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Clinical Pharmacological Approach To Rational Drug Treatment Of Chronic Heart Failure

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Abstract. The clinical pharmacological approach to the rational drug treatment of chronic heart failure (CHF) focuses on optimizing therapeutic strategies to improve patient outcomes. This article examines the pharmacological classes of drugs used in CHF management, including angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, diuretics, aldosterone antagonists, and novel agents. The mechanisms of action, indications, contraindications, and potential adverse effects of these drugs are analyzed. Special emphasis is placed on the importance of individualized treatment, drug interactions, and evidence-based guidelines. Advances in pharmacotherapy and personalized medicine approaches for enhancing the efficacy and safety of CHF treatment are also discussed.
Keywords: Chronic heart failure, rational pharmacotherapy, clinical pharmacology, ACE inhibitors, beta-blockers, diuretics, drug interactions.

Introduction

Unlike other treatments, the effect of diuretics on morbidity and mortality in patients with CHF has not been studied in long-term studies. However, the use of diuretics eliminates symptoms associated with fluid retention (peripheral edema, dyspnea, pulmonary congestion), which justifies their use in patients with CHF regardless of LVEF. Diuretics are recommended to improve HF symptoms and increase physical activity in patients with signs of fluid retention. Fluid retention in the body and the formation of edema syndrome are a typical and most well-known manifestation of CHF, starting from FC II. Therefore, dehydration therapy is one of the most important components of successful treatment of patients with CHF. However, it should be remembered that complex neurohormonal mechanisms are involved in the development of edema syndrome and thoughtless dehydration causes only side effects and "rebound" fluid retention. What is characterized as edema and dyspnea is an accumulation of fluid in the extracellular space [1].

materials and methods

Serious placebo-controlled studies on the use of diuretics have practically not been conducted (with the exception of the AMCRA), therefore all provisions are based on expert opinion. Formally, this corresponds to the degree of evidence C, although, given the vast practical experience in the treatment with diuretics, the validity of their use in all patients with CHF with hyperhydration is beyond doubt.

The main provisions of dehydration therapy, including the use of diuretics, are as follows [2]:

• diuretics are used to eliminate edema syndrome and reduce clinical symptoms in patients with CHF;

• when used correctly, these drugs can reduce the number of hospitalizations, which corresponds to the achievement of two of the 6 main goals in the treatment of CHF:

Most diuretics (except torasemide) do not slow the progression of CHF and do not improve the prognosis of patients. Their impact on the quality of life if prescribed incorrectly (shock doses every 3-4-5-7 days) can even be negative. Torasemide is the most effective and safe loop diuretic with an optimal pharmacokinetic profile. The starting dose of the drug is 2.5-5 mg, which can be increased to 100-200 mg per day if necessary. Torasemide is a typical loop diuretic that blocks the reabsorption of sodium and water in the ascending part of the loop of Henle. In terms of pharmacokinetic properties, it is superior to furosemide (duration of effect up to 18 hours), has better and predictable absorption compared to furosemide (90% versus 50%), and its bioavailability does not depend on food intake and is almost twice as high as that of furosemide [3]. In renal failure, the half-life of torasemide does not change (since it is metabolized in the liver by 80%). But the main positive difference of torasemide from other loop diuretics is its additional

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effects, in particular, associated with the simultaneous blockade of local RAAS and SAS. A dose-dependent blocking effect of torasemide on angiotensin II-stimulated calcium entry into cells has been proven.

Results And Discussion

Thus, torasemide is the first diuretic that can not only affect the symptoms of patients with CHF, but also the progression of the disease and the course of pathological processes in the heart muscle. Recent Russian studies have confirmed the ability of torasemide to affect LV remodeling and normalize the ratio of collagen synthesis/degradation markers. In addition, the use of torasemide helps overcome the main disadvantages of active diuretic therapy: the diuretic effect itself is enhanced and side effects (electrolyte disturbances and activation of the RAAS) are blocked. Long-term smooth diuresis of torasemide (14-18 hours compared to 4-5 hours for furosemide) allows the patient to be mobile, which significantly increases adherence to treatment [4].

Treatment with diuretics begins only with clinical or instrumental signs of congestion (stage II A, FC II according to the NYHA classification). Carbonic anhydrase inhibitors: facial paresthesia, dizziness, dyspepsia, metabolic acidosis, hypokalemia, hyperuricemia, drug fever, skin rash, bone marrow suppression, renal colic with stone formation (rare).

Thiazide and thiazide-like: dyspeptic phenomena, hypokalemia, hyperuricemia, hyperglycemia, impaired glucose metabolism, skin rash, photosensitivity, paresthesia, weakness, increased fatigue, thrombocytopenic purpura, jaundice, pancreatitis, necrotizing vasculitis (rare).

Loop: hypokalemia, hyponatremia, hypomagnesemia, hyperuricemia, hyperglycemia, increased cholesterol. hypochloremic alkalosis, dyspepsia, skin rash, acute hypovolemia (with intravenous administration), ototoxicity (with intravenous administration or high doses).

Direct aldosterone antagonists: hyperkalemia, nausea, vomiting, diarrhea, gastritis, gastric ulcer, gynecomastia, hirsutism, menstrual dysfunction (spironolactone).

Indirect aldosterone antagonists: hyperkalemia, nausea, vomiting, headache, megaloblastic anemia and interstitial nephritis.

Ivabradine is a selective f-channel (if-current) blocker in sinus node cells, reducing heart rate without other hemodynamic effects. Ivabradine preserves myocardial contractility (does not affect the inotropic function of the heart) and diastolic function, and does not affect electrophysiological parameters and carbohydrate and fat metabolism. It is important that ivabradine does not reduce blood pressure (BP) and does not change peripheral vascular resistance. The drug is effective only in patients with sinus rhythm. It has been shown that in patients with sinus rhythm, EF ≤ 35%, symptoms of CHF II-IV FC and heart rate ≥ 70 bpm, despite therapy with recommended (or maximum tolerated) doses of β-blockers, ACE inhibitors/ARBs and MRAs, adding ivabradine to treatment reduces the number of hospitalizations and mortality due to CHF. In addition, in case of beta-blocker intolerance, the use of ivabradine in addition to standard therapy reduces the risk of hospitalization due to CHF in this same category of patients.

The average reduction in the risk of death in patients with CHF in sinus rhythm per every 10 beats of heart rate reduction during ivabradine therapy is 29%, which is comparable to the effects of beta-blockers. This allows us to consider heart rate reduction as a universal mechanism for improving the prognosis of patients with CHF [5].

The recommended initial dose of ivabradine is 5 mg x 2 times a day, with a subsequent increase after 2 weeks to 7.5 mg x 2 times a day. In elderly patients, the dose of ivabradine may be adjusted downwards.

To date, the use of cardiac glycosides in patients with CHF is limited. Currently, digoxin is used in clinical practice in the vast majority of cases, as it has optimal pharmacodynamic properties and proven clinical efficacy. The use of other glycosides for long-term treatment of patients with CHF has no basis. Prescribing digoxin to patients with CHF does not improve their prognosis, but reduces the number of hospitalizations due to CHF, improves CHF symptoms and quality of life. Cardiac glycosides have been used to treat CHF for more than two centuries. Glycosides have 3 main mechanisms of action - positive inotropic, negative chronotropic (which has a different physiological basis for atrial fibrillation and sinus rhythm) and neuromodulatory effects. Although this is a well-known fact for a long time, however, practicing physicians everywhere consider the positive inotropic effect of glycosides to be the main one. A powerful positive inotropic effect of glycosides is manifested when they are used in high doses (for digoxin more than 0.375 mg/day). However, the use of high (more than 0.375 mg) doses of digoxin is fraught with the development

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of intoxication and is a harbinger of a negative impact on the prognosis of patients with CHF. Therefore, digoxin in patients with CHF should always be used in small doses: up to 0.25 mg/day (for patients with a body weight of more than 85 kg - a maximum of up to 0.375 mg/day, and with a body weight of less than 60 kg - up to 0.125 mg/day). In such doses, it acts primarily as a neurohormonal modulator, has a weak positive inotropic effect and does not stimulate the development of cardiac arrhythmia. In cases of renal failure, the daily dose of digoxin should be reduced proportionally to the decrease in creatinine clearance and with a SCF of less than 60 ml/min. In elderly patients, daily doses of digoxin should be reduced to 0.0625–0.125 mg (¼–½ tablet). In all cases, a combination of cardiac glycosides with beta-blockers is preferable, as it provides better heart rate control, reduces the risk of life-threatening ventricular arrhythmias, and decreases the risk of exacerbation of coronary insufficiency. Thus, in CHF with LVEF <40% and sinus rhythm, digoxin use SHOULD be considered if the main treatments for decompensation are insufficiently effective to reduce the risk of rehospitalization.

Dyspeptic symptoms: pain in the epigastric region, anorexia, nausea, vomiting; cardiac dysfunction: bradycardia, AV block, sinoatrial block, ventricular extrasystole or tachycardia; visual impairment: loss of visual fields, photophobia, impaired color perception (xanthopsia), moving spots; neurological symptoms: headache, dizziness, fatigue, anxiety, insomnia, apathy, neuritis, radiculitis; other symptoms: thrombocytopenic purpura, nosebleeds, petechiae; endocrinological disorders: gynecomastia in men, menstrual irregularities in women.

Conclusion

Considering that CHF is a condition that increases the risk of thromboembolism and stroke, anticoagulants play an important role in the treatment of this syndrome. Moreover, according to some researchers, the very presence of CHF due to stasis in the cavities of the heart, observed with LV dilation, is a factor contributing to the development of both peripheral venous and intracardiac thrombosis, as a source of future thromboembolism. Up to 40% of patients with severe CHF have signs of deep vein thrombosis, and in 5.5% of patients, pulmonary embolism complicates the course of decompensation, and the more severe the CHF and the lower the EF, the more likely it is that thrombosis and embolism will occur. Additional factors include dehydration therapy (the more abundant the diuresis, the worse) and the patient being on bed rest (for example, with decompensation).

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