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ETHICAL ASPECTS IN THE MANAGEMENT OF HELICOBACTER PYLORI INFECTION IN CHILDREN

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ABSTRACT. Ethical considerations are critical in medical practice, especially when doctors face the necessity of treating underage patients. Managing Helicobacter pylori infection, the most frequent chronic infection in the world, implies a multidisciplinary approach, and each of the members of the medical team has to act according to the legal provisions and ethical values. Children should be encouraged to involve in medical decisions, under the protection of an adult consent, but particular aspect related to the patient's development have to be carefully considered when discussing minor patient assent.

Keywords*: parental consent, child assent, ethics, Helicobacter pylori*

REZUMAT. ***Aspecte etice privind gestionarea infecţiilor cu Helicobacter pylori la copii.*** Consideraţiile etice sunt esenţiale în practica medicală, mai ales atunci când medicii se confruntă cu necesitatea de a trata pacienţii care nu au vârsta legală pentru a consimţi. Gestionarea infecţiei cu Helicobacter pylori, cea mai frecventă infecţie cronică din lume, implică o abordare multidisciplinară şi fiecare dintre membrii echipei medicale trebuie să acţioneze în conformitate cu prevederile legale şi cu valorile etice. Copiii trebuie încurajaţi să se implice în decizii medicale, sub protecţia consimţământului adulţilor, dar aspectele specifice referitoare la dezvoltarea pacientului trebuie să fie luate serios în considerare atunci când se discută despre acordul pacientului minor.

Cuvinte-cheie: *consimţământul părinţilor, acordul copilului, etică, Helicobacter pylori*

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Introduction

Helicobacter pylori infection is the most common chronic infection in the world, both in adults and children [1]. The infection occurs mainly in childhood, the incidence and prevalence increasing progressively with age and, in the absence of adequate treatment, bacterial colonization persists throughout life [2, 3]. It is estimated that 70% of the population of developing countries and 30-40% of the population of industrialized countries is affected [4]; in developing countries 50% of children are infected by the age of 5 [5].

In 1994, the International Agency for Research of Cancer, classified Helicobacter pylori (Hp) as a class I carcinogen, the infection being considered the most important risk factor in the mechanism of gastric carcinogenesis [6]. Hp plays an important role in the development of adenocarcinomas as well as MALT lymphomas [7], the risk being 3 to 6 times higher than in the uninfected population [8].

A universally accepted cascade of precancerous lesions has been determined: active nonatrophic chronic gastritis-> multifocal atrophy-> intestinal metaplasia-> dysplasia-> invasive carcinoma [9], with a dynamic progression and an individual-dependent speed of progression [10].

Given that in developing countries such as Romania the population is infected in infancy, premalignant lesions could start early, leading to an increased prevalence and onset of gastric cancer at young ages [11, 12]. Therefore, adequate public health programs are needed to prevent infection as well as establishing diagnostic methods and individual treatment according to age. The current pediatric guidelines for the management of Hp infection support upper gastrointestinal endoscopy with biopsies as the best method of diagnosis [13]. The Updated Sydney Classification for gastritis [14] is recommended for the assessment of the histopathological changes of the gastric mucosa [13].

This invasive method raises important ethical issues for the physician. The medical intervention involving pediatric patients must adhere to ethical and legal principles, such as: respect for the patients' rights to self-determination and confidentiality, and ensure good prior information in order to obtain the informed consent and is obliged to take into consideration the anatomical, physiological and psychological features that distinguish the child from an adult patient [15].

Discussions

1. General ethical considerations in the diagnosis and treatment of children

In medical decision making, patients and physicians should work together in an egalitarian partnership [16]. In this process, the patient needs to possess appropriate decisional capacity, and this is a relative matter [17, 18]. Informed

consent involves the provision of relevant information by the doctor so that the patient can exercise the right to make the decision in full knowledge, while respecting the patient's autonomy and the medical-legal needs of the institutions [19].

Informed consent is, however, more than a signed form. It is a process in which the parent of a child is given sufficient information, in order to be able to make a truly informed decision about the elected medical strategies [20]. Effort is required to provide accessible documents, in plain language, at an understanding level of 6 to 12 years [21]. There is evidence that participant comprehension decreases with increasing document length. There must be a balance between providing participants with overwhelming information and giving insufficient information to make an informed choice. [22] Doctors are required to protect children against serious harm, pain and death and parents are obliged to make decisions based on the best interest of their children. If the doctors consider that the parents are making a wrong decision, in order to reach an agreement, they must provide additional explanations and specify the consequences of the inappropriate decision [23].

2. Informed consent versus understood consent

In order to obtain a truly meaningful consent, the physician must spend enough time with the parent of a minor to explain in simple language the stages of treatment, the risks, the benefits and the alternatives for the treatment and to use repetitive techniques to test the understanding. The target should be to secure an "understood consent" [20]. One suggested method is to use a stratified approach, with additional details when needed. There are two complementary processes in obtaining informed consent: the presentation of the written material and the process of explaining it [24]. Even if the combined method, written and verbal, is time consuming, it offers the possibility of identifying parents who, despite repeated corrective feedback, do not understand sufficiently [25]. At the same time, it is necessary to adapt to local cultural norms and levels of education [26].

3. Parental consent versus child assent

Another important ethical aspect that doctors have to consider is the child's assent, not only when treating, but also when conducting pediatric research. It must be correlated with the informed consent of the parent or legal guardian. In this case, the intention is to identify those elements that are important for an adequate voluntary opinion/ of the child [27].

According to the international recommendations, the person who gives his agreement must be aware of the procedures that will be performed, freely choose to submit to the procedures, communicate his clear choice and understand the possibility of withdrawal, when considering medical research [28].

As specified by ethical guidelines, there are three stages of childhood: early, middle childhood and adolescence each associated with a different ability to make logical decisions [29]. Cognitive, emotional and social development should be taken into consideration in the process in order to ensure that the medical decisions are informed, rational and voluntary [16, 30]. An agreement should be reached regarding the age when patients possess the appropriate maturity to take the right medical decision [31].

Ethical considerations in the clinical research involving children

Research involving humans can be done in a therapeutic or purely experimental sense. Research involving children is ethically permissible only if it is carried out for therapeutic purposes, to the benefit of the patients and is subject to informed consent [32].

The unique vulnerability of children as research subjects has been identified since 1970, along with the publication of the article entitled "Ethics and Clinical Research", by Henry Beecher. Based on the ethical principle of respect for persons, the parental permission and the child's opinion work together for the protection of the child [33].

The ethical principle of "scientific necessity" states that research should not be conducted on children unless it is necessary to reach a scientific and / or public health objective that can be beneficial for the health and well-being of children [34].

When the minor is able to understand correctly and fully, he must give his own consent, along with that of the legal representative. Non-therapeutic experiments are morally inadmissible on children. Exceptions are those situations in which the use of an experimental drug represents the last chance to save the life of the child, but these situations are rare and must be rigorously evaluated [33].

Romanian legislation

In Romania, until the 2000s, there was no legislation that specifically referred to the protection of the child in scientific research. Article 19 of the Romanian Law on Patient Rights states that "Persons who are not able to express their will cannot be used for scientific research, except with the consent of the legal representative and if the research is done in the patient's interest". Legal representatives are usually the parents, or one of the parents. But, by adopting the New Civil Code in 2009, Romania has new provisions regard to

minors, to the joint guardianship: both parents must decide on their minor child, whether they are married or not, if they are separated, if divorced or living together with the child [35].

In addition, in 2004 the Law on good conduct in scientific research, technological development and innovation has been elaborated, subsequently modified and supplemented by Law 398/2006. In 2006 Romania implemented the Guide on the clinical investigation of medicines in the pediatric population [36].

In Romania, any clinical study on humans is authorized and supervised by the National Medicine Agency, which has been authorized to develop the "Rules of good practice in the clinical study". A clinical study can start only after obtaining the approval of the National Ethics Commission and / or the local Ethics Committee of the institution where the research is carried out. For the phase I studies it is necessary to obtain the approval of both ethical committees. For the phase II and III studies, the opinion of the local committee and the National Ethics Commission is also required. For phase IV studies, the approval of the local Ethics Committee is sufficient. Regarding the research involving children, according to the European legislation, also adopted by Romania, phase I studies are not allowed in the pediatric population [36].

Particular ethical aspects in the pediatric endoscopy

Endoscopy gains importance in the diagnosis and treatment of pediatric patients and specific rules are needed in the design and management of these units, as this experience affects both the patient and the family. In order to ensure safe and effective pediatric endoscopies, the unit should pay attention to the unique needs of children and should also focus on the goal to reduce anxiety. [37, 38].

Prior to the investigation physicians have to consider the risks and the benefits of the procedure, the agreement with the ethical values, the influence on other methods that may be needed for treatment and the long-term consequences of the procedure [39].

A great variation in types of sedation and analgesia are administered in pediatric endoscopy [40]. As a consequence, endoscopy rooms must provide age-appropriate analgesia and suitable equipment that for appropriate rescue maneuvers. [37]

Also, the patient and the family should be informed about the risks of the maneuver and the associated risks of sedation and informed consent, as well as assent should be obtained when appropriate [41].

As opposed to adults, tissue sampling during esofagogastroduodenoscopy is a routine procedure, biopsies being collected at least from the esophagus, stomach and duodenum; even in the absence of macroscopical findings, they are considered necessary [42, 43, 44]. Moreover, the risks of a subsequent endoscopy associated with sedation are higher than the risk of obtaining biopsies [45].

When considering the diagnostic strategies for the detection of the Helicobacter pylori infection in children, current pediatric guidelines recommend endoscopy whit biopsy as the election method, even though it is an invasive procedure. Other noninvasive methods are also available, with a lower sensitivity and specificity, but patients and their guardians are entitled to be aware of them when considering the diagnostic technique [13].

Particular ethical aspects in the pediatric pathological diagnosis

The most frequent ethical that pathologists are facing are related to confidentiality, privacy and the use of tissue samples in research [46]. Therefore, there is a great need for education in ethics for pathologists [47].

The application of the four basic principles of medical ethics, meaning autonomy, beneficence, nonmaleficence and justice, is mandatory for the pathologists, especially when they are dealing with pediatric patients, even though their interpretation is not as clear as for other medical specialties [48].

Prior to analyzing a sample, the pathologist should ensure that a consent was obtained from the patient or guardians, even though it is assumed that the consent has been obtained by the clinician [49].

The tissue samples that are submitted for pathological evaluation remain the property of the patient, even though the pathologist has the legal rights to process them. The preservation of the tissue for further research has to be done with the explicit permission of the patient [49]. National laws stipulating the storage conditions for biological materials, meaning tissue blocks and slides, must be strictly followed. When managing pediatric patients, pathologists should carefully consider that during the storage period patients may become adults and along with the development of medicine, the patients may require the tissue samples for newly discovered ancillary studies.

There are special situations in which the pathologist cannot provide a 100% accurate diagnosis or in which the laboratory does not have complementary examinations that would help establish a clear-cut diagnosis. In these instances, a second opinion from colleague could be needed, but the change of opinions has to remain confidential [50].

Along with the development of social media, there are numerous platforms used for medical learning. When pathologists post histopathology images of the cases, they should respect their professional standards and pay special attention in respecting the confidentiality of the patient [51, 52].

Conclusion

The pediatric population represents a vulnerable group, which is why special measures are needed in the diagnostic strategies and medical treatment of children, in order to protect their rights and to avoid exposure to unnecessary risks. The management of HP infection in children involves a multidisciplinary team, where each of the specialist doctors, namely pediatrician, gastroenterologist, anesthesiologist, pathologist, must adhere to the medical ethical principles.

Regarding pediatric research there must be a benefit / risk balance and it is recommended for the study to be conducted by experienced researchers, based on informed consent and to be approved by an ethics committee with experience in children's rights and needs.

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