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ANALYSIS OF THE EFFECTIVENESS OF ANTIMICROBIAL THERAPY IN CHILDREN WITH FLUORQUINOLONE

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Annotation
This review will consider the use of antibacterial drugs of the quinolone class, in particular fluorinated drugs (FQ), in the treatment of hospital surgical infections in children in a surgical hospital. Since 1986, clinical data on the efficacy and tolerability of PCs (ciprofloxacin, ofloxacin, levofloxacin) show the possibility and validity of their use in children for the treatment of severe infections with the ineffectiveness of standard antibiotic therapy (ABT) regimens, multidrug resistance of infectious agents and while maintaining their sensitivity to fluoroquinolones.

Keywords: antibacterial, fluoroquinolones (FQ), therapy, infection, pediatrics

Introduction

The urgency of the problem. Therapy of severe forms, hospital and infectious complications is one of the most difficult problems in emergency pediatrics. This problem is aggravated not only by the high requirements for the tolerance and safety of drugs in children, but also by the multi-resistance of the hospital flora [5, 18]. This is facilitated by the rapid increase in the number of antibacterial drugs registered in Uzbekistan. All of the above poses a difficult task for the pediatrician in choosing

acceptable antibacterial drugs for the treatment of nosocomial infections in children, despite the impressive "antibacterial arsenal" of drugs.

It is known that fluoroquinolones, based on experimental data on chondrotoxicity for immature animals (the complication is species-specific and manifests itself in puppies, Beagle dogs, aged 2.5 to 8 months), are contraindicated for use in pediatric practice. Since 1986, clinical data on the efficacy and tolerability of FQs (ciprofloxacin, ofloxacin, levofloxacin) show the possibility and validity of their use in children for the treatment of severe infections with the ineffectiveness of standard antibiotic therapy (ABT) regimens, multidrug resistance of infectious agents and while maintaining their sensitivity to FQ [2,12,26,29,31]. In general, there is a good tolerance of PC in children, a low risk of adverse reactions from the joints (arthropathies). Non-fluorinated quinolones (NFQ - nalidixic, oxolinic, pipemidic acids) in experiments on puppies also exhibit arthrotoxicity. These drugs, even before the fact of cartilage damage was established (the fact was established in 1977-78), were widely used in pediatrics, including among young children. Over a long period of time (since 1962) there have been no cases of severe, especially irreversible, damage to the cartilage tissue, both during therapy and according to follow-up data [4,6,7,25,28,29,31].

In connection with the problem of arthropathies, based on experimental data on NFQ and FQ, the logic of age-related contraindications to the use of NPC in children is unclear: nalidixic acid - up to 3 months, pipemidic acid - up to 1 year, oxolinic acid - up to 2 years. There are no clear justifications for these particular dates in the literature. There are no restrictions for older age groups (unlike FQ). At the same time, all three NFQs are characterized by high experimental chondrotoxicity and from the standpoint of evidence-based medicine are more vulnerable than FC [8,9,10,12,18,28,29].

By the beginning of 2004, the effectiveness of the use of FQ was assessed with positive results in more than 10,000 children, including newborns and children in the first year of life [2,11,15,19,25,27,28,30,31]. At the same time, no data were obtained on FQ damage to cartilaginous or musculoskeletal tissue, impaired growth and development of patients, including follow-up data. In Japan, a special clinical study was conducted to assess the safety and efficacy of norfloxacin in children, and since 1992 this FQ has been approved in Japan for use in pediatrics [1,3,7,12,13,28].

The grounds for the use of FQ in children were:

1) High efficiency in the treatment of severe generalized infections in adult patients;
2) In general, good tolerance of FQ among adult patients;

3) Extensive clinical experience in the use of NFQ in children without revealing any disorders of the osteoarticular system (since 1962);
4) Severe infections with ineffective standard antibiotic therapy (ABT), with multidrug resistance of pathogens with their sensitivity to PC.
In the monograph [26] published in 1994, the question of the possibility of using FQ and NFQ in children and adolescents is considered in detail. One of the important points of the monograph: immature dogs (puppies of any breeds) and rodents (primarily rats), when assessing the arthrotoxicity of quinolones, are not an adequate model for transferring experimental data to the clinic. This position is considered on the example of nalidixic acid, the drug with the highest arthrotoxicity: "Neither rats, nor dogs are a model that determines the possible toxicity (arthrotoxicity) of nalidixic acid in humans" and "these results suggest that arthropathy associated with quinolones (in animals), is not observed in children, even after long courses of therapy" [26]. The monograph provides a series of clinical works on the successful use of PC in pediatrics and analysis of drug tolerance, including in terms of arthralgias and arthropathies. Despite this, some leading world and Russian pediatricians note the exaggerated danger of arthrotoxicity of FQ in children. Today, FQ is used in the treatment of children of different age groups with severe infections: pneumonia, meningitis, sepsis, bacterial diarrhea [2,5,6,11,12,15,18,19,27,28].

Purpose of the Study

To conduct a literary analysis of the use of fluorochonolones for health reasons in children with severe surgical hospital infection in a surgical hospital.

Material and Research Methods

According to the conducted studies, 23 patients were included: underwent abdominal surgery for intestinal obstruction - 4, diffuse peritonitis - 5, traumatic rupture of the intestine - 2 and esophagus - 1; interventions for brain injuries (craniotomy) with hematomas of various localization - 5, with drainage according to Arent - 3; urological operations for congenital ureterohydronephrosis (III-IV degree, chronic renal failure, urosepsis) - 3.
The average age of children was 5.7 + 1.3 years (n-23).
The patients were divided into 3 main groups:
1st with abdominal pathology (n = 12), 7 of them were on mechanical ventilation;
2nd with neurosurgical pathology (n = 8), on ALV-4;
3rd with urological pathology (n = 3), on ALV -1.

A projective study was carried out with the study of bacteriological analysis of various environments of the patient (pharynx, sputum, urine, feces, wound, endotracheal tube, blood, contents from drainages). Microbiological monitoring was carried out for 48-72 hours.

Out of 23 patients, 12 patients (52.2%) were on respiratory support on "SAVINA" and "SULLA" ventilators. The duration of respiratory support in this category of patients averaged 15.1 ± 3.5 days.

Results and its Discussion

Children of the 1st group with abdominal pathology belonged to the category of the most severe ones, they repeatedly underwent repeated operations for the development of intra-abdominal infections (interintestinal abscesses, prolonged peritonitis, intestinal anastomosis incompetence). In the media from the abdominal drainages, multi-resistant Gp-bacteria of the intestinal group were inoculated: E. coli (3), E. faecalis (4), P. aeroginosa (7), Enterobacter (2). All patients received antibiotic therapy (ABT) according to microbiological monitoring data - mainly, these are III-IV generation cefolosporins in combination with III generation aminoglycosides (+ metronidazole).

Patients received several courses of ABT (from 2 to 3), but in the absence of effect from previous antimicrobial therapy, against the background of the progression of intoxication, with the development of purulent foci in the abdominal cavity, the development of surgical sepsis with symptoms of multiple organ failure, patients of this group were transferred to vital indications for fluoroquinolones (FQ). The rationale for transferring patients to FQ were:

1. Progressive deterioration.
2. Lack of effect from previous ABT.
3. High sensitivity of microorganisms to FQ.

In subsequent bacteriological inoculations, polymicrobial resistant hospital flora (P. aureginosa - 10, Enterobacteriaceae - 4, E. coli - 5), highly sensitive to FQ, was sown from various drainages of the patient. The growth of resistant Pseudomonas aeruginosa increased. However, FQ was not immediately introduced into the empiric therapy of nosocomial infections, leaving them with 2-line (or reserve) drugs. Deterioration of the patient's condition on the basis of clinical, laboratory and X-ray data was a reasonable transfer of patients to FQ. In this regard, levofloxacin (Leflocin, Yuria-Pharm, Ukraine), both in isolated use and in combination with metronidazole (possibly a combination with III generation aminoglycosides) was prescribed for the treatment of intra-abdominal infections in patients at different periods of the disease.

Combined antimicrobial therapy was used in children with severe nosocomial infection with involvement of more than 2-3 organs in multiple organ failure syndrome. In patients of this group, the most often developed failures of the organs of the cardiovascular system, the respiratory system and the gastrointestinal tract.

Enteric failure is one of the main causes of persistent endogenous intoxication, systemic inflammatory response syndrome (SIRS), septic shock and multiple organ failure. With enteral insufficiency, the following develop:

1. Critical violations of the water-electrolyte balance.
2. Circulatory hypoxia of the intestinal wall.
3. Dysbacteriosis with proximal microbial colonization of the gastrointestinal tract.
4. Significant violation of antioxidant protection, local immunity and barrier function of the mucous membrane, the phenomenon of progressive "bacterial translocation".

Against this background, there is a decrease in the barrier properties of the intestinal wall with the development of ascending dysbiosis, the phenomena of endogenous microbial intoxication due to the increased formation of biologically active substances, cytokines and transient translocation of microbes into the blood. Therefore, in this group, in 83.3% of cases, combined antimicrobial therapy was carried out, aimed at suppressing both anaerobic and aerobic infections. It should be noted that against the background of the development of surgical sepsis with multiple organ failure syndrome, 7 patients were on respiratory support. The immediate postoperative period in this subgroup of children was complicated by the addition of ventilator-associated pneumonia (VAP). From the endotracheal tube of these patients, a multiresistant hospital flora was inoculated: Stafilococcus aureus-1, Klebsiella-5, Pneumonia aureginosa-2, also highly sensitive to PC. When treated with leflocin at a dose of 20 mg / kg / day. every 12 hours intravenously in combination with metronidazole (netromycin 7-8 mg / kg / day, 2 times), a good clinical effect (decrease in temperature and intoxication, no negative X-ray dynamics, normalization of laboratory parameters) was obtained in 86.5% of cases. Complete elimination of microbes or bacteriological effect was achieved in 73.3% of cases. 2 patients died with progressive multiple organ failure on the background of prolonged peritonitis, surgical sepsis, and repeated relaparotomies (one of them was a one-year-old child with an underlying pathology - closed abdominal trauma, intestinal rupture, fecal peritonitis, who died on the 37th day of illness).

Group 2 - neurosurgical, was mainly represented by children with a cerebral coma of II-III degree, who were on mechanical ventilation (n = 4). The postoperative period was complicated by the development of secondary purulent meningitis. From the drains of patients in this group, multi-resistant hospital flora was sown: Klebsiella-2,

P. aureginosa-4, Enterobacter-2, also highly sensitive to FQ. In children who were on respiratory support, by the 5th day, the clinic of VAP-pneumonia developed, from the endotracheal tube of these patients, multidrug-resistant hospital flora was sown: S. aureus-2, Klebsiella-3, P. aureginosa-1. The developed infection was resistant to therapy with various combinations of cephalosporins (CEP) in combination with aminoglycosides (AG). After unsuccessful previous antibiotic therapy, mainly after 1-2 courses, leflocine was prescribed. When treated with leflocin at a dose of 20 mg / kg / day. intravenously in combination with ceftriaxone, a good clinical effect was obtained in 87.5% of cases. Complete elimination of microbes or bacteriological effect was achieved in 75% of cases. In 6 children, recovery was observed, in 1 child during treatment, a therapeutic effect was obtained, however, there was a recurrence of infection - after removal of the drainage and re-administration of leflocin, recovery was achieved. Another 1 patient died after repeated neurosurgical operations due to open craniocerebral trauma, cerebral coma against the background of secondary purulent meningoencephalitis and hospital pneumonia.

3rd group uro-nephrological with urinary tract infection. This group is represented by patients with congenital anomaly of the UT - grade III-IV ureterohydronephrosis, chronic renal failure. The condition of children after plastic urological operations in the early postoperative period worsened due to exacerbation of urosepsis with the development of multiple organ failure. In the urine, feces, from the drainage tubes of patients, multi-resistant flora was seeded: Enterobacter spp.-2, P. aureginosa-1, E. coli-1, Proteus mir.-2, Candida alb.-1 (except for Candida alb.). This microflora was highly sensitive to FQ. After unsuccessful previous antimicrobial therapy, leflocine was included in the regimen. The therapeutic effect was achieved in 100% of cases, including according to the data of microbiological studies. Not a single patient in this group died during treatment. In the process of research and treatment, it was revealed that with progressive surgical hospital infectious complications in the early postoperative period, microbial associations were inoculated in children, including 2 or more opportunistic microorganisms in 51.2% of cases. The effectiveness of leflocin therapy in pure form and in the form of combinations was 87%. Combined antimicrobial therapy was used in children with severe nosocomial infection with involvement of more than 2-3 organs in multiple organ failure syndrome. Mortality 13% (3 children). The death of patients was due to the main severe surgical pathology, an immune deficiency state with the subsequent development of hospital infectious complications. As noted above, with unsuccessful previous antimicrobial therapy (2-3 courses), they switched reasonably (based on microbiological monitoring - from the point of view of evidence-based medicine) to treatment with leflocin, given the high

sensitivity of the detected Gp-microorganisms to it. During therapy, the patients did not have complaints of pain in the joint area, no swelling and pain in the joints were revealed. In recovered children, according to clinical and radiological studies, there were no violations in the development of the skeletal system, the presence of arthropathies or an increase in the volume of joints. Follow-up control over 10 months did not reveal any deviations from the norm in the development of children. 9 patients were monitored for 2 years - no diseases or abnormalities in the development of the osteoarticular system were found.

Conclusion

The presented data from the studied literature, based on microbiological analysis, clinical laboratory and X-ray studies, indicate a fairly high efficacy of leflocin in the treatment of life-threatening surgical hospital infections in children in the early postoperative period in a surgical hospital. The effectiveness of antimicrobial therapy was 87%. The presented studied literature data on the appointment of leflocin coincide with many world studies in pediatrics. Thus, it can be assumed that the appointment of leflocin to a sick child with a clinic, a progressive surgical hospital infection caused by gram-negative flora (peritonitis, interintestinal abscess, sepsis, meningitis), in the absence of the effect of previous antimicrobial therapy of cephalosporins and aminoglycosides of the latest generations of microorganisms + high sensitivity FQ. We believe that in the presence of microbiological confirmation of multidrug-resistant Hr-hospital strains (Enterobacter, P. aeruginosa, Klebsiella spp.) And cases of prolonged patient stay in a surgical hospital, leflocin is indicated in the treatment of the above life-threatening conditions in children.

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