THE ADVANTAGES OF ANTIBIOTIC PROPHYLAXIS IN NEUROSURGERY

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Prophylactic use of antibiotics in neurosurgery means the use of antibiotics in order to prevent infections of wounds and internal operative structures.

The research was conducted at the Clinic for Neurosurgery in Niš, during 2018, in 44 patients operated with L4-L5 and L5-S1 disc herniation. In 26 patients, antibiotic prophylaxis was used. In the remaining 18 patients, antibiotic prophylaxis was not applied and they were grouped into a control group. The average duration of the operation was 50 minutes. The antibiotic is used in one dose, the first generation Cephalosporin - Cefazolin 1 g iv for patients with body weight less than 80 kg and 2 g for patients with body weight more than 80 kg.

We observed the occurrence of wound infections and internal operational structures, the occurrence of unwanted effects and financial aspects.

The goal of the work was to demonstrate that antibiotic prophylaxis is more favorable due to shorter time use of antibiotics, less side effects and overall financial benefit comparing to continuous antibiotic therapy.


Key words: antibiotic prophylaxis, neurosurgery, wound infections

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Introduction

Infection means the penetration of microorganisms into the body, with all the consequences of their mutual reactions, with both actors trying to maintain it.

An important condition for the emergence of infection is that a certain number of pathogenic or conditionally pathogenic microorganisms come into contact with sensitive tissue and there to multiplies.

Surgical infections always penetrate the tissue through the front door in which local defense inflammatory reaction of the tissue has primary role, and then it is quickly associated with the general reaction of the organism. For the development of a surgical infection significant factors are: the amount of inoculated microorganisms, i.e. their reproduction and excretion properties, and the resistance of the patient's organism to infection, which has been reduced in people with atherosclerotic blood vessels and chronic patients. Hospital infections are one of the leading causes of increased morbidity and mortality of hospitalized patients (1-5), malnourished patients, hypoproteinemic and anemic, as well as those with malignant diseases.

The causative agents of the bacterial infection in neurosurgically operated patients usually come from the immediate environment, such as the patient's bacterial flora or in the presence of aerobic bacteria in the operating room during surgical work and those represent a high risk for the development of the infection. In neurosurgical patients at 3-4% of cases infection occurs (6,7).

Antibiotic prophylaxis involves the use of antibiotics before the onset of infection, to prevent contamination of the operative wound by bacteria that represent a normal skin flora such as S. aureus, S. epidermidis, P. acnes, or contamination of pathogenic bacteria from the patient's environment during and after the procedure.

The use of antibiotics prophylactically aims to achieve sufficient concentration of bactericides in the tissue during intervention and for the first 3-4 hours postoperatively. Another way of using antibiotics prophylactically, is to use a few days before and after surgery and It is not justified because it represents a realistic modality for spreading resistance in a hospital setting (8).

The most common causes of infection at the Clinic for Neurosurgery in Niš are:
- S. epidermidis
- S. aureus
- P. aeruginosa
- Citrobacter
- P. vulgaris
- P. mirabilis
- Acinetobacter

Prophylaxis has been used in neurosurgery since 1925, before the age of antibiotics, when Hexamine-antiseptic was used. Harvey Cushing, a pioneer of neurosurgery, had a rate of postoperative infections of 1% using only water and soap. From Cushing’s era, all neurosurgeons use aseptic techniques in all types of operations (9).

**Materials and methods**

The research was carried out at the Clinic for Neurosurgery KC Niš. During this study, we examined the effects of antibiotic prophylaxis in patients treated with lumbar disc hernias. The study was performed in 44 patients with their consent. In 26 patients, antibiotic prophylaxis was used. For the remaining 18 patients antibiotic prophylaxis was not used and they were assigned to the control group. We followed the movement of laboratory parameters of inflammation: CRP, sedimentation and leukocytes before and after surgery in 44 patients.

The average duration of the operation was 50 minutes. Antibiotic is used in one dose, the first generation Cephalosporin - Cefazolin 1 g iv for patients with body weight less than 80 kg and 2 g for patients with body weight more than 80 kg.

**Results**

There was no statistically significant difference in wound infection depending on the use of antibiotic therapy ($\chi^2 = 1.076; p = 0.583$) (Table 1.).

<table>
<thead>
<tr>
<th>Infections</th>
<th>Wound infections</th>
<th>Infections of deeper structures</th>
<th>No infections</th>
<th>Total</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis</td>
<td>1 (33.3%)</td>
<td>0 (0.0%)</td>
<td>25 (62.5%)</td>
<td>26 (59.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous antibiotic therapy</td>
<td>2 (67.3%)</td>
<td>1 (100.0%)</td>
<td>15 (37.5%)</td>
<td>18 (40.9%)</td>
<td>1.076</td>
<td>0.583</td>
</tr>
<tr>
<td>Total</td>
<td>3 (100.0%)</td>
<td>1 (100.0%)</td>
<td>40 (100.0%)</td>
<td>44 (100.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A statistically significant difference in the distribution of side effects was determined depending on the use of antibiotic therapy ($\chi^2 = 15.634; p = 0.001$). A significantly higher number of patients who had antibiotic prophylaxis were without side effects, while patients with continuous antibiotic therapy more often had nausea and vomiting, diarrhea and stomach pain (Table 2.).

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Nausea and vomiting</th>
<th>Diarrhea</th>
<th>Pain in the stomach</th>
<th>No side effects</th>
<th>Number of patients</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis</td>
<td>2 (33.3%)</td>
<td>1 (14.3)</td>
<td>0 (0.0%)</td>
<td>23 (82.1)</td>
<td>26 (59.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous antibiotic therapy</td>
<td>4 (66.7%)</td>
<td>6 (85.7)</td>
<td>3 (100.0%)</td>
<td>5 (17.9)</td>
<td>18 (40.9)</td>
<td>15.634</td>
<td>0.001</td>
</tr>
<tr>
<td>Total</td>
<td>6 (100.0%)</td>
<td>7 (100.0%)</td>
<td>3 (100.0%)</td>
<td>28 (100.0%)</td>
<td>44 (100.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A statistically significant difference in funding was found, depending on the use of antibiotic therapy ($\chi^2 = 14.123; p <0.001$). Patients in whom for antibiotic therapy were spent funds up to 2000 dinars were more likely to have antibiotic prophylaxis, while those with over 2000 dinars spent, more often had continuous antibiotic therapy and associated therapy (Table 3.).
Table 3. Financial aspects

<table>
<thead>
<tr>
<th>Funds</th>
<th>Up to 2000 dinars</th>
<th>More than 2000 dinars</th>
<th>Number of patients</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis</td>
<td>26(72.2%)</td>
<td>0(0.0%)</td>
<td>26(59.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous antibiotic therapy and</td>
<td>10(27.8%)</td>
<td>8(100.0%)</td>
<td>18(40.9%)</td>
<td>14.123</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>associated therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>36(100.0)</td>
<td>8(100.0)</td>
<td>44(100.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Postoperative infections are the main source of morbidity and mortality of surgical patients. Prophylactic use of antibiotics is indicated in neurosurgical operations where the risk of infection is greater than the risk of using antibiotics.

In neurosurgery, there is generally a low risk of infection compared to other surgical branches, only 3-4%, due to surgical strategies, technological quality and progress (10,11). Postoperative infections in neurosurgical patients can be dramatic, rapidly progressive forms of meningitis, epidural abscess, subdural empyema, brain abscess, ventriculitis, sepsis. Therefore, the prophylactic use of antibiotics has proven to be very useful (12-14).

However, some studies have shown that prophylactic use of antibiotics in neurosurgery is still controversial. In practice, there is a "struggle" between advances in aseptic procedures and the abuse of high-dose antibiotics of the broad spectrum as a "standard".

Our study showed that there was no statistically significant difference in wound infection depending on the use of antibiotic therapy ($\chi^2 = 1.076; p = 0.583$) (Table 1.). According to the results of numerous studies (7,16), antibiotic prophylaxis leads to a reduction in the incidence of operative site infections. In contrast, this association in some other studies has not been confirmed (17, 18). Surgical infection increases the length of hospital stay (19). Prophylaxis has the potential to shorten hospital stay. There are several randomized studies that monitor the duration of hospital stay as a measure of outcome. They have shown that prevention of wound infection is associated with a faster return to normal activity after being discharged from the hospital (20).

A statistically significant difference was found during our study in the distribution of side effects depending on the use of antibiotic therapy ($\chi^2 = 15.634; p = 0.001$) (Table 2). A significantly higher number of patients who had antibiotic prophylaxis were without side effects, while patients with continuous antibiotic therapy more often had nausea and vomiting, diarrhea and stomach pain. Antibiotics can cause disturbance of bacterial equilibrium in the intestines and allow the development of strains of bacteria that cause gases in the intestines and lead to inflammation. Sometimes antibiotics significantly destroy the normal intestinal flora, so the Clostridium difficile bacteria can accumulate and multiply in the intestines. It illuminates a very harmful substance in the human intestines and leads to a much more serious form of inflammation of the intestines called Pseudomembranous colitis. Diarrhea occurs during or shortly after taking antibiotics. Pseudomembranous colitis may occur practically after the administration of any antibiotic, or most commonly after the increase of Ampicillin, Clindamycin, Cephalosporin of the third generation and Fluoroquinolone (21). Exposure to systemic antibiotics leads to a disorder of normal colon flora and an increase in sensitivity to colonization and toxin production by Clostridium difficile and increases the risk of symptomatic Clostridium by 2 to 16 times (22). The unreasonable consumption of antimicrobial drugs is harmful to the health of patients, it cause possible side effects, toxic reactions and interactions with other drugs and lead to increased resistance of microorganisms to antibiotics (23). Therefore, we concluded that antibiotic prophylaxis should be applied in neurosurgery due to shorter time use of antibiotics, less over-all dose, and less frequent appearance of serious complications due to prolonged use of antibiotics. Several published guidelines (24-28) say that for all clean and most pure-contaminated procedures (the main problem of bacterial contamination of the skin), Cefazolin is the first choice medication due to its external action on gram-positive coca, which mainly constitutes skin contamination.

Very few prospective randomized studies of surgical prophylaxis included economic evaluation within the research. During our research, a significant statistical difference was found in financial resources depending on the use of antibiotic therapy ($\chi^2 = 14.123; p <0.001$). Antibiotic therapy was used for prophylactic purposes and reduced the length of patients' stay in the hospital and did not cost more than 2000 dinars, while the continuous use of antibiotics extended hospitalization and it costed financially more. For most operations, however, prophylaxis only reduces short-term morbidity. Surgical infection increases the length of stay in the hospital (28). The additional length of stay depends on the type of surgery. Prophylaxis has the potential to shorten the stay in the hospital. There is little direct evidence to suggest that, a few randomized studies of (29,30) included the length of stay in the hospital as a measure of outcome. This is the evidence that the prevention of wound infection is associated with a faster return to normal activity after being discharged from the hospital.

Based on our research it is mandatory to provide optimum protection in the work by...
respecting the principle of asepsis, use prophylactic antibiotics after the patient’s consent by giving a minimum dose adjusted for the risk of infection and the status of the patient, before the beginning of operation and 24 hours after surgery.

It should be noted that the prophylactic use of antibiotics is different from continuous antibiotic therapy; the use of high-dose broad-spectrum antibiotics has long been used as a standard but should be avoided.

**Conclusion**

Antibiotic prophylaxis should be applied in neurosurgery for the following reason:

- shorter time of use of antibiotics,
- less overall dose of used antibiotics,
- rarely occurrence of severe complications of long-term use of antibiotics (enteric infection with C. difficile, development of resistance),
- economic benefit comparing to continuous antibiotic therapy.

**References**

PREDNOSTI ANTIBIOTSKE PROFILAKSIJE U NEUROHIRURGIJI

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Profilaktička upotreba antibiotika u neurohirurgiji znači upotrebu antibiotika u cilju sprečavanja infekcija rana i unutrašnjih operativnih struktura. Istraživanje je sprovedeno na Klinici za neurohirurgiju u Nišu, tokom 2018. godine kod 44 pacijenata koji su operirani sa hernijom diska L4-L5 i L5-S1. Kod 26 pacijenata primenjena je antibiotска profilaksa. U preostalih 18 pacijenata nije provedena antibiotска profilaksa i oni su grupisani u kontrolnu grupu. Pravecele trajanje operacije bilo je 50 minuta. Antibiotik se koristi u jednoj dozi, Cefalosporin prve generacije - Cefazolin 1 g iv za pacijente sa telesnom težinom manjom od 80 kg i 2 g za bolesnike sa telesnom težinom većom od 80 kg.

Primetili smo pojavu infekcija rana i unutrašnjih operativnih struktura, pojavu neželjenih efekata i finansijske aspekte. Cilj rada je bio pokazati da je antibiotска profilaksa povoljnija zbog kraće upotrebe antibiotika, manje nuspojava i ukupne finansijske koristi u poređenju sa kontinuiranom antibiotskom terapijom.


Ključne reči: antibiotска profilaksa, neurohirurgija, infekcije rana