Interdisciplinary Pharmacoeconomic Research Concerning the Pharmacotherapy of Alcoholic Hepatitis in Conditions of Covid-19 Pandemic

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Abstract. Substantiated the relevance and necessity of the chosen research topic as a result of a review of the scientific literature on the epidemiology and pharmacotherapy of patients with alcoholic hepatitis. Contradictory evidence exists regarding the association between international and national clinical protocols for the management of alcoholic hepatitis in the context of the COVID-19 pandemic. Author undertook the present study to justify the procurement of drugs for patients with alcoholic hepatitis based on pharmacoeconomic calculations for hospitals. This study is based on pharmacoeconomic, organizational and legal, forensic and pharmaceutical approaches to pharmacotherapy with using literature review. Clinical and pharmacological analysis of basic therapy of alcoholic hepatitis was performed. Pharmacoeconomic studies have been conducted. According to the results of the ABC analysis, group A includes one drug (INN Ursodeoxycholic acid). According to the results of VEN analysis, it was proved that one drug (INN Prednizolone) belongs to category V (Vital). This study provides an opportunity to make administrative and managerial decisions in determining the pharmacotherapy of patients with alcoholic hepatitis to improve the use of drugs in hospitals.

Keywords: COVID-19, drugs, alcoholic hepatitis, pharmacotherapy, interdisciplinary pharmacoeconomic research.

Introduction. Coronavirus 2019 (COVID-19) resulted in an unprecedented pandemic affecting with a mortality rate at the time of writing this manuscript. In the context of the COVID-19 pandemic, timely pharmacotherapy of alcoholic hepatitis will significantly improve the quality of medical services and reduce the cost of medical care. COVID-19 resulted in an unprecedented pandemic affecting with mortality rate at the time of writing this manuscript. Despite numerous publications on COVID-19, at present, conceptual thinking of the problem is only at a nascence stage. New data from Public Health England suggests that the COVID-19 vaccines used in the UK are as effective at preventing symptomatic disease in the majority of people with underlying health conditions compared to the rest of the population [1-7].

Treatment of patients with alcoholic hepatitis during the COVID-19 pandemic is one of the most relevant issues. Further analysis of COVID-19 among patients with alcoholic hepatitis is important. Excessive alcohol consumption is an important problem worldwide. Alcoholic hepatitis is diagnosed among 10-35% of patients with alcohol dependence. Alcoholic hepatitis includes a wide range of nosologies from uncomplicated steatosis to liver cirrhosis caused by the systematic use of the psychoactive substance alcohol [8-13].

Today it is important to use modern, effective and safe drugs for pharmacotherapy of alcoholic hepatitis. Further analysis of COVID-19 among patients with alcoholic hepatitis is important. Pharmacoeconomic methods of analysis, in particular, ABC/VEN analysis, are used to select effective, safe and affordable drugs [14-16].

The purpose of this study was to conduct an interdisciplinary pharmacoeconomic study of the pharmacotherapy of alcoholic hepatitis based on experimental clinical and pharmacological, organizational and legal, marketing and VEN analysis

Materials and methods. The study was carried out between March 2021 and March 2023. It was conducted in selected public healthcare facilities in Ukraine. The facility-based quantitative descriptive cross-sectional study was conducted using a standard data collection tool. Experimental data were processed on the basis of the Department of Pharmacy of the Luhansk State Medical University. Study Design is based on pharmacoeconomic, organizational and legal, forensic and pharmaceutical, clinical and pharmacological approaches to pharmacotherapy with using literature review.

The research of the article is a fragment of research works of Kharkiv Medical Academy of Postgraduate Education on "Improving the organizational and legal procedure for providing patients with drugs from the standpoint of forensic pharmacy, organization and management of pharmacy" (state registration number 0116U003137, terms 2016-2020) and "Pharmaceutical and medical law: integrated approaches to the system of drug circulation from the standpoint of forensic pharmacy and organization of pharmaceutical business" (state registration number 0121U000031, terms 2021-2026); Petro Mohyla Black Sea National University on the topic "Conceptual interdisciplinary approaches to the drug circulation system, taking into account organizational and legal, technological, biopharmaceutical, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, pharmacotherapeutic aspects" (state registration number 0123U100468, implementation period 2023-2028); Luhansk State Medical University "Conceptual interdisciplinary approaches to pharmaceutical provision and availability of drugs, taking into account organizational and legal, technological, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, marketing, social and economic competencies" (state registration number 0123U101632, terms 2023-2027).

Results and discussion. The work is a continuation of the previous study on the meta-analysis of pharmacotherapy of alcoholic hepatitis [17].

*Study Population and Sample***.** The study population included accounting the hospitals' comprehensive medicine list development by the pharmaceuticals and therapeutic committee for patients with alcoholic hepatitis. During the study of the medical records of patients, prescribed drugs for marketing and pharmacoeconomic analysis were allocated. The study processed pharmaceuticals from 170 medicine cards of patients with alcoholic hepatitis who attended public healthcare clinics in Kharkiv region, Kyiv region, Rivne region of Ukraine. The study population included selection of clinical and pharmacological groups of drugs for basic pharmacotherapy of alcoholic hepatitis according to clinical protocols of Ukraine. All drugs were purchased using a budget drug fund in public health clinics between 2021 and 2022. Drugs were listed using Microsoft Excel.

Sampling and Sample Size. The study subjects were all pharmaceuticals for pharmacotherapy of patients with alcoholic hepatitis. The USAID delivery project logistics indicator assessment tool was employment to determine the sample size of health facilities. It recommends a minimum of 15% of the total health facilities inclusion [18].

According to the clinical and pharmacological group for pharmacotherapy of patients with alcoholic hepatitis were selected drugs that have the diagnostic code ATC-Classification (ATC): A05AA02 «Ursodeoxycholic acid»; A11H A03 «Tocopherol acetate (Vitamin E); C04AD03 «Pentoxifyline»; H02AB06 «Prednizolone» [19].

ABC analysis was applied as a method for classifying drugs based on cost incurred. A structured data collection from Management science for health was used to collect the necessary data for ABC analysis [20]. VEN analysis was applied as a method of prioritizing drugs based on public health importance as vital, essential and non-essential [14, 15, 21]. A structured data collection from Management science for health was used to collect the necessary data for VEN analysis. VEN data were generated from hospitals comprehensive medication cards development by the pharmaceuticals and therapeutic committee [22].

Study Procedure. For ABC analysis to assess the cost of pharmacotherapy for patients with alcoholic hepatitis. ABC analysis was performed as a tool to study the cost of purchasing drugs [22, 23]. ABC analysis involves the distribution of drugs from the most to the least expensive depending on their share among the indicators of the general purpose of drugs.

For VEN analysis to assess the effectiveness of drug use, a VEN analysis was performed to classify drugs into categories V (vital), E (essential) and N (non-essential), taking into account regulatory documents: medical care standards, clinical protocols, State formulary of medicines [24]. National List of Essential Medicines [25] and principles of evidence-based medicine (evidence of efficacy, quality, safety, economy, affordability). The following approach was used in this analysis: the division of drugs into categories V – "Vital"; E – "Essential" and N – "Non-essential".

The quantity of all drugs for ABC analysis was entered, the percentage of total value was calculated in descending order by value starting at the top with higher value. Then the cumulative percentage by value, and items were computed, and cutoff points for pharmaceuticals A, B, C were determined based on the Pareto principle. Finally, the ABC-VEN matrix was developed.

International, national, organizational and legal, medical, pharmaceutical, clinical and pharmacological, marketing and pharmacoeconomic approaches were used to conduct a multidisciplinary study. The research design according to the methodology of interdisciplinary research in pharmacotherapy developed at the Department of Medical and Pharmaceutical Law, General and Clinical Pharmacy of Kharkiv Medical Academy of Postgraduate Education during 2012-2022 and them at the Department of Pharmacy of Luhansk State Medical University (from 2023 to the present) was proposed (Table 1).

General Characteristics.Organizational and legal analysis of drugs for pharmacotherapy of alcoholic hepatitis. Alcoholic hepatitis has the code of the International Classification of Diseases 10 edition (ICD-10) – K70.1 and the code of the International Classification for the Primary Care (ICPC-2) – D97. In the database of the Ministry of Health of Ukraine as of March 20, 2021 there is no information and official translation of international clinical protocols for pharmacotherapy of alcoholic hepatitis. Based on the Ukrainian unified clinical protocol of primary, secondary (specialized) medical care "Alcoholic hepatitis" (approved by Order of the Ministry of Health of Ukraine, dated November 06, 2014 No. 826), basic pharmacotherapy of alcoholic hepatitis includes drugs by INN: Pentoxifyline, Prednizolone, Tocopherol acetate, Ursod.

Table 1. Design of a multidisciplinary pharmacoeconomic study for pharmacotherapy of alcoholic hepatitis.

Phases of the study	Content of the study
1	2
1.	Formulation of the goal
2.	Choice of objects and research methods
3.	Organizational and legal experiment. Normative and legal, documentary analysis of international and national medical and technological documents on standardization of medical care for pharmacotherapy of alcoholic hepatitis
4.	Organizational and legal experiment. Regulatory and legal analysis of scientific sources
5.	Clinical and pharmacological experiment. Clinical and pharmacological analysis of drugs for pharmacotherapy of alcoholic hepatitis
6.	Marketing experiment. Marketing research of drugs that are allowed for medical use in Ukraine (by trade names of drugs, manufacturers, dosage forms, registration certificates and terms of their registration in Ukraine)
7.	Pharmacoeconomic experiment. ABC analysis for price classification of costs. The classification is based on the Pareto principle
8.	Pharmacoeconomic experiment. VEN-analysis (Vital, Essential, Non-essential) – directive segmentation of the "necessity" of the range of drugs
9.	Description and evaluation of the obtained data, formulation of conclusions, proposals and recommendations

Clinical and pharmacological analysis of drugs для for pharmacotherapy of alcoholic hepatitis. Clinical and pharmacological analysis of drugs for basic therapy of patients with alcoholic hepatitis was performed according to the national Ukrainian clinical protocol. In this study, the results of clinical and pharmacological analysis showed that for basic therapy of alcoholic hepatitis have the following diagnostic codes of the ATC Classification (ATC): A05 – Agents used in diseases of the liver and biliary

tract; A11 – Vitamins; C04 – Peripheral vasodilators; H02 – Corticosteroids for systemic use. Each ATC-system code had a similar codification inside. For example, code A – "Drugs that affect the digestive system and metabolism"; A05 "Agents used in diseases of the liver and biliary tract", A05A "Agents used in biliary pathology", A05AA "Bile acids and their derivatives", A05AA02 "Ursodeoxycholic acid"; A11 "Vitamins", A11H-A11NA "Other simple preparations of vitamins", A11H A03 Tocopherol acetate (Vitamin E). Similarly, code C – "Agents affecting the cardiovascular system"; C04-C04A – "Peripheral vasodilators"; C04AD – "Purine derivatives"; C04AD03 – "Pentoxifyline". Similar to code H – "Hormone preparations for systemic use (excluding sex hormones and insulins)"; H02 – "Corticosteroids for systemic use"; H02A – "Simple corticosteroid preparations for systemic use"; H02AB – "Glucocorticoids"; H02AB06 - "Prednisolone" [16].

Marketing analysis of drugs for pharmacotherapy of alcoholic hepatitis. Marketing research of drugs for pharmacotherapy of alcoholic hepatitis (Table 2) was carried out.

Table 2. Marketing analysis of drugs for pharmacotherapy of alcoholic hepatitis.

No.	INN	Trade name / Manufacturer	Dosage form, strength, amount per unit	Number, validity period from/until according to the registration certificate of the medicines
1	2	3	4	5
1.	Pentoxifyline	Pentoxifilin-Darnitsa / PRAT "Pharmaceutical company" Darnytsya ", Ukraine	Tablets, 200 mg	UA/4041/01/01 Unlimited from 13.05.2020
2.	Prednizolone	Prednizolon-darnytsya / PRAT "Pharmaceutical company" Darnytsya ", Ukraine	Tablets, 5 mg	UA/2587/02/01 Unlimited from 12.04.2017
3.	Tocopherol acetate (Vitamin E)	Vitamin E 200-Sanofi / AT "Saneka Pharmaceuticals", Slovak Republic	Capsules, 200 mg	UA/3392/01/01 Unlimited from 21.03.2019

4.	Ursodeoxycholic acid	Ursolizin / Mitim S.r.l., Italia	Capsules, 150 mg	UA/8078/01/01 Unlimited from 13.12.2017

According to marketing analysis (Table 2) for pharmacotherapy of alcoholic hepatitis use solid dosage forms (tablets and capsules) take 100% of doctors' prescriptions. All tested drugs have an unlimited validity of registration certificates. Countries ranking of manufacturers of studied drugs follow: Ukraine – 50%; Italy and Slovenia – by 25% each.

*Pharmacoeconomic research of drugs for pharmacotherapy of alcoholic hepatitis: ABC/VEN analysis***.** Pharmacoeconomic studies using ABC/VEN analysis made it possible to allocate drugs by the cost of pharmacotherapy and evaluate the effectiveness of drug use in hospitals (Table 3, Table 4). Using ABC analysis drugs were classified in the order of expense, where group A drugs were the most expensive, group B – less expensive, group C – least expensive.

Table 3. ABC analysis of drugs for pharmacotherapy of patients with alcoholic hepatitis.

INN	Cost per unit dose (UAH)	Specific weight (%)	ABC group
Ursodeoxycholic acid	1343.00	85.03	A
Total for group A:	1343.00	85.03	
Tocopherol acetate (Vitamin E)	109.50	6.93	B
Prednizolone	94.00	5.95	B
Total for group B:	203.5	12.88	
Total for groups AB:	1546.5	97.91	
Pentoxifyline	33.00	2.09	C
Total for group C:	33.00	2.09	
Total for groups ABC:	1579.5	100.00	

According to the results of the ABC analysis (Table 3), group A includes one drugs INN (Ursodeoxycholic acid). The cost per unit dose is 1343.00 UAH, which is 85.03% specific weight of the total cost of treatment of the patient. Group B includes two drugs INN (Tocopherol acetate, Prednizolone). The total unit cost is 203.5 UAH (12.88%). Group C includes one drugs INN (Pentoxifyline) costing 33.00 UAH per unit dose (2.09%).

Table 4. VEN analysis of pharmaceuticals for pharmacotherapy of patients with alcoholic hepatitis.

INN	VEN group
Pentoxifyline	E
Prednizolone	V
Tocopherol acetate (Vitamin E)	E

Ursodeoxycholic acid	E

Pharmacoeconomic research of drugs for pharmacotherapy of alcoholic hepatitis: VEN analysis.

According to the results of VEN analysis (Table 4), it was proved that one drugs INN (Prednizolone) belong to category V (Vital). In categories E (Essential) were included three drugs INN (Pentoxifyline, Tocopherol acetate, Ursodeoxycholic acid). In category N (Non-Essential) the studied drugs were no doctor's appointments and costs of pharmacotherapy.

Distribution according to the results of VEN-analysis of studied drugs for pharmacotherapy of alcoholic hepatitis follows. The studied drugs in 25% (Prednizolone) included in pharmacotherapy as vital (category V), in 75% (Pentoxifyline, Tocopherol acetate, Ursodeoxycholic acid) – as essential (category E).

Based on the ABC/VEN analysis, a matrix of the consolidated ABC/VEN analysis was developed (Table 5).

Table 5. Matrix of consolidated ABC-VEN analysis of drugs for pharmacotherapy of alcoholic hepatitis.

Drugs' group	Quantity of drugs	Vital		Quantity of drugs	Essential		Quantity of drugs	Non-Essential	
		Drug prescription			Drug prescription			Drug prescription	
		UAH	%		UAH	%		UAH	%
A	-	-	-	1	1343,00	85,03	-	-	-
B	1	94,00	5,95	1	109,50	6,93	-	-	-
C	-	-	-	1	33,00	2,09	-	-	-
Total:	1	94,00	5,95	3	1485,50	94,05	-	-	-

Studies show that INN of drugs for category E accounted for the largest costs 94.0%, for category V – 5.95%, for category N – no costs. The share of distribution of drugs for alcoholic hepatitis by doctor's appointments and therapy costs by categories was calculated: A/E (85.03%) is the largest share of the total rate of doctors' appointments and the cost of maintenance therapy (Ursodeoxycholic acid). Niche of the B/V matrix (5.95%): one drug is included in the niche (Prednizolone). Niche of the B/E matrix (6.93%): one drug is included in the niche (Tocopherol acetate).

Conclusions. The relevance and necessity of the chosen research topic as a result of a review of the scientific literature on the epidemiology COVID-19 and pharmacotherapy of patients with alcoholic hepatitis was substantiated in the study. The results of the study provide an opportunity to make administrative and managerial decisions in determining the pharmacotherapy of patients with alcoholic hepatitis to improve the use of drugs in hospitals. Further researches in area needed, including analysis of the most important side effects of appointed drugs in comparing them with their costs. The results of the study provide an opportunity to make administrative and

managerial decisions in determining the pharmacotherapy of patients with alcoholic hepatitis to improve the use of drugs in hospitals. Further researches in area needed, including analysis of the most important side effects of appointed drugs in comparing them with their costs.

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