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ANALGESIA AS A FACTOR IN IMPROVING THE QUALITY OF LIFE OF PALLIATIVE PATIENTS

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Background. Palliative and hospice care (PHC) is provided to patients with incurable diseases in the last period of their life. PHC should reduce suffering and improve the quality of life of palliative patients themselves and their relatives. Pain relief is one of the main needs of palliative patients.

The purpose of the work is to analyze, generalize, and systematize the information of professional literature and normative legal acts of Ukraine regarding chronic pain in palliative patients and adequate analgesia depending on the main palliative disease.

Materials and methods. It was used system analysis, bibliosemantic method, and materials of PubMed and Google Scholar.

Results. The study showed the imperfection of the practice of organizing palliative care for palliative patients in Ukraine: national standards for the treatment of chronic pain, reimbursement of analgesic drugs practice. An objective assessment of the results of the aid organization is provided by surveys on the quality of life with standard and modified SF-36 questionnaires.

Conclusions. In order to organize full-fledged analgesia for the majority of palliative patients in Ukraine, it is necessary to review the list of palliative diagnoses with its recognition at the legislative level, as well as further development of the PHC system within the framework of the reform of the entire health care system. Increasing the availability of adequate pain relief for palliative patients should be facilitated by the legalization of medical cannabis, revision of protocols for the treatment of chronic pain in adults and children, improvement of the practice of reimbursement of the cost of medical drugs from the state budget, and further scientific research on the effectiveness of health care organization measures.

Key words: palliative and hospice care, basic palliative diagnosis, reimbursement, literature review.

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ЗНЕБОЛЕННЯ ЯК ФАКТОР ПОКРАЩЕННЯ ЯКОСТІ ЖИТТЯ ПАЛІАТИВНИХ ПАЦІЄНТІВ
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Паліативна та хоспісна допомога (ПХД) надається хворим з невиліковними захворюваннями для покращення якості їхнього життя та зменшення страждань. Дослідження проведене з метою вивчення питань хронічного болю у паліативних хворих, адекватного знеболення залежно від основного паліативного захворювання. Огляд літературних джерел та нормативно-правових актів України показав недосконаліть практики організації знеболення паліативних хворих в Україні порівняно з практикою країн із розвиненими системами ПХД. Препарати для знеболення лише частково підлягають реімбурсації. Оцінити результати організації знеболення дозволяють стандартні та модифіковані опитувальники про якість життя SF-36. Для покращення організації знеболення необхідні перегляд переліку паліативних діагнозів, подальша розбудова системи ПХД у межах реформи всієї системи охорони здоров'я.

Ключові слова: паліативна та хоспісна допомога, основний паліативний діагноз, реімбурсація, огляд літератури.

Statement of the problem. Most of the diseases that are responsible for a long life with disability in the world [1–3] are accompanied by moderate to severe pain that lasts until the last days of patients' lives. A significant proportion of these diseases are incurable and belong to the palliative care category. These diseases include malignant tumours, HIV/AIDS, severe trauma, rheumatoid arthritis, strokes, demyelinating diseases (multiple sclerosis, amyotrophic lateral sclerosis), epilepsy (including treatment-resistant epilepsy in children), cerebral palsy, congenital malformations, and others. Palliative care patients need treatment and care that should reduce their suffering in the last years and days of life [4; 5]. Palliative care patients with chronic pain need to receive narcotic painkillers on a regular basis, which is often difficult to ensure in countries with strict anti-drug policies. To provide greater access to narcotic painkillers, countries trying to improve the situation of palliative care patients are decriminalising the possession of a certain amount of narcotic drugs for personal use, developing national palliative and hospice care systems (PHC), legalising medical cannabis, and reimbursing the cost of painkillers from the state budget [6–8]. Ukraine is one of them, and the reform of the PHC system was activated along with the reform of the entire healthcare system in 2014 [9]. However, there are a number of unresolved issues in healthcare organisation that prevent the majority of palliative care patients from receiving treatment. Firstly, it is an understanding of what diseases Ukraine is ready to consider palliative in order to organise the necessary palliative treatment and care for these patients. Secondly, it is how hospice and outreach palliative care, "hospices at home" are organised. What kind of treatment coverage do palliative patients have? Thirdly, how pain relief is organised and whether it is adequate to the needs of the main categories of palliative care patients. What is the regulatory and legal framework for pain relief, what narcotic and non-narcotic drugs are available to patients, and what part of their cost is reimbursed by the state.

We have studied the first issue and will not discuss it in detail in this review. It is known that the list of palliative diagnoses in Ukraine primarily includes oncological (malignant) diseases of the last stages, as well as conditions with direct damage to the central and peripheral nervous system as a result of injuries and neurodegenerative diseases. However, countries with developed PHC systems are expanding the list of palliative care diseases within the list recommended by the World Health Organization (WHO). For adults, it also often includes cardiovascular diseases (I00–I99 according to the International Classification of Diseases, 10th Revision, ICD-10), kidney disease (N00-N15, N20-N23) tuberculosis (A15-A19), HIV/AIDS (B20-B24), diabetes mellitus (E10-E14), rheumatoid arthritis (M05-M06), liver fibrosis and cirrhosis (K74), chronic obstructive pulmonary disease (J43-J47), epilepsy (G40-G41). For children – cardiovascular diseases, diabetes mellitus, tuberculosis, HIV/AIDS, as well as congenital malformations, severe perinatal conditions (Q00-Q99), cerebral palsy (G80), inflammatory diseases of the central nervous system (G00, G03, G04, G06, G08, G09), chronic hepatitis (K73, K75.2, K75.3), phenylketonuria (E70.0), cystic fibrosis (E84), mucopolysaccharidoses (E76). Palliative care patients in these categories are provided with both pathogenetic treatment and symptomatic treatment (including adequate pain relief) in countries with developed PHC systems when treated in hospice and palliative care facilities, hospice units and wards of general and specialised clinics, nursing homes and home hospices [10].

In our 2021–2023 study, we determined the need for palliative care in adults and children in Ukraine with the above listed diseases, with the exception of epilepsy. We also made a forecast of the need for PHC for the following years, and were subsequently able to verify and refine this forecast using various methods. We found that the best method for forecasting is the creeping trend method with a constant smoothing segment, which allowed us to determine most of the indicators of need within the 95% confidence interval [11–13]. We had significant difficulties in calculating the need for PHC for adult patients with dementia (F00-F03) and children with severe and profound mental retardation (F72-F79), which was caused by the cessation of statistical data collection for these patients in Ukraine since 2018.

We estimate the total number of palliative care patients before the start of the full-scale war to be 242,800, including 194,500 adults and 48,300 children. The possibility of underestimating this number was determined by us within 25%, which was due to incomplete statistical data on the nosologies included in the calculation, as well as nosologies that were not calculated (epilepsy and multiple sclerosis) [14; 15]. Thus, at the preliminary stages of the study, we were able to identify a list of diseases that Ukraine should recognise as palliative care. However, we did not find any publications on the relevance of such lists of diseases to the types of chronic pain and pain relief, the adequacy of which would be confirmed by quality-of-life indicators.

The aim of our study is to investigate the features of chronic pain in palliative care patients depending on the underlying palliative disease and to organise adequate pain management.

Materials and methods. The literature and regulatory sources were analysed using the bibliosemantic method with a search for the thematic keywords "chronic pain in palliative care patients", "pain management in palliative care patients" on PubMed and Google Scholar, in Ukrainian and English. For the analysis, 20 sources were selected using the relevant keywords in Ukrainian and English in Google Scholar and in English on PubMed. The vast majority of sources corresponded to the period of the last 5 years (2020–2024). Of the 120 sources pre-selected for analysis, 46 were finally selected, which belonged to the categories of regulatory legal acts of Ukraine on financing pain relief for palliative patients with chronic pain; scientific publications on the need for pain relief, and assessment of pain relief effectiveness according to quality-of-life indicators. The final selection of sources was based on their credibility (for example, WHO analytical reports were selected) and relevance to the Ukrainian model of pain management for palliative care patients (for example, the choice of available painkillers). To systematise and evaluate the data, we used the method of systematic analysis with minimal detail of steps and feedbacks according to E.P. Golubkov [16], which has the following successive

stages: problem statement; research; analysis; preliminary judgement; confirmation; final judgement; implementation of the decision.

Results and discussion. The procedure for the provision of palliative care in Ukraine is regulated by the Order of the Ministry of Health of Ukraine No. 1308 of June 04, 2020 "On Improving the Organisation of Palliative Care in Ukraine" [17]. According to this order, palliative care should be provided on the principles of succession and continuity (for which special routes are drawn up for patients to move between doctors of different specialties or to those medical institutions where patients consistently receive the necessary care). PHC is provided to "alleviate patient suffering through early identification and assessment of symptoms, pain relief and other physical, psychosocial and spiritual problems" by general practitioners, internists, pediatricians, etc., junior medical specialists, or multidisciplinary teams consisting of doctors, social workers, psychologists, volunteers, and clergy. Palliative care requires "the treatment of pain, associated symptoms and complications, and the resolution of physical, psychological, spiritual and social problems" of the patient. The patient's family and friends have the right of round-the-clock access to a palliative patient who is being treated in any medical institution. Forms of palliative care include inpatient (including hospice) care, mobile care and "hospice at home". A medical institution must ensure that parents or guardians stay with a child with a palliative diagnosis until the end of his/her life. Healthcare facilities treating palliative care patients should establish chronic pain treatment rooms.

The literature review makes it clear that the reform of the PHC system in Ukraine is ongoing, even despite the war, which is confirmed by key aspects of the organisation of medical care: the allocation of funds for palliative care for adults and children by the National Health Service of Ukraine (NHSU) and a gradual increase in this funding over 2021–2024. For example, a study of the section "Contracting (2021–2025)" on the NHSU website [18] showed that the list of healthcare packages for 2021 [19] included only the inpatient palliative care for adults and children. In 2022, funding for mobile palliative care for adults and children also began [20]. In addition, package funding for the treatment of people with mental and behavioural disorders due to opioid use with a substitution maintenance therapy drugs has begun, which is relevant for a significant number of palliative care patients with chronic pain who have been receiving narcotic pain relief for a long time [21–23].

According to the list of palliative diagnoses we have compiled, the following funding packages of the National Health Service of Ukraine, which appeared in the list of the medical guarantees programme, are relevant for adults and children in need of palliative care: "Diagnosis and treatment of adults and children with tuberculosis in outpatient and inpatient settings"; Chemotherapy and radiological treatment and support for adults and children with cancer in outpatient and inpatient settings; "Psychiatric care provided by mobile multidisciplinary teams" (for palliative care patients with dementia, for patients who have side effects of long-term use of narcotic painkillers); "Medical rehabilitation of infants born prematurely and/or sick during the first three years of life" (for children with severe perinatal conditions); "Inpatient medical care for patients with acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2" (the abbreviation stands for Severe acute respiratory syndrome-related coronavirus 2); "Comprehensive rehabilitation care for adults and children in inpatient settings"; "Surgical operations for adults and children in inpatient settings"; "Inpatient care for adults and children without surgery". It should be noted that packages of direct funding for palliative inpatient and mobile medical care for adults and children are not always used by the chief physicians who ordered them for the needs of palliative patients, when these funds go to the accounts of hospitals with palliative and non-palliative departments [24] (it occurs not only in Ukraine [25]). However, in order to obtain the NHSU's consent to fund palliative care packages, a hospital must already have a significant number of staff and material and technical resources. Therefore, palliative care patients in non-hospice facilities actually use not only the equipment and medicines received by hospitals as part of "palliative" packages. At the same time, the list of services included in the palliative packages, in our opinion, does not cover all clinical needs of palliative patients (especially in terms of medication), so chief physicians of clinics and heads of their palliative units can also use the funds of the packages for profiles that correspond to the main palliative diagnosis, but are not directly intended for palliative patients. This also concerns several diagnostic packages: "Mammography"; "Hysteroscopy"; "Esophagogastroduodenoscopy"; "Colonoscopy"; "Cystoscopy"; "Bronchoscopy".

In 2023, the requirements for medical services under the medical guarantees programme provided by NHSU contracts were improved, and 2 fundamentally new funding packages were added: "Readiness and provision of medical care to the population in the territory where hostilities are taking place" and "Readiness of a healthcare facility to provide medical care in emergency situations" [26]. The opportunities provided by these packages to heads of healthcare facilities are important for saving the lives of palliative care patients with limited mobility in regions where active hostilities are ongoing or which are under constant Russian shelling [27].

In 2024, the requirements for implementers of the Medical Guarantee Programmes improved. The tools for ordering services were also developed. In particular, a cost calculator was introduced, which makes it especially easy to apply the coefficients set out in the law [28]. When concluding a contract with the NHSU, a provider of inpatient and mobile medical services for palliative care patients is obliged to "assess, prevent and treat chronic pain syndrome (including the use of narcotic drugs, psychotropic substances and precursors)" with constant access to painkillers, and to anaesthetise all diagnostic and therapeutic invasive interventions. The provider of inpatient services should also ensure round-the-clock nursing supervision of palliative care patients, constant access to an adult palliative care patient for relatives and friends, constant joint stay of parents or guardians with a palliative care child, and oxygen support if necessary.

Reimbursement ("full or partial reimbursement to pharmacies of the cost of medicines or medical devices dispensed to patients on the basis of a prescription at the expense of the state healthcare guarantee programme" [29]) plays an important role in providing effective pain relief for most palliative care patients, namely, inclusion of the medicines necessary for pain relief in the reimbursement list and a significant percentage of reimbursement. Reimbursement of medicines in Ukraine is carried out within the framework of the "Affordable Medicines" NHSU. In 2023, the NHSU reimbursed medicines for the treatment of outpatient diseases that are often the main palliative diseases (those that are incurable and directly lead to the death of patients): cardiovascular, cerebrovascular, diabetes mellitus, chronic lower respiratory diseases, mental and behavioural disorders, epilepsy, Parkinson's disease. On 31 August 2023, targeted reimbursement of painkillers for palliative care patients was launched. In the current year of 2024, reimbursement is carried out for a number of directly analgesic drugs, as well as other drugs which use may affect the presence and intensity of pain, as well as its subjective perception. These include anticonvulsants, antispasmodics, non-steroidal anti-inflammatory drugs and other adjuncts [30]. The list of medicines subject to reimbursement and the amount of reimbursement are shown in the table 1. Test kits for patients with diabetes mellitus are also reimbursed [31], which is included in the list of palliative diseases and is accompanied by chronic pain in the presence of diabetic polyneuropathy [32; 33].

The analysis of the list of medicines to reimbursement in 2024 suggests that it is limited for the treatment of palliative care patients, and the reimbursement percentage is insufficient, despite the relatively low cost of commercial drugs included in the reimbursement list. The limited number of medicines limits the training of healthcare professionals providing care to palliative care patients. After all, it is advisable to start studying medicines for the categories of patients treated by a healthcare professional from the list of medicines reimbursed by the state. We were unable to find scientific publications analysing the list of drugs included in evidence-based clinical guidelines, standards and protocols for the treatment of palliative care diseases.

The standards of care "Chronic pain syndrome in adults and children" [34] recommends following the WHO Three-step Analgesic Ladder [35] for the choice of painkillers, according to which non-narcotic painkillers (non-steroidal anti-inflammatory drugs, acetaminophen, adjuvant drugs) are used on the first step (for mild pain); on the second step (for severe pain) (for moderate pain) weak opioids (hydrocodone, codeine, tramadol) are used; the third step (for severe pain) uses strong opioids (morphine, methadone, fentanyl, oxycodone, buprenorphine, tapentadol, hydromorphone, oxymorphone), to which non-opioid analgesics and adjuvants are added, if necessary. Of this list, Ukraine reimburses a small portion (primarily acetylsalicylic acid and tablet morphine), which is not enough to implement the three-step strategy.

The introduction of such a profession as a palliative care physician into the classification of professions in Ukraine is unreasonably delayed, and no training for palliative care physicians is provided [14]. However, a significant number of doctors come into contact with palliative care patients, as the actual number of such patients fluctuates around 300,000 (about 1%) of the actual population of the country [11]. All doctors face the ethical issue of pain management with the use of new drugs whose efficacy and side effect risks have not been sufficiently tested. These issues are linked to other difficult questions of pharmacotherapy for patients, their guardians and doctors: when to stop treatment of the underlying palliative disease (most often cancer), when to stop resuscitation. Besides the instructions of clinical protocols, the physician must take into account the wishes of the patient and his/ her family, their religious, cultural and family traditions [36; 37].

An objective assessment of the effectiveness of care and treatment of palliative patients should be carried out using the ShortForm-36 Health Status Survey (SF-36)

Table 1

Medicines that can be used to directly or indirectly reduce pain in palliative care diagnoses, which are included in the list of those subjected to reimbursement in 2024

International chemical name	Action, group of chemical compounds, possible use	Reimbursement amount, %*
Amitriptyline	Tricyclic antidepressant and analgesic; in neuropathic pain	100–49
Valproic acid	In bipolar disorders, secondary epilepsy	100–81
Haloperidol	Antipsychotic drug of the group of butyrophenone derivatives, a powerful antagonist of central dopamine type 2 receptors; for combined therapy of postoperative nausea and vomiting	100–43
Carbamazepine	Antiepileptic anticonvulsant, in idiopathic neuralgia of the trigeminal glossopharyngeal nerve, in neuralgia in multiple sclerosis	100–56
Acetylsalicylic acid	Analgesic and antipyretic	100–45
Clozapine	Neuroleptic; hypnotic and sedative effect	100–69
Lamotrigine	Antiepileptic; anticonvulsant; for treatment of adults and children	100–35
Morphine	Narcotic analgesic, opioid; for severe pain	100–70
Phenytoin	Antiepileptic; anticonvulsant; muscle relaxant	100**
Fluoxetine	Antidepressant; analgesic; for treatment of adults	100–49

Notes: * – drugs from different manufacturers are reimbursed differently; the calculation result is rounded to whole numbers; ** – if a single commercial drug is reimbursed, not an interval, but a single reimbursement value in % is calculated.

questionnaire, which is valid for different age groups, highly informative and sensitive, allows simultaneous assessment of physical and mental health indicators of healthy people and patients with various diseases (general health, mental health, physical functioning, role-based physical functioning, role-based emotional functioning, social functioning, intensity of physical pain and vital activity) [38–41]. The 36 questions of the SF-36 demonstrate 8 concepts of health. Assessment of the general condition allows to determine the prospects for treatment, physical functioning – the ability to self-care. Role functioning is assessed in relation to possible physical and emotional obstacles to performing daily activities, which may increase the time spent on them, reduce their volume and quality. Social functioning is defined as the ability to communicate, which may be limited due to physical or emotional conditions related to the disease. Pain is assessed by its intensity and impact on the ability to perform daily activities. Self-assessment of vital activity refers to the self-perception of own energy, ranging from overflowing with energy to complete exhaustion. Mental health self-assessment refers to the patient's predominant mood.

For palliative care patients with oncological and neurological treatment profiles, we proposed minor modifications to the questionnaire that took into account the serious condition of patients and the limitation of their mobility up to complete immobility while in bed [42; 43]. Physical activity is considered by the survey as the ability to perform certain types of activities (work) outside the home (climbing stairs, carrying loads), which can be perceived emotionally negatively by immobile patients. A preliminary assessment of the quality of life of Kharkiv hospice patients in 2022 showed that adequate pharmacotherapy can not only improve the quality of life of palliative patients and reduce pain, but also have a positive impact on the disease itself. Besides the direct pain relief, the level of pain can be reduced by proper symptomatic and pathogenetic treatment [44–46].

Thus, in accordance with the chosen research model using the systematic analysis method and the goal set, we have formulated a preliminary judgement about the insufficient pain relief for palliative care patients in Ukraine. The main reason for this fact is the insufficiently detailed list of palliative diseases, which we proposed to expand at the previous stages of the study. The second reason for insufficient pain relief is the imperfection of national standards for the treatment of chronic pain. As a result of the analysis of literature sources (scientific publications and regulatory acts of Ukraine), we received confirmation of our preliminary judgement and formulated a final judgement that states the fact of insufficient pain relief, details the problem and suggests a way to improve pain relief for palliative care patients in Ukraine, which is presented in the conclusions.

Conclusions. The overwhelming majority of palliative diseases in adults and children are accompanied by chronic pain, the impact of which on the psyche, emotional state, social functioning, and ability to self-care can be objectively determined by the SF-36 questionnaire. Adequate pharmacotherapy, using narcotic and non-narcotic painkillers and adjuvant medications (sedatives, anticonvulsants, tranquillisers, etc.), can significantly improve the quality of life of palliative patients. We have identified the inconsistency of national standards for the treatment of chronic pain in adults and children with the strategy of package financing of palliative and hospice care and reimbursement of pharmaceuticals that can be used for pain relief in palliative care. It is proposed to expand the list of painkillers and adjuvants in palliative medicine, which should help improve the quality of life of palliative patients.

Conflict of interest. The authors declare no conflict of interest.

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