Ethical aspects of child's enrolment in clinical trial

Introduction

Clinical trials are one of the most important tools for research and for the development of new drugs. It is the validation, demonstration of efficacy and safety of potential medicines or treatments developed under detailed testing conditions in the laboratory. Clinical trials are conducted before a drug is approved for marketing authorisation and before it enters the market. Clinical trials do not always guarantee a positive outcome and sometimes carry risks. Because of the risks, it is sometimes difficult for an adult to decide whether or not to take part in a clinical trial. And it is particularly difficult for parents to decide when a clinical trial is offered to their child. The aim of this essay is to highlight the ethical aspects of child participation in clinical trials. To determine what are the ethically correct steps to maintain good relationships between health care professionals, parents and minor patients during clinical trials. According to this theme, different studies and articles were compared and summarized.

1. Basic definition and concepts of Health care ethics

Advances in medical knowledge and medical technology bring with them new and important moral questions. Moral issues include the clinical relationship between health professional and patient, biomedical and behavioural research on human subjects, organ harvesting and transplantation, euthanasia, abortion and the allocation of health services. Medical ethics is a branch of applied ethics that deals with a wide range of moral decision-making situations that arise in medical practice in addition to the procedures and policies that are intended to guide that practice. Understanding the most important ethical principles and methods of moral decision-making is essential to understanding the moral issues that arise in the context of health care delivery. Decisions are applicable to such moral issues and which serve to guide our moral decision-making. (STEPHEN C. TAYLOR, 2018 , online)

1.1. An ethical problem and the procedure for solution

There are three recommended steps in solving an ethical dilemma. First, get technically clear about what is at stake. In our case, it is the parents, the health professionals and the Child. The second step is to gather all possible arguments for and against. Which in our study are provided by various studies and literature. In the last step we will try to formulate our own opinion which will be well argued. I will summarize most of my opinions in the conclusion. (HEŘMANOVÁ, 2012, page 9)

2. Communication by minor patients and their legal representatives

A number of professional studies have looked intensively at what psychological factors influence the treatment process. Modern medicine clearly points to the fact that if a health professional can communicate appropriately with a patient, he or she can significantly influence virtually all aspects of the treatment process and ensure his or her satisfaction.

2.1. Minor patient and their rights

The period from birth to 18 years of age is the period of childhood and adolescence. Children are considered vulnerable individuals not only because they are more vulnerable to negative factors in their environment due to their immature bodies, but also because they do not have the physical, cognitive and often social skills to effectively defend themselves as adults, which can lead to harm. Ethical issues that may be related to this age period include the question of protecting the rights of the hospitalized child, information and decision-making options for certain medical interventions, especially for adolescents, communication between medical personnel and parents, etc. (HEŘMANOVÁ, 2012, page 120)

In the case of a minor patient, the necessary information and the necessary decision-making are discussed primarily with his/her legal guardians, who are usually the parents. It can also be another person who has been appointed as the child's legal representative or an adoptive parent. This does not mean that the doctor or other medical personnel do not communicate with the minor patient at all and everything is discussed only with the minor's legal guardians. On the contrary, communication with the minor is necessary and, from the point of view of the minor himself, becomes more important as he grows older and more mature. Under Article 6 of the Convention on Human Rights and Biomedicine, if a minor lacks legal capacity, the procedure cannot be carried out without the consent of his or her legal guardian, an official or other person legally entitled to do so. The opinion of the minor shall be taken into account as a factor whose severity increases with age and level of maturity. (PTÁČEK, 2011, page 455)

Furthermore, the rights of child patients are set out in the Charter of Rights of Hospitalized Children. The rights listed in the Charter apply to all sick children regardless of their illness, age or disability, origin or social or cultural background, or the possible reason for treatment or the form or place of treatment, whether they are inpatients or outpatients. The European Association for Children in Hospitals (EACH) is an umbrella organisation for organisations that seek to improve the living conditions of children in situations that are in some way related to hospitalisation. EACH currently has 19 full members from 17 European countries and Japan. I would like to mention Articles 4 and 5. Article 4 states that children and parents have the right to be informed in a manner appropriate to their age and understanding. Measures should be taken to alleviate physical and emotional stress. Article 5 states that children and parents have the right to informed participation in all decisions concerning their health care. Every child must be protected from unnecessary medical treatment and examination. The last sentence tells us that the benefits must always outweigh the risks, and this applies to clinical trials as well. (AIF, 2022, online and EACH, 2022, online)

The rules of good clinical practice set out in the Convention on Biomedicine must be followed when children enter a study in which a clinical trial of a medicinal product is being conducted. The ethics committees of organisations that guarantee good clinical practice in a study must oversee the appropriate ethical conduct of the investigating physicians. Efforts to treat the child ethically should not end with the approval of the study by the ethics committee. It is important to use non-traumatic procedures, especially when obtaining biological material. For example, when taking blood. It is also necessary to choose painless procedures using

analgosedation or at least local anaesthesia in the form of numbing plasters or ointments. It is recommended to choose laboratory methods that work with a minimum volume of biological material. These are the so-called micromethods. These should not be studies that require repeated collection of tens of millilitres of blood. There are studies that test the antibody response to the vaccine administered. (PTÁČEK, 2011, page 155)

In a Japanese clinical study, children's ability to consent to treatment was assessed. The results of the study say that children should be allowed to give consent and their opinions should be respected. Involving children in decision-making promotes more open communication and transparency between health professionals, parents and children. The researchers used the method of children divided into three age groups (6-10 years, 11-14 years and 15-18 years) with three categories of disease severity. Possible correlations between the number of children, the age of the children, the level of education of the parents and the attitudes of the parents were investigated. The method was provided by a semi-structured Internet survey on parents' opinions and attitudes and preferences regarding involvement in medical research. Possible correlations between the number of children, the age of the children, the level of education of the parents and the attitudes of the parents were investigated. (FUKUDA, 2018, online)

In another clinical study, potential determinants of children's competence to consent to clinical research and the extent to which they explain differences in judgments of competence were examined. In the study, age was found to be the factor that explained most of the variance in children's competence to consent, followed by intelligence. Experience of illness did not affect competence in this study, nor did other variables. The study lasted 2 years, and pediatric patients aged 6 to 18 years, eligible for clinical research studies, were enrolled prospectively in various internal and outpatient pediatric departments. Children's competence to consent was assessed using the MacArthur Competency Assessment Tool for Clinical Research. Potential determining variables for children included age, gender, intelligence, disease experience, ethnicity, and socioeconomic status. Of 209 eligible patients, 161 were included. The mean age was 10.6 years and 47.2% of the men participated. Age, socioeconomic status, intelligence, ethnicity, complexity, parental assessment of competence, and study participation were univariately associated with competence. Results showed that age was a key factor explaining most of the variance in children's competence to consent. IQ is a second important contributing factor. Other factors that could potentially contribute to causality (gender, experience of illness, ethnicity) did not contribute significantly to the explained variance in competence, nor did contextual factors. The high contribution of age to the assessment of children's competence to consent complements recent findings on age. Previous work has shown that competence to consent is unlikely for children younger than 9.6 years and competence is likely for children older than 11.2 years. These findings offer a rationale for appropriate age boundaries in child consent policies. (HEIN, 2015, online)

2.2. Parents

An autonomous person is capable of conscious autonomous action, which is crucial to the fulfilment of the principle of autonomy in relation to the acceptance or refusal of medical care, unlike parents who decide according to the duty of responsibility whether or not their child

should participate in a clinical trial. This fundamental difference between trials in adult and pediatric medicine, relatively little is known about how the specific role of parents influences communication about the trial. Most parents want what is best for their child, but not knowing what the best course of action is can affect their response to a clinical trial. To the investigator, this may appear to be a misunderstanding of the rationale for the trial because parents are constructing the situation in a way that is acceptable to their need to protect their child. Some parents will see the trial as a threat to their child or fear that they will regret their decision, while others will see the trial as a hope for better treatment for their child. Almost all parents value their role in protecting their children and want to ensure the best outcome for them, but many recognise the complexity of the medical and research context and how this limits their ability to fulfil this role. Conducting studies with children can benefit from a better understanding of the special situation of parents and their particular need for support to enable them to maintain a sense that they have protected their child's interests. (SHILLING, 2009, online)

The Brazilian study by Carvalho and Costa also confirms that parents are not sufficiently informed. They aimed to understand how mothers perceived the processes of informed consent and randomization in a randomized control trial that divided uncooperative children into three intervention groups (physical restraint, sedation, and general anesthesia) for dental rehabilitation. Mothers' perceptions of the processes of informed consent and randomization in the clinical trial are characterized by a lack of understanding of these research steps, vulnerability in accepting the randomized intervention, conflicting feelings of belief, fear, helplessness, coercion, and a tendency to overlook their feelings to ensure the completion of their children's dental treatment. Participants in their study were mothers of children younger than 3 years who were recruited in randomized clinical trials to receive dental care under physical restraint, mild sedation, or general anesthesia. The children had early childhood caries, a severe oral disease that causes primarily pain and chewing difficulties, and their oral problems were not addressed by other public or private dental care services. Dental treatment with physical restraint and without sedation is considered ethical in Brazil due to the unavailability of facilities that provide pharmacological behavioral management. (CARVALHO, 2013, online)

2.3. Health care professionals

Health professionals who are in frequent contact with the parents of a hospitalized child must find a balance between a friendly and impersonal approach. A balanced relationship is a professional one, one that inspires trust in the parents, but also respect for the work of the health professionals and the whole team. The health worker can be sensitive to the parents, encouraging, educating and listening to their concerns, but aware of the purpose and goal of their shared care for the sick child. The health worker must maintain a professionally balanced relationship, which they must also maintain with the children. This requires not only a good knowledge of paediatric nursing but also of the laws of psychomotor development. He must not take patients' reactions personally and it is important that he does not avoid negative reactions from children. The principle of fairness must be applied in the provision of care. Every patient must be treated equally. (HEŘMANOVÁ, 2012, page 130)

Improper practice or malpractice in the exercise of a health care professional's profession can lead to patient harm. This includes the odd choice of communication. In the case of a clinical trial, inadequate explanation and disclosure of information regarding the clinical trial may lead to the patient or parents not consenting to participate in the trial. Healthcare professionals must have high moral credit and continually cultivate their personality. Negligence can only be prevented if morality is internalized. (KUTNOHORSKÁ, 2009, page 62-63)

3. Informed consent

According to Ptáček, informed consent is a practical application of the principle of the aspect of human autonomy. Treatment without informed consent is an unethical and illegal interference with the patient's physical and mental integrity, even if it is successful. The denial of informed consent is not a denial of the right to medical care, but of the right to make a free decision. In practice, an ethical dilemma can lead to conflict between two or more people who hold opposing views. Abandonment of the principle of beneficence is characterised by an ethical crisis. Beneficence is perceived as benefiting the patient. The solution is valid informed consent. It represents a compromise between conflicting principles and prevents ethical conflicts, including frustration on the part of the patient that can lead to complaints and lawsuits. (PTÁČEK, 2011, page 111)

In contrast to Ptáček, bioethicists and others point out that informed consent did not evolve to protect autonomy; rather, its primary purpose is to preserve well-being. Allmark and Spedding suggest that parental consent for clinical trials is important as a social recognition of the role of parents, but offers little additional protection for children beyond that provided by appropriate ethical, safety monitoring and research governance procedures. From this perspective, the quality of parental consent may be less critical. (ALLMARK, 2007, page 318-323)

Obtaining informed consent is also important for taking photographs of underage patients for medical research and experimentation. They are valuable material because they enrich teaching, research and advocacy and in many cases are necessary, but they can also have negative consequences. Children's safety and privacy could be compromised if compromising photographs identify children and their location, given that the images, if not adequately protected, could then reappear in the public press. Caution must always be exercised to avoid harm, the rights of the child being the paramount consideration. (DEVAKUMAR, 2013, online)

Conclusion

The aim of this essays was to highlight the ethical aspects of enrolling a child in a clinical trial, which are described in several points from the perspective of health professionals, parents and children. Various scientific articles and literature show that it is necessary to respect children's rights, to provide them with sufficient information in a clear and age-appropriate manner, and it is important not to neglect the child's wishes and decisions during the clinical trial. Children, and even parents, cannot make independent decisions. Parents are burdened with a duty of responsibility. The role of the health professional is to provide parents and their child with truthful and sufficient information so that they are able to make rational decisions on the basis of that information. Inadequate information provided around clinical trials is a

common problem, according to the articles. For this reason, every clinical trial should begin with informed consent in order to avoid communication errors, ethical crises and ensure patient welfare. When photographing patients, especially children, for clinical trials, we must be careful not to do so without the patient's informed consent as well. The most important argument is that the benefits of a clinical trial should always outweigh the risks.

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