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Study of the Quality of Medical Therapy and Adherence in Patients with Chronic Heart Failure (According to the COMPLIANCE Study)

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Aim. Assess the medical therapy quality in patients with chronic heart failure (CHF) and patients' adherence to the treatment depending on the previous observation in a specialized medical center as part of an outpatient registry.

Materials and methods. An analysis of the medical therapy quality in patients with CHF was carried out as part of the COMPLIANCE prospective observational study (NCT04262583). 72 patients with CHF verified according to the protocol were included in the study. The average age of the patients was 69.1 ± 9.5 years (31% of women and 69% of men). Patients were divided into groups: those who first applied to a specialized department during the period of the study inclusion, or those who were previously observed in a specialized department. The general adherence assessment to medical therapy was carried out using the original questionnaire «The adherence scale of the National Society for Evidence-Based Pharmacotherapy» which was supplemented with questions to assess the actual adherence to specific medical drugs recommended for patients with CHF.

Results. According to the results of the study, beta-blockers were prescribed to 70 (97.2%) patients. Angiotensin converting enzyme inhibitors (ACEi)/angiotensin receptor blockers (ARBs) were recommended in 68 (94%) patients. Mineralocorticoid receptor antagonists were included in therapy in 6 out of 9 patients who were shown to be prescribed (66.6%). The choice of medical drugs within the group was not always adequate. For example, ACEi/ARBs with proven efficacy in patients with CHF were prescribed only in 72% of patients. Comparative analysis of adherence to medical therapy between patients of the selected groups demonstrated a higher adherence to the recommended therapy in patients who were previously observed in a specialized center.

Conclusion. The medical therapy quality for patients with CHF doesn't always comply with current clinical guidelines. The choice of a medical drug within a group is not always adequate. Regular observation in a specialized center contributes to a higher adherence to the recommended therapy.

Key words: quality of drug therapy, chronic heart failure, clinical guidelines, adherence to treatment, registry.

For citation: Guseynova E.T., Kutishenko N.P., Lukina Yu.V., Tolpygina S.N., Voronina V.P., Blagodatskih S.V., Drapkina O.M., Martsevich S.Yu. Study of the Quality of Medical Therapy and Adherence in Patients with Chronic Heart Failure (According to the COMPLIANCE Study). *Rational Pharmacotherapy in Cardiology* 2021;17(5):738-742. DOI:10.20996/1819-6446-2021-10-10.

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Received: 26.09.2021
Accepted: 07.10.2021

Introduction

The issues of the medical therapy quality are still relevant despite the development of an increasing number of clinical guidelines and treatment regimens for various diseases. This also applies to the treatment of patients with chronic heart failure (CHF). The comorbidity of such patients makes it necessary to take into account variety of nosologies and the peculiarities caused by them when choosing a drug within a class, therefore the task of patients' high-quality treatment with CHF becomes even more difficult.

Several large foreign registries of CHF patients have shown that such patients don't receive all the medical drugs required according to the guidelines, including specific medical drugs within the class in the recommended target doses.

The CHAMP-HF registry (USA), which includes 2588 outpatients with CHF with intermediate and reduced ejection fraction (EF), showed that during 12 months of observation, less than 1% of patients simultaneously received target doses of blockers of the renin-angiotensin-aldosterone system (RAAS): angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs)/angiotensin and neprilisin receptor inhibitors (ANRI), beta-blockers (BB) and mineralocorticoid receptor antagonists (MRA) [1].

The OPTIMIZE-HF registry, which includes 20441 patients with CHF, analyzed mortality one year after the last hospitalization. In-hospital prescription of BB, MRA, or implantation of a cardioverter-defibrillator were associated with a better clinical outcome and were used to determine the care quality in the hospital [2].

The aim of this work is to assess the medical therapy quality and adherence to the treatment in patients with CHF depending on the previous observation in a specialized medical center new patients.

Materials and methods

The assessment of the medical therapy quality in patients with CHF was carried out as part of the COMPLIANCE study (Assessment of adherence to Medical therapy and its influence on long-term outcomes in patients with Chronic heart failure in the outpatient registry; NCT04262583). The COMPLIANCE study was carried out on the basis of the PROFILE register, a register of a specialized cardiological department of a research center [3]. The study included patients with verified CHF who

applied to a specialized cardiology department in the period from December 01, 2019, to December 31, 2020. The protocol and the first results of the study were described earlier [4].

We analyzed the treatment quality in 72 patients with CHF, verified according to the protocol. Clinical guidelines of the European Society of Cardiology 2016 for the treatment of patients with CHF were taken as the basis [5].

The assessment of general adherence to medical therapy was carried out using the original questionnaire «The adherence scale of the National Society of Evidence-Based Pharmacotherapy» which was supplemented with questions to assess the actual adherence to specific medical drugs recommended for patients with CHF [6].

Patients were divided into groups: those who first applied to a specialized department during the period of the study inclusion (new patients), and those who were previously observed in this department and who consulted a doctor during the specified period (established patients).

The main criteria for quality medical therapy were the prescription of recommended medical drugs, the prescription absence of non-recommended drugs according to clinical guidelines; the correct choice of medical drugs within the class; lack of polypharmacy.

The statistical analysis was performed using IBM SPSS Statistics 20.0 software (IBM USA). The main descriptive statistics for categorical and ordinal variables were the frequency and proportion (%); mean, standard deviation, minimum (min.), and maximum (max.) or median; and interquartile range for quantitative variables. Comparative analysis of qualitative variables was performed using the well-known significance criteria [paired Student's t-test, Mann-Whitney's test, χ^2 test, and others]. Differences were considered statistically significant at $p < 0.05$.

Results

The clinical characteristics of the patient groups are presented in Table 1.

Evaluation of the prescribed therapy quality revealed that BB were prescribed to 70 (97.2%) patients with CHF (30 primary and 37 repeated patients; Table 2). However, BBs with proven efficacy according to clinical guidelines were prescribed only in 85.7% of cases ($n=60$). The target dose was not achieved in any of the patient groups. Comparison of BB prescriptions between patient groups did not reveal a statistically significant difference

in achieving the target dose between primary and repeated patients.

ACE inhibitors/ARBs were prescribed in 94% (n=68) of patients, while medical drugs with proven efficacy in CHF were prescribed in 72% of patients (n=49). 18 patients (11 primary and 7 repeated patients) were prescribed medical drugs that were not included in the clinical guidelines (Table 3). Only 12% (n=8) of patients received targeted doses of ACE/ARBs inhibitors of all patients to whom they were prescribed. Enalapril preparations from ACE inhibitors were more often prescribed in the target dose to repeated patients ($p=0.004$). There was no statistically significant difference in the prescriptions for the remaining medical drugs. We also note the rare prescription of the preparation sacubitril/valsartan.

The comparative analysis results of adherence to the recommended treatment of CHF new patients and established patients are shown in Table 4. Patients who were followed up in a specialized center for a long time turned out to be more adherent to therapy in general than those who first applied to a center. Adherence to BB intake didn't differ in patients of the study groups.

Discussion

In general, the results obtained in the study demonstrated that the main problems of reducing the medical treatment quality for CHF are the wrong choice of medical drugs and failure to achieve the recommended target doses of medical drugs.

This is consistent with the results of the large CHAMP-HF and QUALIFY registers [1,7]. In the QUALIFY register, the therapy quality was also determined by prescribing medical drugs according to clinical guidelines and by reaching the recommended dose of medical drugs. Patients with CHF received the recommended dose of ACE inhibitors only in 27.3% of cases, ARBs – in 49.9%, BB – in 48.5%

Table 1. Clinical characteristics of patients with CHF (n = 72)

Characteristics	New patients (n=32)	Established supervised patients (n=40)
Men, n (%)	18 (56.3)	33 (82.5)
Smoking, n (%)	7 (21.9)	7 (17.5)
AH, n (%)	29 (90.6)	35 (87.5)
BMI, n (%)		
Norm (<25 kg/m ²)	6 (19.0)	5 (12.5)
Overweight (25-29.9 kg/m ²)	11 (34.0)	15 (37.5)
Obesity of the 1st degree (30-34.9 kg/m ²)	11 (34.0)	18 (45.0)
Obesity of the 2nd degree (35-39.9 kg/m ²)	3 (9.4)	2 (5.0)
Diabetes mellitus, n (%)	8 (25.0)	11 (27.5)
AF, n (%)	17 (53.1)	15 (37.5)
History of myocardial infarction, n (%)	14 (43.8)	26 (65.0)
History of PCI, n (%)	8 (25.0)	17 (42.5)
History of CABG, n (%)	4 (12.5)	3 (7.5)
LV aneurysm, n (%)	2 (6.3)	6 (15.0)
COPD, n (%)	10 (31.3)	9 (22.5)
VPB and/or SPB (>10000/day), n (%)	2 (6.3)	3 (7.5)
Thyroid diseases requiring medical therapy, n (%)	6 (18.8)	3 (7.5)

AH – arterial hypertension, BMI – body mass index, CHF – chronic heart failure, AF – atrial fibrillation, PCI – percutaneous coronary intervention, LV – left ventricle, CABG – coronary artery bypass grafting, COPD – chronic obstructive pulmonary disease, VPB – ventricular premature beats, SPB – supraventricular premature beats

[7]. According to the CHAMP-HF register, most patients with CHF also didn't receive medical drugs indicated in accordance with clinical guidelines in target doses [1].

In the CIBIS-ELD study, the target doses of bisoprolol and carvedilol after 12 weeks of treatment were achieved only in 25% of patients with CHF [8]. Failure to achieve target doses and the associated lack of CHF therapy effectiveness negatively affects the prognosis of patients with this nosology. For example, the BIOSTAT-CHF registry has shown that achieving <50% of the target dose of

Table 2. Prescribed therapy with beta-blockers in the studied groups

Medical drug	New patients (n=32)		Established supervised patients (n=40)		Target daily dose (mg) [6]
	mg/day	n	mg/day	n	
Bisoprolol	5 [2.5;5]	15	2.5 [5;5]	22	10 mg once a day
Carvedilol	25 [19;25]	3	25 [25;25]	5	25-50 mg twice a day
Metoprolol	21.9 [38.0;50.0]	6	37.5 [50.0; 125.0]	7	200 mg once a day
Nebivolol	–	0	5 [5; 5]	2	10 mg once a day
Sotalol	40 [40;100]	3	160	1	*

Data are presented as Me [25%; 75]
n – number of patients who were prescribed medical drugs, * the medical drug is not included in the current clinical guidelines

Table 3. Prescribed therapy with RAAS blockers in the studied groups

Πpenapar	New patients (n=32)		Established supervised patients (n=40)		Target daily dose (mg)
	mg/day	n	mg/day	n	
ACE inhibitors					
Enalapril	5 [5;7,5]	3	20 [20;20]	11	20 mg twice a day
Lisinopril	10 [3,75;20]	5	10	1	20-35 mg once a day
Ramipril	6,25 [7,5; 8,75]	2	7,5 [5;10]	6	10 mg once a day
Perindopril	5 [5;6,5]	7	5 [5;5]	6	*
Fosinopril	n=0	0	20(n=1)	1	*
Angiotensin receptor blockers					
Losartan	50 [50;100]	6	25 [25;81,3]	6	150 mg once a day
Valsartan	90 [60;130]	4	40 [40;80]	5	160 mg twice a day
Candesartan	16 [12;20]	3	n=0	0	32 mg once a day
Azilsartan	40	1	n=0	0	*
MRA					
Spironolactone	25 [25;25]	12	25 [25;25]	15	50 mg once a day
Eplerenone	25	1	50 [25;50]	3	50 mg once a day

Data are presented as Me [25%; 75]

* the medical drug is not included in the current clinical guidelines [6]

n – number of patients who were prescribed medical drugs, RAAS – renin-angiotensin-aldosterone system, MRA – mineralocorticoid receptor antagonists

Table 4. Adherence to treatment in the studied groups

Medical drug group	New patients	Established supervised patients	p
BB	70.0% (21 out of 30)	83.8% (31 out of 37)	0.395
ACEi	32.3% (10 out of 31)	76.9% (30 out of 39)	0.001
MRA	38.5% (5 out of 13)	100% (18 out of 18)	0.001
General adherence to therapy	15.6% (5 out of 32)	72.5% (29 out of 40)	0.001

The calculation was based on the patients' number who received the prescribed therapy.

BB – beta-blockers, ACEi – angiotensin-converting-enzyme inhibitors, MRA – mineralocorticoid receptor antagonists

medical drugs in the patients' treatment with CHF is associated with a high risk of hospitalizations and cardiovascular mortality in such patients [9].

In addition, a decrease in the CHF therapy effectiveness is possible as a result of insufficient patient adherence to the recommended treatment. According to the results of

our study, the most vulnerable in terms of adherence to treatment were patients who first visited a specialized cardiology department of a research center, compared with established supervised patients.

Conclusion

The medical therapy quality for patients with CHF doesn't always correspond to the current clinical guidelines, and the medical drug choice within a group is not always adequate. Established supervised patients at a specialized center contributes to a higher adherence to the recommended therapy.

Relationships and Activities: none.

Funding: The study was performed with the support of the National Medical Research Center for Therapy and Preventive Medicine.

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