

Berezhna Antonina, Makarova Victoria, Chumachenko Tetyana. The practices of antibiotics application in neurosurgical patients in Ukraine: a cohort study. *Journal of Education, Health and Sport*. 2021;11(06): 291-300. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2021.11.06.032> <https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.06.032> <https://zenodo.org/record/5585770>

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

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The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 21.05.2021. Revised: 03.06.2021. Accepted: 30.06.2021.

THE PRACTICES OF ANTIBIOTICS APPLICATION IN NEUROSURGICAL PATIENTS IN UKRAINE: A COHORT STUDY

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Abstract

Introduction. The outcomes of potential complications of surgical interventions in neurosurgical patients can cause a death. Efficient antibiotic prophylaxis decreases the risks of infection and improves the quality of health care.

Purpose. To estimate the appropriateness of prescribing antibiotics in a neurosurgical ward from the perspective of evidence-based medicine.

Material and method. A retrospective cohort study has been carried out in a neurosurgical ward of multidisciplinary healthcare setting of Ukraine. Data from 131 in-patient medical cards (MC) of neurosurgical patients has been analyzed. Descriptive statistics methods have been used for data analysis. The relative risk (RR) with the 95% confidence interval (95% CI) has been calculated.

Results. We found that among the patients, females prevailed ($n = 81 / 61.8\%$). The patients' mean age was 49.83 ± 13.90 years. The frequency of antibiotics prescriptions was higher significant in patients, who received surgical procedures in comparison with patients,

who did not receive surgical procedures (RR = 1.827; 95% CI: 1,137 – 2.935). Antibiotics were prescribed mostly during the postoperative period. The use of interchangeable antibiotics of the same group has been occurred. The use of antibiotics for prevention in the most cases was of unreasonably long duration.

Conclusion. The practice of the use of antibiotics in neurosurgical ward does not correspond to scientifically founded recommendations. It is needed to clearly define the indications for prescribing antibiotics. Duration of antibiotic use should depend on specialization of wards in multidisciplinary healthcare setting. It is expedient to conduct an audit on the use of antibiotics at healthcare settings on a regular basis with involving a specialist in infection control, a clinical pharmacist, and a clinical microbiologist.

Key words: healthcare-associated infections; antibiotic prophylaxis; cephalosporins; multidisciplinary healthcare setting.

Introduction. The discovery of antibiotics has become a considerable achievement of humankind and modern medicine. Apart from drastic decrease in mortality level from bacterial diseases, surgical sciences got further development, with surgical interventions having become a routine method of treatment, which enabled saving millions of lives [1-2]. Nevertheless, the use of antibiotics at healthcare settings for the reason of prophylaxis is often unfounded, incorrect, and does not correspond to international standards [3-7]. Along with decrease in antibiotics' clinical efficacy, their unreasonable use may facilitate forming of resistant strains of microorganisms, including agents of healthcare-associated infections [8, 9]. Special attention should be paid to the issue of antibiotic prophylaxis in surgery. When carrying out surgical procedures, healthcare workers often apply antibiotics as an additional means to prevent development of infectious complications. Using antibiotics in neurosurgical patients is a separate topic for discussion, for despite of quite a low frequency of development of nosocomial infections of the central nervous system, the consequences of potential complications can lead to death. A higher occurrence of infections complications due to neurosurgical interventions is associated with the type and duration of operation, the implanting of drainage or liquor shunt systems [10]. Neurosurgical patients may need ensuring a permanent vascular access, bladder catheterization, mechanical ventilation, which leads to additional infection risks and to development of healthcare-associated infections, for instance catheter-related bloodstream infections [11]. This stipulates the importance of choosing the optimal course of antibiotic prophylaxis in neurosurgical patients.

Purpose. To estimate the appropriateness of prescribing antibiotics in a neurosurgical ward from the perspective of evidence-based medicine.

Materials and methods. A retrospective cohort study was carried out in a neurosurgical ward of multidisciplinary healthcare setting of Ukraine. We studied 131 medical cards (MC) of in-patients who obtained a treatment in 2019. The object of the study was the practice of using antibiotics in patients with neurosurgical pathology.

An additional criterion for MC selection was patients' treatment at anesthesiology and intensive care unit (AICU). The use of this criterion was determined by several reasons. Firstly, at the AICU, mostly moderate and serious condition patients are treated, who may experience a need in being prescribed antibiotics. Secondly, the AICU receives patients following surgical procedures. This enables to establish the approaches to organizing antibiotic prophylaxis, by which healthcare workers are guided when performing operations and invasive manipulations. Also, it makes possible establishing the sequence in prescribing antibiotic therapy to patients in two wards of the same healthcare setting. The data analysis of MC was carried out with the use of the authors' expert evaluation method [12]. Apart from the general information related to the patients' age, gender, length of hospital stay, the state of their health in dynamics (changes that occurred during the treatment period), the diagnosis, the expert estimation form contained data regarding the use of antibiotics, performing of surgical and other procedures at the healthcare setting.

Predominantly used antibiotics groups, duration of the use of antibiotics, frequency of assigning pre-surgery and post-surgery antibiotic prophylaxis were determined. The cases of using metronidazole, chlorophilipt, and nifuroxazide were excluded from the general analysis. It is due to the fact that the mentioned medications, despite the present antibacterial action, do not pertain to any antibiotic group. Repetitive prescribing of the same antibiotic during the patient's stay in hospital was considered as the new one on condition that the previous treatment with this antibiotic had been completed.

To facilitate the analysis of the data obtained and to avoid advertising proliferation, the active substances nomenclature was used, rather than antibiotics' trade names.

For information systemizing and statistical procession, a database was formed through applying the Microsoft Excel 2016 and Epi Info™ for Windows (version 7.2) software. Descriptive statistics methods have been used for data analysis. The relative risk (RR) with the 95% confidence interval (95% CI) has been calculated [13].

In order to preserve data confidentiality and observe the bioethics principles, the information about healthcare setting is not disclosed, and the patients' information is depersonified and generalized.

Results and discussion. It was established that among the patients, females prevailed ($n = 81 / 61.8\%$). The patients' mean age was 49.83 ± 13.90 years (mode = 58; median = 52). All the patients' hospitalizations were planned, of them 111 people (84.7%) were hospitalized for the first time that year concerning a neurosurgical pathology, while 15.3% ($n = 20$) – recurrently. The mean length of hospital stay was 19.47 ± 11.85 bed-days (mode = 16; median = 17). Within the structure of illnesses, neoplasms (tumors) of brain and the spinal cord prevailed (51.2% / $n = 67$) as well as lower back dorsopathy (22.1% / $n = 29$). Rare cases of the radial nerve and the sciatic nerve neuropathy, traumatic brain injury, arteriovenous malformation, occlusive hydrocephalus also were occurred. The surgical procedures were performed on 88.5% of patients ($n = 116$). Most patients received surgical procedures once during their hospital stay (90.5% / $n = 105$). All surgical procedures were pre-planned. In total, 131 operations were made. Lumbar drainages, draining or liquor shunt systems were installed to ten patients (7.6%). Spinal fusion was made on three patients (2.3%). Overall, sluggish wounds with secondary intention elements were observed in two patients. The sluggish wound with a serous reaction signs was observed in one patient. A raise in the body temperature (37.0°C and higher) exceeding two days was recorded in 35.1% of patients ($n = 46$ of 131).

It was established that most patients' treatment regimens ($n = 121 / 92.4\%$) included antibiotics. Notably, in most cases ($n = 113 / 93.4\%$), patients received surgical procedures. The frequency of antibiotics prescriptions was higher significant in patients, who received surgical procedures in comparison with patients, who did not receive surgical procedures (RR = 1.827; 95% CI: 1,137 – 2.935). Among patients who received surgical procedures with subsequent appointment of antibiotic prophylaxis, a considerable proportion ($n = 109$ of 113 / 96.5%) started taking antibiotics in the post-surgery period on the day of the surgical procedure. In 2.6% of cases ($n = 3$), antibiotics were prescribed in the post-surgery period after 1.5 days and later following the surgical procedure. In one case (0.9%), antibiotics were prescribed in the post-surgery period on the day of carrying out the second surgical procedure. Apart from the post-surgery antibiotic prophylaxis, 8 patients (7.1%) also received antibiotic in the pre-operation period. Only 2.6% of patients of the total number of the operated persons

(n = 3 of 116) were not prescribed whatever antibiotics in the course of their hospital stay at all.

It was established that among the patients who were prescribed antibiotics during their hospital stay, 43.0% of persons (n = 52) obtained one antibiotic, 36.4% of persons (n = 44) were given two antibiotics, 15.7% of persons (n = 19) obtained three antibiotics, and 3.3% of persons (n = 4) obtained four antibiotics. One-time (0.8%) application of correspondently 6 and 8 antibiotics was registered in a patient who was being treated at AICU for a long time due to intra-brain abscess and its consequences. Therefore, 227 antibiotics prescriptions were issued in total. It was established that within the structure of antibiotics prescribed by doctors, 3rd generation cephalosporins prevailed (50.2% / n = 114). The second ranking by the frequency of prescribing (27.8% / n = 63) were 3rd generation cephalosporins in combination with the β -lactamase inhibitor, sulbactam. Fluoroquinolones were prescribed 35 times (15.4%). The other 6.6% of prescriptions (n = 15) were made for antibiotics of other groups, in particular penicillin antibiotics (n = 4), lincozamids (n = 3), glycopeptides (n = 2), carbapenems (n = 2, including one medication in combination with cystalatine, an inhibitor of dehydropeptidase), etc. It was established that ceftriaxone was the antibiotic, which doctors prescribed for their patients most often (n = 90). In combination with sulbactam, ceftriaxone was prescribed in nearly one quarter of cases (n = 53), cefoperazon in combination with sulbactam was prescribed in 10 cases. Another antibiotic of the 3rd generation cephalosporins, cefixim, was prescribed 18 times. As to antibiotics from other groups, levofloxacin should be noted, which was prescribed in 27 instances. The detailed information concerning all antibiotics, prescribed to the patients, is gathered in Table 1.

Also, it was established that one-third of patients (34.7% / n = 42 of 121) during the treatment obtained two different antibiotics of the cephalosporins group. Ceftriaxone and ceftriaxone/sulbactam were applied in 54.8% (n = 23) of these cases. During the treatment patients were obtained three different antibiotics of the cephalosporins group in 7.4% of cases (n = 9 of 121). When prescribing two antibiotics to the same patient, only in 27.3 % of cases (n = 12 of 44) the medications pertained to different groups. A considerable number of antibiotic prescriptions and the use of two or more antibiotics of the same group were mostly linked with changing the antibiotics when patients were transferred from one ward to another, or within the same ward. Thus, in particular, in 33.1% of cases (n = 40), interchange of antibiotics with the medications of same group was made, of which in 12.5 % of cases (n = 5), the interchange of medications took place within the same ward.

One of the reasons, which partially influenced the antibiotics interchangeability, was the medications stock available to the hospital wards.

Table 1. The frequency of prescribing antibacterial medications to neurosurgical patients

No	The name of antibiotics	Number of prescriptions, n	Proportion, %
1.	Azithromycin	1	0.44
2.	Amikacin	1	0.44
3.	Amoxicillin	1	0.44
4.	Amoxicillin/clavulanic acid	2	0.88
5.	Ampicillin	1	0.44
6.	Vancomycin	2	0,88
7.	Gatifloxacin	4	1.80
8.	Imipenem/cylastatin	1	0.44
9.	Co-trimoxazol	1	0.44
10.	Levofloquacin	27	11.89
11.	Lincomycin	3	1.32
12.	Meropenem	1	0.44
13.	Norfloxacin	1	0.44
14.	Rifampicin	1	0.44
15.	Cefixim	18	7.93
16.	Cefoperazone/sulbactam	10	4.40
17.	Ceftazidime	6	2.64
18.	Ceftriaxone	90	39.64
19.	Ceftriaxone/sulbactam	53	23.34
20.	Ciprofloxacin	3	1.32
	Total	227	100.00

Considering the aforementioned, the mean duration of the antibiotics use was calculated for the most often prescribed antibiotics groups (Table 2).

Table 2. Duration of the use of antibiotics of different groups in neurosurgical patients

Duration of the use of antibiotics, days	Class or group of antibiotics		
	3 rd generation cephalosporins (n = 114)	combined cephalosporins (n = 63)	fluoroquinolones (n = 35)
Mean ± standard deviation	5.75 ± 3.51	6.37 ± 4.00	7.01 ± 4.65
Median	5.5	6.5	6
Mode	1	1	two modes: 3 and 5
Minimum	0.5	1	1
Maximum	14	19.5	24
Range	13.5	18.5	23
Total	655.5	401.5	248.0

It was also established that 52.2% of those whom more than one antibiotic was prescribed (n = 36 of 69), received at least two antibiotics simultaneously.

We found, that 7.4% of patients (n = 9 of 121) got recommendations concerning the use of antibiotics after their hospital discharge. The analysis of 119 epicrisis issued to the patients on their discharge demonstrated that in 40.3% of cases (n = 48), taking of antibiotics was not documented, in 31.1% of cases (n = 37) not all antibiotics were written in the epicrisis, in 4.2% (n = 5) of cases the names of the antibiotics differed from those actually taken. In the other 4.2% of the discharge epicrisis (n = 5), it was indicated that the patients were prescribed antibiotics therapy without mentioning the names of the issued medications. Information on antibiotics taking with indicating the names of the issued antibiotics was documented only in 22.7% (n = 27) of the discharge epicrisis. It should be noted that documenting the antibiotics taking anamnesis prior patients' hospitalization is virtually nonexistent in the studied healthcare setting. In 97.7% of MC (n = 128 of 131), information on previous taking of antibiotics was absent. In 1.5% of MC (n = 2), information on antibiotics taking was indicated in the copies of the discharge epicrisis issued by other healthcare settings. In only one MC (0.8 %) did the attending doctor document the anamnesis of the previous antibiotics taking. Information on previous antibiotics prescribing can be useful for controlling antibiotics rotation. The results of scientific studies concerning expediency in antibiotics rotation within the strategic complex of antibiotics resistance prophylaxis at healthcare settings are disputable. A correct interpretation of the obtained results is affected by the non-uniformity of different studies and insufficient level of their organizing [14]. Although some authors do not recommend a routine antibiotics rotation [15], we think it expedient to clarify the history of antibiotics prescriptions for every patient. The individual approach to prescribing antibiotics will enable decreasing the number of repetitive use of the same antibiotics. That is why, when choosing optimal antibiotic for prophylaxis and treatment, gathering and documenting of anamnesis information concerning the use of antibiotics should be carried out.

According to the "Clinical practice guidelines for antimicrobial prophylaxis in surgery", it is recommended to use antibiotics to prevent a neurosurgery infection one hour prior the surgical procedure. When performing liquor shunting procedures, a one-time antibiotic prophylaxis (with one dose) or by treatment regimen should be made in the period of 24 – 48 hours after the procedure [10]. An important step at prescribing antibiotics is neurosurgery wounds classification. It enables estimating possible infection risks and

selecting the optimal antibiotics and regimens for using them [16]. It is recommended to use cefazolin, a medication of the 1st generation cephalosporins for antibiotic prophylaxis in most surgical procedures in the head and neck area [10].

So, the use of antibiotics for prevention in the most cases was of unreasonably long duration. Preference is given to antibiotics (ceftriaxone, ceftazidime, levofloxacin), which according to the World Healthcare Organization's AWaRe classification should be used as the first and second choice medications for empirical treatment of a limited number of infection syndromes ("Watch" group antibiotics) [17].

Conclusions. Neurosurgical patients are most often prescribed such antibiotics: 3rd generation cephalosporins, combined cephalosporins, and fluoroquinolones. Despite a need in carrying out the pre-surgery antibiotic prophylaxis, we identified inobservance of this requirement by most doctors. We also identified excessive use of antibiotics in the post-operation period and antibiotics interchangeability with medications of the same group. It is needed to clearly define the indications for prescribing antibiotics with obligatory documenting in the MC. Duration of antibiotic use should depend on specialization of wards in multidisciplinary healthcare setting. It is expedient to conduct an audit on the use of antibiotics at healthcare settings on a regular basis with involving a specialist in infection control, a clinical pharmacist, and a clinical microbiologist.

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