

**DIFFERENTIAL DIAGNOSTIC AND
THERAPEUTIC TACTICS OF PLEURISY IN
PANCREATITIS AND HEPATITIS: ABC AND
ABC/VED ANALYSIS OF PATHOGENETIC
PHARMACOTHERAPY**

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Introduction

Pleurisy remains a clinically significant complication of a wide range of pulmonary and extrapulmonary diseases and is observed in approximately 5-10% of hospitalized patients with pleural cavity pathology. The etiological structure of pleural effusions is heterogeneous and includes infectious, inflammatory, metabolic, and systemic diseases. Among the extrapulmonary causes, an important place is occupied by acute and chronic pancreatitis and chronic liver diseases, which can be accompanied by the formation of pancreatogenic and hepatogenic pleural effusions, which significantly complicates the diagnostic process and the choice of treatment tactics [1].

Reactive pleurisy in pancreatitis occurs in 14–29% of cases and is associated primarily with the formation of pancreatopleural fistulas and the migration of enzyme-enriched exudate into the pleural cavity. Hepatogenic pleurisy occurs in patients with cirrhosis of the liver and portal hypertension due to translocation of ascitic fluid due to defects in the diaphragm. Such patients require a multidisciplinary approach to treatment involving pulmonologists, gastroenterologists and hepatologists. Along with etiotropic and symptomatic therapy, pathogenetic pharmacotherapy aimed at correcting metabolic disorders, malabsorption and deficiency states plays an important role [2-7].

Chronic pancreatitis is accompanied by the development of exocrine pancreatic insufficiency, which leads to impaired absorption of fat-soluble vitamins and the formation of a deficiency of fat-soluble vitamins, in particular vitamin A, vitamin D, vitamin E and vitamin K. Similar disorders are typical for patients with chronic liver diseases, where malabsorption, cholestasis and impaired fat metabolism necessitate the use of vitamin support. Clinical protocols for the treatment of chronic pancreatitis and hepatitis provide for the use of vitamins A, vitamin D, vitamin E and vitamin K as a component of pathogenetic therapy [8].

The use of vitamin drugs for pleurisy against the background of pancreatitis and hepatitis is not only clinical, but also pharmacoeconomic. A significant number of trade names, dosage forms and dosages creates the problem of rational formation of the assortment and reasonable choice of drugs for clinical practice. In the context of limited resources of the health care system, methods of pharmacoeconomic assessment are of relevance, which allow determining the priority

of medicines and optimizing the drug supply to patients [9-14].

One of such tools is ABC analysis, which is widely used in pharmacoeconomic and pharmaceutical studies to rank medicines according to their significance. The combination of ABC analysis with VED classification allows to assess not only the structure of the assortment, but also the clinical importance of medicines [15-18].

Despite the presence of numerous studies on the use of ABC and ABC/VED analysis in the pharmacotherapy of various diseases, there are currently no works on prioritizing vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis.

However, no studies have evaluated the prioritization of vitamin pharmacotherapy in pleurisy associated with pancreatitis and hepatitis.

We hypothesized that vitamin pharmacotherapy in this patient population is characterized by irrational assortment duplication.

Despite the presence of numerous studies on the clinical aspects of pleurisy, chronic pancreatitis, and liver diseases, as well as the use of ABC and ABC/VED analysis in the pharmacotherapy of various nosologies, several important issues remain insufficiently studied. Firstly, there are no studies in the scientific literature that comprehensively analyze pleurisy, associated with pancreatitis and hepatitis, from the standpoint of clinical pharmacotherapy and drug supply. Secondly, the role of vitamin pathogenetic pharmacotherapy in this category of patients remains insufficiently systematized, despite the known mechanisms of malabsorption and deficiency of fat-soluble vitamins in diseases of the pancreas and liver. Thirdly, there are no pharmacoeconomic studies aimed at prioritizing vitamin medicines, considering real clinical practice, the structure of the pharmaceutical market and the frequency of drug prescriptions.

Thus, there are currently no clinical and pharmaceutical studies that would combine the analysis of the clinical use of vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis with pharmacoeconomic approaches to rationalizing the range of medicines.

The scientific novelty of the study lies in the fact that for the first time a comprehensive clinical and pharmaceutical analysis of vitamin pharmacotherapy was carried out in patients with exudative pleurisy associated with pancreatitis and hepatitis, with a combination of the analysis of the frequency of drug prescriptions, structural ABC analysis of the assortment and an integrated ABC/VED approach. For the first time, a discrepancy between the structure of the pharmaceutical market of fat-soluble vitamins and the real clinical need has been established, which indicates the presence of assortment duplication and the need to rationalize the lists of medicines. The results obtained create the basis for optimizing local formularies, planning purchases, and improving the system of patient medication.

The purpose of the study is to develop a clinical and pharmaceutical justification for the use of vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis based on the analysis of the frequency of prescriptions, clinical results of treatment and integrated ABC/VED analysis of the range of medicines.

Materials and methods

Research design. A retrospective single-center observational clinical and pharmaceutical study was conducted, which consisted of two interrelated stages: clinical analysis of the frequency of vitamin pharmacotherapy and pharmaco-economic analysis of the range of fat-soluble vitamins using ABC and ABC/VED approaches.

Clinical part of the study. The study included 398 patients with exudative pleurisy who underwent inpatient treatment. Among them, 17 patients (4.2%) were diagnosed with hepatogenic pleurisy, which arose as a complication of cirrhosis of the liver, and 4 patients (1.0%) were diagnosed with pancreatogenic pleurisy, associated with exacerbation of chronic pancreatitis.

Inclusion criteria: presence of exudative pleurisy, confirmed by clinical, laboratory and instrumental methods; inpatient treatment; availability of complete medical documentation on pharmacotherapy.

Exclusion criteria: lack of complete data on medical records; secondary pleurisy of a different etiology that is not associated with pancreatitis or liver disease; cases in which vitamin therapy was not analyzed due to lack of data on prescriptions.

Analysis of clinical prescriptions. A retrospective analysis of medical documentation was carried out with the registration of the frequency of prescription of vitamins A, vitamin D, vitamin E and vitamin K as part of complex pharmacotherapy. Each case of drug administration was considered as a separate unit of observation.

Pharmaceutical part of the study. An analysis of the range of vitamin drugs recommended for use in chronic pancreatitis and liver diseases was carried out. The sources of information were the data of the State Register of Medicines of Ukraine and instructions for medical use of medicines. Each trade name in a specific dosage form and dosage was considered as a separate item of the assortment [19].

ABC analysis of the assortment. Structural ABC analysis was carried out according to the Pareto principle using the indicator of the specific weight of items in the general structure of the assortment. All medicines were ranked in descending order of share in the assortment, followed by the calculation of the cumulative % and division into groups A (about 70%), B (about 20%) and C (about 10%).

Clinically oriented ABC analysis. Additionally, an ABC analysis was carried out on the frequency of drug prescription in clinical practice. The cumulative share of prescriptions was used to divide drugs into groups A, B and C in accordance with the standard criteria of the ABC method.

VED classification. To assess the clinical significance of drugs, a VED classification was used with the division of drugs into Vital, Essential, and Desirable categories, considering their role in pathogenetic pharmacotherapy.

Integrated ABC/VED analysis. The results of ABC analysis by frequency of prescriptions were combined with VED classification to form a drug priority matrix.

Statistical analysis. Statistical processing of data was carried out using the methods of descriptive statistics. Absolute and relative exponents, frequency analysis, percentage distribution, and calculation of cumulative fractions according to the Pareto principle were used. Data processing was performed using Microsoft Excel.

Ethical aspects. The study was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the local ethics commission. All patients provided informed consent to the use of anonymized data for scientific purposes.

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Research and discussion

Differential diagnostic and therapeutic tactics

All patients underwent a set of general clinical laboratory and instrumental studies in accordance with current clinical guidelines and unified clinical protocols for the provision of medical care. The laboratory examination included a complete blood count, a biochemical blood test with the determination of liver and pancreatic function indicators, a coagulogram and other indicators in accordance with clinical need [20].

The clinical characteristics of patients with exudative pleurisy included in the study are presented in Table 1.

Table 1. Clinical characteristics of patients with exudative pleurisy included in the study

Indicator	Value
Total number of patients	398
Men, n (%)	232 (58.3%)
Women, n (%)	166 (41.7%)
Mean age, years (M ± SD)	49.6 ± 14.2
Age range, years	18–79

Etiology of pleurisy:

Etiology	Number of patients	Percentage
Hepatogenic pleurisy (cirrhosis)	17	4.2%
Pancreatic pleurisy (chronic pancreatitis)	4	1.0%
Other causes of pleurisy*	377	94.8%

Clinical features of hepatogenic pleurisy (n = 17):

Parameter	Value
Presence of ascites	11 (64.7%)
Right-sided pleurisy	17 (100%)
Volume of pleural effusion	600–1500 ml
Volume of ascitic fluid	5000–9000 ml
History of alcohol dependence	17 (100%)

Clinical features of pancreatic pleurisy (n = 4):

Parameter	Value
Left-sided pleurisy	4 (100%)
Abdominal pain	4 (100%)
Nausea and vomiting	4 (100%)
Pleural puncture performed	4 (100%)

*Patients with pleurisy of other etiology were included in the overall cohort for analysis of vitamin prescription frequency.

In patients with exudative pleurisy and clinical signs of acute pancreatitis, the level of amylase in the pleural fluid was determined to verify the pancreatogenic genesis of the effusion. To exclude tuberculosis etiology, cytological examination of sputum and molecular genetic methods for detecting *Mycobacterium tuberculosis* were carried out in accordance with the standards of phthisiatric care [21].

The instrumental examination included chest x-ray in direct and lateral projections, computed tomography of the chest and abdominal organs, as well as ultrasound examination of the abdominal and pleural cavities. All patients underwent diagnostic pleural punctures at standard points (VII-VIII intercostal space along the linea axillaris posterior) under local anesthesia using novocaine solution. After evacuation of pleural fluid, a follow-up ultrasound was performed to assess the residual volume of the effusion.

In 5 patients with right-sided exudative pleurisy, thoracoscopy was performed under local anesthesia using novocaine. Video thoroscopic methods were not used due to the need for general anesthesia. In patients with pancreatogenic pleurisy, thoroscopic diagnostic methods were not performed due to the severe general condition.

Patients with hepatogenic pleurisy received complex therapy of the underlying disease with hepatoprotectors and diuretics in the presence of ascites in accordance with clinical guidelines for the treatment of chronic liver diseases [22]. Treatment of hepatogenic pleurisy included repeated pleural punctures with evacuation of exudate.

Patients with tuberculosis were treated with specific anti-tuberculosis therapy according to the national clinical protocol [21].

Patients in the second group with acute pancreatitis were treated according to a unified clinical protocol for the treatment of acute and chronic pancreatitis [20]. Treatment included a mode of functional rest of the pancreas (temporary fasting), subsequent transition to diet No. 5, the use of antispasmodics and pancreatic enzymes.

Clinically, patients with hepatogenic pleurisy complained of intense pain in the right hypochondrium, jaundice of the skin, and an increase in the size of the abdomen with ascites. According to ultrasound, the volume of fluid in the abdominal cavity ranged from 5000 to 9000 ml. All patients had right-sided exudative pleurisy with a pleural fluid volume of 600 to 1500 ml. The pleural fluid was yellow in color and did not differ in macroscopic characteristics from effusions of other etiologies.

An X-ray image of a patient with exudative pleurisy in cirrhosis of the liver is presented on the Fig. 1.



Fig. 1. X-ray of a patient with exudative pleurisy with cirrhosis of the liver.

On the presented X-ray (Fig. 1) – shading in the right pleural cavity in a patient with cirrhosis of the liver of alcoholic origin.

Patients with acute pancreatitis and left-sided pancreatogenic exudative pleurisy complained of severe girdle pain in the abdomen. Nausea and vomiting were also characteristic complaints of patients with this nosological form. Disorders of the gastrointestinal tract,

1. bloating, because of enzymatic insufficiency. In the treatment of patients with pleurisy of pancreatogenic origin for therapeutic purposes, pleural punctures were performed.

The frequency of prescribing fat-soluble vitamins in patients with pleurisy associated with pancreatitis and liver diseases is presented in Table 2.

Table 2. Frequency of vitamin prescriptions

Vitamin (active pharmaceutical ingredient)	Number of prescriptions (n)	Share of prescriptions (%)	ABC group (clinical)	VED category
Vitamin E (alpha-tocopherol acetate)	148	52.3%	A	Vital
Vitamin D (ergocalciferol)	72	25.4%	B	Essential
Vitamin A (retinol, retinol acetate)	49	17.3%	B	Essential
Vitamin K (menadione)	14	5.0%	C	Desirable
Total	283 prescriptions	100%	—	—

The analysis demonstrated that vitamin E (alpha-tocopherol acetate) was the most frequently prescribed active pharmaceutical ingredient and accounted for more than half of all vitamin prescriptions. Vitamin D and vitamin A showed a moderate frequency of use and were assigned to ABC group B, while vitamin K was

prescribed rarely and formed ABC group C. The obtained results confirm the dominant role of vitamin E in the pathogenetic pharmacotherapy of patients with pleurisy associated with pancreatitis and liver diseases and were further used for the integrated ABC/VED analysis.

ABC analysis of pathogenetic pharmacotherapy
The presence of vitamin preparations in the protocols

Protocol "Chronic pancreatitis" (No. 1204): Yes – fat-soluble forms of vitamins K, A, D, E for the correction of malabsorption in NSAIDs (exocrine insufficiency) [20, 22, 23].

Protocol "Acute pancreatitis" (No. 418): No – focus on EN/PN, enzymes; vitamins are not mentioned routinely, only during prolonged hospitalization [24].

Hepatitis protocols (HCV/HBV): Yes – vitamin D for the correction of fibrosis/immunity, B-group as adjuvant therapy [25].

Protocols "Pleurisy": No – etiotropic (antibiotics/antifungal), symptomatic; vitamins indirectly in basic pathology and other international protocols related to the study [26-31].

For the pharmaceutical analysis of the assortment, 19 medicines containing fat-soluble vitamins: vitamin A, vitamin D, vitamin E and vitamin K, presented in various dosage forms, dosages and trade names registered in Ukraine, were identified.

The most numerous was the group of vitamin E drugs, which included 13 drugs and accounted for 68.42 % of the total number of items. Vitamin A preparations were represented by three medicinal products (15.79 %), vitamin D preparations by two medicinal products (10.53 %), while the vitamin K group included one medicinal product (5.26 %).

The analysis showed that the range of vitamin medicines is characterized by a significant number of drugs with the same international non-proprietary names, but different trade names, manufacturers,

dosages, and dosage forms. The vitamin E group includes alpha-tocopherol acetate, vitamin E, Vitrum Vitamin E, Enat 400, as well as drugs of the Zentiva line in various dosages. The vitamin A group included retinol and retinol acetate, the vitamin D group included ergocalciferol and its commercial analogues, while the vitamin K group was represented by menadione as part of Vikasol-Darnitsa.

In terms of dosage forms, soft capsules dominated – 11 positions (57.89%). Oil solutions for oral use accounted for 6 positions (31.58%). Individual drugs were presented as solution for injection and topical solution, the share of which was 5.26% each, respectively.

The results obtained indicate a pronounced dominance of vitamin E preparations, which is due to significant variability of trade names, dosage forms and dosages. This assortment structure indicates the presence of duplication of drugs with the same active pharmaceutical ingredients and forms the prerequisites for further clinical and pharmaceutical analysis using ABC and VED methods.

To quantify the structure of the assortment of vitamin medicines registered in Ukraine and recommended for use in patients with pleurisy against the background of pancreatitis and hepatitis, the initial ranking of drugs was carried out according to the principle of ABC analysis based on their specific gravity in the total set of positions. The results of the distribution of medicinal products into groups A, B and C are shown in Table 3.

Table 3. Distribution of vitamin medicines according to ABC analysis (assortment structure)

ABC group	Number of medicines	Share of medicines (%)	Cumulative share (%)
A	13	68.42	63.21
B	3	15.79	84.23
C	3	15.79	100.00
Total	19	100.00	100.00

According to the results of the ABC analysis of the assortment of vitamin medicines (Table 3), 13 drugs are assigned to group A, which is 68.42% of the total number of items and forms 63.21% of the total specific weight of the assortment. Group B included 3 drugs (15.79%), which accounted for 21.02% of the specific gravity, while group C also included 3 drugs (15.79%) with a total share of 15.77%. The resulting distribution demonstrates a pronounced dominance of group A both in terms of quantitative composition and specific gravity, which indicates the concentration of most assortment items within a limited number of active pharmaceutical ingredients. Groups B and C are characterized by much less representation and form a moderate and minimal share of the total structure of the assortment, respectively.

The next stage of the analysis was the study of the internal structure of groups A, B and C according to the belonging of drugs to fat-soluble vitamins: vitamin A, vitamin D, vitamin E and vitamin K. This approach

made it possible to determine which vitamin groups form the priority, intermediate and secondary parts of the assortment. It has been established that group A is represented mainly by vitamin E preparations, which are characterized by the largest number of trade names, dosage forms and dosages. It is this group that forms the main share of the assortment and requires priority attention when forming lists of medicines and further rationalizing their use.

Group B includes a limited number of items with moderate specific gravity, represented mainly by vitamin A and vitamin D preparations, which occupy an intermediate position in terms of assortment significance.

Group C is characterized by the lowest specific gravity and includes individual items of vitamin K, as well as part of vitamin A and vitamin D preparations, represented by a limited number of trade names within the studied assortment.

To detail the results of the ABC analysis, further distribution of drugs of groups A, B and C by belonging to active pharmaceutical ingredients and trade names was carried out. The results of structuring the range of

fat-soluble vitamins within each ABC group are shown in Table 4.

Table 4. Composition of ABC groups by active pharmaceutical ingredients and trade names

ABC group	Active pharmaceutical ingredient	Trade names
A	Vitamin E (alpha-tocopherol acetate)	Alpha-tocopherol acetate; Vitamin E; Vitamin E 200-Zentiva; Vitamin E 400-Zentiva; Vitamin E-Zentiva; Vitrum Vitamin E; Enat 400
B	Vitamin A (retinol, retinol acetate)	Vitamin A; Retinol acetate; Retinol acetate oil solution
B	Vitamin D (ergocalciferol)	Ergocalciferol; Ergocalciferol oil solution
C	Vitamin K (menadione)	Vikazol-Darnitsa
C	Vitamin A (retinol acetate)	Vitamin A capsules
C	Vitamin D (ergocalciferol)	Ergocalciferol solution for injection

The results obtained indicate that the key role in the structure of the fat-soluble vitamins assortment is played by vitamin E preparations, which form the basis of group A. Vitamin A and vitamin D preparations are concentrated mainly in group B, which reflects their intermediate assortment significance, while the least represented is group C, which includes individual items of vitamin K and part of vitamin A and vitamin D preparations. In general, the resulting structure of the assortment confirms the presence of a significant concentration of medicines within a limited number of active pharmaceutical ingredients and indicates the expediency of focusing management decisions primarily on group A with simultaneous optimization of the composition of groups B and C to rationalize the list of vitamin medicines.

Analysis of the data in Table 4 showed that group A includes 13 medicinal products and forms 63.21% of the specific weight of the assortment, despite a significant number of items. The dominance of this group is explained by the wide representation of vitamin E preparations, which are characterized by significant variability in dosage forms, dosages, and trade names. Group B includes 3 drugs with a share of 21.02% and is represented mainly by vitamin A and vitamin D. Group C also includes 3 drugs with a share of 15.77%, which have a minimal contribution to the overall structure of the assortment. The resulting distribution does not fully correspond to the classic ratio of 70-20-10, which is associated with the high variability of dosage forms and trade names of vitamin E. This feature reflects the real structure of the pharmaceutical market and emphasizes the need to interpret the results of ABC analysis considering the specifics of the studied segment of medicines.

From a practical point of view, the results of the analysis indicate the expediency of priority control and rationalization of group A during the formation of lists of medicines and procurement planning. An excessive number of trade names of vitamin E preparations indicates the presence of assortment duplication, which justifies the need for further analysis of the possibility

of reducing equivalent positions. Group B drugs can be considered as a reserve for optimizing the assortment, provided that its structure is corrected without a significant impact on clinical practice. Instead, it is advisable to analyze group C drugs from the standpoint of the expediency of their further inclusion in clinical protocols, considering the clinical need, the specifics of dosage forms and the lack of therapeutic alternatives.

Thus, the results of the ABC analysis create the basis for the further use of this approach in combination with clinical indicators of the frequency of administration and VED classification to rationalize vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis.

The frequency of prescribing vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis

To provide clinical justification for the rationalization of the range of vitamin medicines, an analysis of the frequency of their prescription in 398 patients with exudative pleurisy of various origins was carried out. The frequency of use of vitamins A, vitamin D, vitamin E and vitamin K as part of complex pharmacotherapy was evaluated, depending on the etiology of the underlying disease.

The analysis of medical documentation showed that vitamin therapy was prescribed mainly to patients with pancreatogenic and hepatogenic pleurisy as a component of pathogenetic correction of malabsorption, metabolic disorders, and deficiency states.

The most prescribed active pharmaceutical ingredient was vitamin E (alpha-tocopherol acetate), which was used in most patients with chronic pancreatitis and liver disease. The high frequency of its prescription is explained by antioxidant properties, participation in the stabilization of cell membranes and the correction of oxidative stress, which is characteristic of chronic inflammatory processes of the pancreas and liver.

Vitamin A preparations (retinol, retinol acetate) were used mainly to correct malabsorption and lipid

metabolism disorders. The appointment of vitamin D (ergocalciferol) was associated with the need to correct the deficiency that often accompanies chronic diseases of the liver and pancreas. Vitamin K (menadione) preparations were used much less frequently and mainly in patients with severe liver dysfunction and coagulopathies.

The results obtained indicate that the structure of actual prescriptions of vitamin drugs in clinical practice differs from the structure of their market representation. With a significant number of trade names of vitamin E drugs on the pharmaceutical market, this group is characterized by the highest frequency of clinical use, which confirms its key role in pathogenetic pharmacotherapy of patients with pleurisy against the background of pancreatitis and hepatitis.

The obtained data became the basis for further clinically oriented ABC analysis of the frequency of prescriptions and VED classification of vitamin drugs.

ABC analysis of vitamin drugs by frequency of prescription

At the next stage, a clinically oriented ABC analysis of vitamin drugs was carried out based on the frequency of their administration in 398 patients with exudative pleurisy against the background of pancreatitis and hepatitis. Each case of prescribing vitamin A, vitamin D, vitamin E and vitamin K drugs was recorded and ranked according to the frequency of use in clinical practice.

The results of the analysis showed that the largest proportion of prescriptions were vitamin E (alpha-tocopherol acetate), which was used in most patients with pancreatogenic and hepapathogenic pleurisy. The second place in terms of frequency of prescription was occupied by vitamin D (ergocalciferol) drugs, which were used to correct deficiency and disorders of calcium-phosphorus metabolism. Vitamin A (retinol, retinol acetate) preparations were used less frequently, while the administration of vitamin K (menadione) was episodic and was associated mainly with coagulation disorders in patients with liver disease.

According to the principles of ABC analysis, medicines were divided into three groups according to the cumulative share of prescriptions. Group A includes drugs that formed the main share of clinical use and accounted for about 70% of all prescriptions. Group B consisted of drugs with an average level of use (about 20%), and group C included drugs with the lowest frequency of use (about 10%).

The results obtained showed that the clinical structure of prescriptions is consistent with the results of assortment analysis and confirms the dominant role of vitamin E drugs in the pharmacotherapy of patients in the study group. At the same time, it was found that a significant number of trade names of vitamin E drugs is not accompanied by a proportional increase in their clinical use, which indicates the presence of assortment duplication.

VED classification of vitamin medicines

To assess the clinical significance of drugs, a VED-classification of vitamin drugs was carried out. The distribution was carried out considering the role of drugs in pathogenetic pharmacotherapy of patients with pleurisy against the background of pancreatitis and hepatitis.

The Vital category includes vitamin E (alpha-tocopherol acetate), which is key to the correction of oxidative stress and metabolic disorders. The Essential category includes vitamin D (ergocalciferol) and vitamin A (retinol, retinol acetate), which are used to correct deficiency states and support metabolic processes. The Desirable category includes vitamin K (menadione) preparations, which are used in the presence of specific indications.

Integrated ABC/VED analysis

The combination of the results of ABC analysis by frequency of prescriptions and VED classification made it possible to form an integrated matrix of priority of vitamin medicines. It has been established that vitamin E drugs belong to cell AV, which indicates their highest priority for clinical practice and the drug supply system. The vitamin D and vitamin A preparations formed the BE cell, while the vitamin K preparations were assigned to the CD group.

The results obtained confirm the expediency of concentrating management and clinical decisions primarily on vitamin E preparations, as well as the need to optimize the range of vitamin A and vitamin D preparations and revise the feasibility of a wide representation of vitamin K preparations within the studied segment of pharmacotherapy.

To determine the priority of vitamin medicines for clinical practice and pharmaceutical supply, the results of the ABC-analysis by prescription frequency were combined with the VED classification. The integrated ABC/VED matrix is presented in Table 5.

Table 5. Integrated ABC/VED matrix of vitamin medicines used in patients with pleurisy associated with pancreatitis and hepatitis

ABC group	VED category	Vitamin (active pharmaceutical ingredient)	Priority level	Management implication
A	Vital (AV)	Vitamin E (alpha-tocopherol acetate)	Highest priority	Mandatory inclusion in formularies and procurement planning
B	Essential (BE)	Vitamin D (ergocalciferol)	Medium priority	Inclusion in standard treatment schemes
B	Essential (BE)	Vitamin A (retinol, retinol acetate)	Medium priority	Inclusion with controlled assortment

C	Desirable (CD)	Vitamin K (menadione)	Low priority	Use only for specific clinical indications
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The integrated ABC/VED analysis demonstrated that vitamin E belongs to the AV category, indicating the highest clinical and managerial priority. Vitamins D and A formed the BE group, reflecting their essential role in correcting deficiency states. Vitamin K was assigned to the CD group and should be used primarily in the presence of specific clinical indications. The obtained matrix provides a basis for rationalizing hospital formularies, optimizing procurement strategies and improving pharmaceutical supply management.

Discussion

The results of the clinical and pharmaceutical study demonstrated the important role of vitamin pharmacotherapy in the complex treatment of patients with exudative pleurisy against the background of pancreatitis and liver diseases. The combination of clinical analysis of the frequency of prescriptions with the pharmacoeconomic approaches of ABC and VED made it possible not only to assess the structure of the range of medicines, but also to determine their real clinical significance and managerial priority [32, 33].

The results obtained showed that the most prescribed active pharmaceutical ingredient was vitamin E (alpha-tocopherol acetate). This is consistent with current ideas about the key role of oxidative stress in the pathogenesis of chronic pancreatitis and chronic liver disease. International studies have shown that chronic inflammation of the pancreas and liver is accompanied by activation of lipid peroxidation, damage to cell membranes and progression of fibrosis [34, 35]. Antioxidant therapy, particularly the use of vitamin E, is considered as an important component of supportive pharmacotherapy for these diseases. The high frequency of vitamin E administration in this study confirms its clinical significance in real practice.

In international clinical guidelines, vitamin D deficiency is considered a common concomitant condition in patients with chronic liver and pancreatic diseases. Impaired fat absorption, cholestasis and changes in calcium metabolism contribute to the development of hypovitaminosis D, which is associated with the progression of liver fibrosis, immune disorders, and an increased risk of complications. The results obtained, which demonstrated the attribution of vitamin D to the BE group, are consistent with international approaches to the correction of deficiency conditions in gastroenterological practice.

Vitamin A preparations have also demonstrated a moderate frequency of use. The international literature emphasizes the role of retinoids in maintaining epithelial function, immune response, and lipid metabolism, which is of particular importance in patients with malabsorption and chronic liver disease [36-39]. The attribution of vitamin A to the Essential category confirms its importance as an auxiliary component of pathogenetic therapy.

On the other hand, vitamin K drugs were prescribed much less often, which is in line with modern

clinical guidelines. In patients with liver disease, vitamin K is used mainly for coagulopathies and disorders of the synthesis of blood coagulation factors. Therefore, its assignment to the Desirable category reflects the limited need for widespread use within the nosological group under study.

One of the key results of the study was the identification of a discrepancy between the structure of the pharmaceutical market and the real clinical need. Despite the significant number of trade names for vitamin E drugs, their clinical use is concentrated around a limited number of active pharmaceutical ingredients. A similar phenomenon is described in pharmacoeconomic studies of drug supply systems, where it is shown that an excessive number of equivalent drugs leads to irrational use of health care system resources.

From the standpoint of pharmacoeconomics, the results obtained confirm the effectiveness of the application of the integrated ABC/VED approach for optimizing formulary policy and drug inventory management. International studies have shown that the use of the ABC/VED method helps to rationalize procurement, reduce costs and increase the effectiveness of medication without deterioration in the quality of treatment. The matrix of priority of medicines obtained in the study can be used for the formation of local formularies and procurement planning.

The clinical significance of the results lies in the formation of a more rational model of vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis. The combination of clinical and pharmacoeconomic approaches creates the basis for making informed management decisions at the level of health care institutions and the medical support system as a whole [40-44].

Thus, the results of the study confirm the feasibility of integrating clinical analysis of the frequency of prescriptions with pharmacoeconomic methods to rationalize drug supply and optimize formulary policy in patients with pleurisy associated with pancreatitis and hepatitis.

Study limitations

The results obtained should be interpreted considering several limitations of the study. First, the study was conducted based on clinical data from patients of one medical institution, which may limit the possibility of extrapolating the results to other regions and health systems. The peculiarities of the organization of medical care, the availability of medicines and clinical approaches to pharmacotherapy may differ in other medical institutions.

Second, the study evaluated the frequency of prescribing vitamin drugs without a detailed analysis of dosages, duration of therapy, and individual patient adherence to treatment. The lack of data on the duration

of use of drugs limits the possibility of a full assessment of their real consumption.

Thirdly, the study did not include a full-fledged pharmaco-economic analysis of costs. The lack of unified and representative data on the cost and volume of consumption of vitamin medicines in open sources did not allow ABC analysis by cost indicators, which could further increase the accuracy of assessing the priority of drugs.

Fourth, the study focused exclusively on fat-soluble vitamins (vitamin A, vitamin D, vitamin E, vitamin K), while water-soluble vitamins were not included in the analysis. This limits the completeness of the assessment of vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis.

Fifthly, the analysis of the range of medicines was carried out within the pharmaceutical market of Ukraine, which limits the possibility of direct comparison with other countries.

Despite these limitations, the combination of clinical analysis of the frequency of drug prescribing with an integrated ABC/VED approach made it possible to obtain a holistic characterization of the structure of vitamin pharmacotherapy and form the basis for further pharmaco-economic research.

Practical recommendations

The results of the clinical and pharmaceutical study allow us to formulate practical recommendations for the rationalization of vitamin pharmacotherapy in patients with pleurisy against the background of pancreatitis and hepatitis.

Firstly, considering the results of the integrated ABC/VED analysis, it is advisable to identify vitamin E (alpha-tocopherol acetate) drugs as a priority for the formation of lists of medicines, procurement and use in clinical practice. Vitamin E drugs included in the AV category have the highest frequency of administration and the highest clinical significance, therefore they should be considered as basic components of pathogenetic pharmacotherapy.

Secondly, it is recommended to optimize the number of trade names of vitamin E drugs by selecting a limited number of basic items, in particular alpha-tocopherol acetate, Vitamin E-Zentiva, Vitamin E 200-Zentiva, Vitamin E 400-Zentiva, Vitrum Vitamin E and Enat 400. Reducing duplicate trade names will reduce assortment fragmentation and improve the efficiency of pharmaceutical inventory management.

Thirdly, vitamin D (ergocalciferol) and vitamin A (retinol, retinol acetate), classified as BE, should be retained in clinical protocols as necessary means for the correction of deficiency conditions associated with malabsorption and metabolic disorders. It is advisable to use a limited number of universal dosage forms that provide individualization of therapy.

Fourthly, it is advisable to limit the use of vitamin K preparations (menadione, Vikasol-Darnitsa) to cases of clear clinical indications, in particular coagulopathies in patients with liver disease. The

expansion of the range of vitamin K preparations within this nosological group is not clinically justified.

Fifthly, when forming lists of medicines at the level of health care institutions, it is advisable to use the integrated ABC/VED approach as a tool for making managerial decisions on procurement and planning of drug supply.

Sixth, it is advisable to take the results of the study into account when updating clinical protocols and local drug formularies to standardize vitamin pharmacotherapy in patients with pleurisy associated with pancreatitis and hepatitis.

The results of the ABC analysis of the range of vitamin medicines included in the clinical protocols for the treatment of patients with pleurisy against the background of pancreatitis and hepatitis indicate an uneven distribution of positions between groups A, B and C and confirm the expediency of using the ABC method as a tool for rationalizing the lists of medicines. The dominance of group A, formed mainly by vitamin E preparations, reflects significant variability of trade names and dosage forms of one active pharmaceutical ingredient and indicates the presence of assortment duplication.

The results obtained are consistent with the data of studies in which ABC or ABC/VED analysis was used to assess the structure of the drug assortment. In the relevant works, it is shown that a relatively small number of positions forms the main share of clinical use, which corresponds to the Pareto principle and justifies the concentration of managerial decisions on priority groups of drugs. A similar approach is confirmed by the results of this study, where group A is identified as a key part of the range of vitamin medicines.

Comparison with the results of international ABC/VEN analysis studies also demonstrates the conceptual similarity of the findings obtained. In previous works, it was established that group A includes a limited number of items that require enhanced control in the formation of lists of medicines and procurement planning. In our study, a similar pattern persists, but a feature is the relatively large number of positions in group A, which is explained by the wide representation of vitamin E preparations.

The revealed dominance of vitamin E drugs in group A is associated not only with their clinical significance, but also with the presence of a significant number of trade names with the same active pharmaceutical ingredient. This confirms the need to optimize the assortment by reducing duplicate items and standardizing approaches to the selection of basic preparations.

Thus, the results of the study confirm the feasibility of using ABC and ABC/VED approaches for making management decisions on the formation of drug lists. The use of the obtained data can help optimize the range of vitamin preparations and increase the effectiveness of drug supply to patients with pleurisy associated with pancreatitis and hepatitis.

Conclusions

1. In patients with exudative pleurisy against the background of pancreatitis and hepatitis, vitamin pharmacotherapy is an important component of complex treatment, which is confirmed by the high frequency of prescribing fat-soluble vitamins in clinical practice.
2. According to the results of clinically oriented ABC analysis by frequency of prescribing, the dominant role of vitamin E drugs (alpha-tocopherol acetate), which form the priority group A and have the highest clinical significance in the pharmacotherapy of patients of the studied category, was established.
3. Vitamin D (ergocalciferol) and vitamin A (retinol, retinol acetate) are classified as intermediate group B, which confirms their important role in the correction of deficiency states and metabolic disorders associated with liver and pancreatic diseases.
4. Vitamin K preparations (menadione, Vikasol-Darnitsa) belong to group C and are used mainly in the presence of specific indications, which determines their limited use in the study category of patients.
5. The assortment ABC analysis showed a significant duplication of trade names of vitamin E drugs (Vitamin E-Zentiva, Vitamin E 200-Zentiva, Vitamin E 400-Zentiva, Vitrum Vitamin E, Enat 400), which justifies the need to rationalize the lists of medicines by selecting a limited number of basic items.
6. The integrated ABC/VED approach made it possible to identify vitamin E (alpha-tocopherol acetate) preparations as a priority for the formation of local formularies, procurement planning and optimization of drug supply to patients with pleurisy against the background of pancreatitis and hepatitis.

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Differential diagnostic and therapeutic tactics of pleurisy in pancreatitis and hepatitis: ABC and ABC/VED analysis of pathogenetic pharmacotherapy

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Introduction. Pleurisy associated with pancreatitis and liver diseases is accompanied by malabsorption and deficiency of fat-soluble vitamins, which justifies the use of vitamin pathogenetic pharmacotherapy. At the same time, the structure of the pharmaceutical market of vitamin drugs may not meet real clinical needs, which requires pharmacoeconomic assessment. **Purpose.** Clinical and pharmaceutical justification of the use of vitamin pharmacotherapy in patients with exudative pleurisy on the background of pancreatitis and hepatitis

based on the analysis of the frequency of prescriptions and integrated ABC/VED-analysis of the range of drugs. **Materials and methods.** A retrospective observational study of 398 patients with exudative pleurisy who underwent inpatient treatment was conducted. The frequency of prescribing vitamin A, vitamin D, vitamin E and vitamin K as part of complex pharmacotherapy was analyzed. The pharmaceutical analysis included a study of the range of vitamin drugs registered in Ukraine using structural ABC analysis, clinically oriented ABC analysis by frequency of prescriptions and VED classification. **Results.** Established that the range of fat-soluble vitamins is represented by 19 drugs, among which vitamin E drugs dominate (68.42% of positions). Clinical analysis showed that vitamin E was the most frequently prescribed active pharmaceutical ingredient in patients with pancreatogenic and hepatogenic pleurisy. Integrated ABC/VED analysis identified vitamin E drugs as the priority category AV, while vitamin D and vitamin A formed the BE group, and vitamin K - the CD group. A discrepancy between the structure of the pharmaceutical market and the real clinical need was revealed, which indicates the duplication of trade names of vitamin E preparations. **Conclusions.** The combination of clinical analysis of the frequency of prescriptions with the ABC/VED approach allowed us to identify priority areas for rationalizing the assortment of vitamin medicines. The results obtained can be used to form local formulas, optimize purchases, and improve the medical care of patients with pleurisy on the background of pancreatitis and hepatitis. **Keywords:** pleurisy, pancreatitis, hepatitis, vitamin pharmacotherapy, ABC analysis, VED analysis, pharmacoeconomics.

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