therapy in skin grafts seems to be unquestionable. This type of treatment should be also introduced in concomitant infections or progressing symptoms of burn disease, which can be in some way predicted when observing a significant increase in blood PCT or CRP level. At the same time, the use of first and second-generation cephalosporins seems to be the most reasonable [9].

## CONCLUSIONS

- Routine antibiotic prophylaxis in burn injuries has no effect on the risk of infection complications and does not reduce the treatment time. It should be limited to perioperative prophylaxis in the case of skin grafts and to patients with progressing symptoms of burn disease or with concomitant infections.
- Implementation of guidelines specifying strict recommendation for supplementation of antibiotics significantly reduces the frequency of administration of these drugs in the patients with burns.

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The authors have no potential conflicts of interest to declare.