



## Controversies and dilemmas in the treatment of malignant pain

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According to the definition of the International Association for the Study of Pain (IASP), pain is noticeably uncomfortable and emotional experience, combined with actual or potential tissue damage, or described at the time of such damage (1). The pain is extremely unpleasant emotional experience that is described as one of the oldest phenomena of human life. It is a completely subjective experience, which depends on personal perception of the pain. Making proper attitude about pain is under various cultural, ethnic and linguistic influences, and therefore the pain has a subjective component as well as multi-dimensional.

Patients are often unable to adequately evaluate pain (2). Also, they are often prone to the denial of pain (3). The reasons are multiple, such as denial of illness, fear that pain means deterioration of illness, belief that »suffering« of pain »strengthens their« spirit, etc. In countries with dominant Catholic religion, there is particularly strong belief in the suffering and voluntary acceptance of pain. On the other hand, there is evidence that medical staff underestimated the patient's pain, and experiences it less severe than it is presented by the patient. The big issue in the assessment of pain is the lack of objective biological markers for pain. Often, the only tool to detect the occurrence of pain or change in intensity of pain remains a patients' behavior tracking. Mood swings, agitation, restlessness, insomnia, fatigue, depression or irritability are some of signs that can draw attention to the occurrence of pain.

Treatment of pain is based on the guidelines adopted by the IASP (International Association for or the Study of Pain) 2005. year (4). Despite the existence of guidelines pain treatment is extremely complex, with a lot of dilemmas and controversies that are already reflected in drug selection and decisions about how to implement the therapy of pain.

In the treatment of cancer pain use of corticosteroids is common, although the number of studies is too small to safely confirm their effectiveness (5). Their use in practice has shown to have powerful anti-inflammatory effect, to raise the mood and appetite and that are useful in the treatment of specific pain syndrome (reduction of intracranial pressure, reduction of compression of the nerves, etc) (6, 7). With their application it is possible to reduce the dose of opiates that are needed for the reducing of pain. In treating pain it is extremely important to achieve prompt elimination of pain or if it is impossible, to relieve feelings of pain which is successfully achieved with corticosteroids. However, the use of corticosteroids has serious side effects which make big part of clinicians to oppose to their use (8). Their use is based on clinical

tradition and the unchecked statements. Existing studies are too old, with too small number of patients, and poorly designed. Further scientific research will give us proof whether corticosteroids really have an impact in the treatment of pain or it is a mistake. Until then, their use remains open to options and decisions about their use as a personal choice. In doing so, we must take into account how long it will be used corticosteroid therapy, what dose would be applied and what are the possible side effects of the therapy in certain patients.

Next dilemma we face in treating cancer pain is opioid rotation (9). We use opioid rotation when we're not satisfied with pain control, and the patient has distinct side effects of used drug. Opioid rotation helps to avoid severe side effects and better pain control. (10). Opponents of opioid rotation consider that opiates should not be viewed as the sole treatment for pain, but greater importance should be given to use of co-analgetics, adjuvant drugs and psycho stimulants (11).

Particular problem is pain in the elderly population (12). Older people rarely acknowledge the pain, harder describe pain and its characteristics (13). Big part of elderly patients have sensory and cognitive impairments, and sometimes they are unable to express the pain they suffer. Therefore, absence of pain reporting must not be accepted as a »no pain« state, and we should examine whether a patient suffers pain.

In addition to sensory and cognitive disorders characteristic of older populations and co-morbid diseases, are often multiple. Heart failure, coronary heart disease, generalized atherosclerosis, diabetes, and stroke are just some of the conditions that frequently occur in the elderly population. Co-morbid diseases must be treated in parallel with the treatment of pain. Consequently the number of side effects is greater, and their interpretation more complicated. It is necessary to avoid polipragmacism and good knowledge of the mechanisms of action of drugs is required to not harm the patient. Also in elderly patients is necessary to take into account the reduced renal and liver function, which does not necessarily have to be manifested as abnormal laboratory findings. Therefore, identification and treatment of pain in these patients is real challenge (13).

All known treatment options of pain are in accordance with the moral principles of the Hippocratic Oath (14). What are inconsistent with the Hippocratic Oath is to use a placebo rather than medication. However, the results obtained using placebos in practice are often encouraging and represent a major ethical dilemma for any doctor. By definition, a placebo is a substance or procedure that is objectively without specific activity for the state that is trying to heal (16). It has been scientifically proven that the patient's recovery can be accelerated if the patients suggest improvement of his condition. Therefore, a placebo may be part of the treatment of pain or treatment of anxiety. Placebo action is manifested through the placebo effect that was first scientifically confirmed in 1978 year (17). Advances in medicine and the use of functional brain images using magnetic resonance imag-

ing proved that the use of placebo, leading to activation and increased correlation between these parts of the brain: area cingulata, prefrontal, orbitofrontal, and insular cortex, nucleus accumbens, amygdala, periaqueductal gray matter and spinal cord (18).

Prefrontal area of the brain could be responsible for reminding the patient that he took a placebo, and thus lead to a cognitive understanding of his work. Anterior area cingulata and its effect on subcortical structures could be associated with an expectation of a potentially painful stimulus (18). Placebo effect depends on how it is presented. A substance that acts as a muscle relaxant if it is presented in another way it can achieve the effect of muscle tension (19). Furthermore, the placebo effect depends on whether the patient believes in the effect of substance that he receives. The length of the placebo effect is different. As a remedy for panic disorders placebo can be effective over 8 weeks, 6 months for angina pectoris and even two and a half years as an analgesic in rheumatoid arthritis (20). Placebo effect after verbal suggestions for mild pain may be much stronger and last even after ten applications. Placebo effect is not the same in all patients, which is not surprising because neither effect a real cure is not always the same in all patients (21). The application of placebo in terms of analgesia will cause a positive response in 35% of patients. Almost the same percentage (36%) of patients will respond to therapy with low to medium doses of morphine (4–8 mg) (22). The use of placebo in the treatment of pain has shown that the result is better as the pain intensified (23). Usage of placebo extends period of time through which patients can support pain. According to the VAS scale with use of placebo patients will feel pain lower by 2 to 5 point (24). However, the use of placebo is morally, ethically and scientifically questionable. Basically, usage of the placebo is deception. It undermines honest relationship and trust between doctor and patient which make an extremely important link in the treatment.

Giving a placebo instead of drug is unethical and interfere with the Hippocratic Oath which all doctors swear. Consciously giving placebos to patients for a condition that can be adequately treated, which prejudice the right of patients to the best care possible, opens up many bioethical issues. After all, how do we know which patient will respond to placebo? Those who do not respond will be subjected to unnecessary pain which is unacceptable.

Special entity is treating malignant pain at home. It is substantially different from treatment in hospitals or in hospices (25). Taking care for such a patient is within the domain of family physicians and palliative care team. Treatment is based on the basic principles of supportive and palliative medicine, which means quickly and effectively remove the pain, the treatment of »total« pain and pain treatment plan (26). As is often performed on patients who are in poor physical and mental condition and not able to make independent decisions the application of ethical principles of autonomy is often questionable, and sometimes impossible (27).

In conclusion we can say that the treatment of pain in oncology patients is a great professional challenge. Numerous treatment options that exist, makes often decision more difficult. Insufficient number of scientific studies on pain, its pathophysiological mechanisms and cause-effect situations to which it leads, raises practical and ethical dilemmas. Notwithstanding all mentioned nothing can prevent us to provide to every patient the best care possible and to eliminate their pain or if it is impossible to reduce it. It is allowed to use a wide range of medicines and methods, with adherence to ethical principles and rules.

Numerous scientific studies on the mechanisms and treatment of pain, and clinical observations will certainly lead to changes and updates guidelines for pain management on a global level (IASP 2005). We believe that a number of controversies and dilemmas in the treatment of pain to be elucidated. However, some will remain within the limits of vague areas that the doctors involved in treating pain put dilemmas and challenges. Therefore, we have a duty and obligation to communicate our experiences and reflections so that future guidelines for the treatment of pain were more comprehensive.

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