Digoxin was almost Abandoned in HFrEF Therapy. Is that Entirely Justified?

Vjeran Nikolić Heitzler

INTRODUCTION

Digoxin is a positive inotropic agent, the only one suitable for chronic oral administration in patients with systolic heart failure (HFrEF <45-50%) with or without atrial fibrillation. Neuro-humoral properties are also significant by suppressing excessive activity of the sympathetic and renin-aldosterone systems. Numerous studies confirm that it achieves exceptional hemodynamic effects by increasing displacement graft (EF), cardiac index by reducing pulmonary capillary pressure. It slows down the heart and neutrally affects blood pressure. Therefore, unlike beta-blockers and ACEs / ARBs, it can be safely used in patients with lower blood pressure. Digoxin is also associated with an improvement in renal function, estimated to increase glomerular filtration rate by 20%. Therefore, unlike renin-angiotensin-aldosterone inhibitors, it can be administered to patients with borderline renal function without the risk of further renal impairment (1,2,3,4,5)

Keywords: digoxin, Heart failure with reduced ejection fraction (HFrEF), mortality, hospital readmission.

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I. INTRODUCTION

Digoxin is a positive inotropic agent, the only one suitable for chronic oral administration in patients with systolic heart failure (HFrEF <45-50%) with or without atrial fibrillation. Neuro-humoral properties are also significant by suppressing excessive activity of the sympathetic and renin-aldosterone systems. Numerous studies confirm that it achieves exceptional hemodynamic effects by increasing displacement graft (EF), cardiac index by reducing pulmonary capillary pressure. It slows down the heart and neutrally affects blood pressure. Therefore, unlike beta-blockers and ACEs / ARBs, it can be safely used in patients with lower blood pressure. Digoxin is also associated with an improvement in renal function, estimated to increase glomerular filtration rate by 20%. Therefore, unlike renin-angiotensin-aldosterone inhibitors, it can be administered to patients with borderline renal function without the risk of further renal impairment (1,2,3,4,5)

II. DISCUSSION

It was the drug of first choice for many years until a 1997 DIG study showed that digoxin did not reduce mortality in that population (NYHA III-IV with LVEF≤40% or NYHA II with LVEF≤ 30% with or without atrial fibrillation), but contributes to the reduction of symptoms and the frequency of hospitalizations. The DIG study may complain that beta-blockers and aldosterone antagonists were not used in the treatment of heart failure at that time, and relatively high doses of digoxin were prescribed, which are not common today. Negative remarks on DIG study /1997/.

1. HF therapy without beta-blockers and aldosterone antagonist
2. High digoxin doses 0.25 mg
3. Distribution of NYHA class I = 13.3%
   II = 53.%
   III = 30.7%
   IV = 2.2%

small percentage representation of more severe HF cases.

1. 44,1% of the patients assigned to digoxin were on digoxin before study entry.
2. 44,6% of the patients allocated to placebo were previously on stable, chronic digoxin therapy without a wash-out period (6,7)

In the last twenty years alone, the use of digoxin in HFrEF therapy has dropped by rather than two thirds. According to a US study (GWTH-HF) on 250,000 patients with HFrEF, the frequency of digoxin use in discharge therapy decreased from 33.1% of patients in 2005 to 10.7% in 2014. (8).

Current European IIb and American Guideline IIa recommend digoxin in patients with HFrEF who have persistent symptoms despite optimal therapy, in order to reduce the frequency of hospitalizations. Small doses equivalent to a serum concentration <0.9 ng / ml are recommended when digoxin is administered.

In studies with stable HFrEF when digoxin therapy was discontinued, symptoms worsened, exercise tolerance decreased, and a decrease in EF was recorded. In extremely severe cases of HFrEF, the introduction of digoxin was able to remove

mechanical circulatory support and intravenous inotropic drugs (9,10,11,12).

Heart failure therapy has changed greatly in the last twenty years or so. In addition to modern therapy: angiotensin receptor neprilysin inhibitor (ARNI) sacubitril/valsartan is now preferred compared to ACEI/ARBs and sodium-glucose cotransporter-2 inhibitors (SGLT2) are now an option for patients with or without diabetes after ARNI/ACEI/ARB and BB treatment has started. Finally, mechanical support and heart transplantation are today a possibility in advanced stage of the disease, if every other therapy fails(14).

III. CONCLUSION

The clinician faces the dilemma of relying on the quality of data arising from clinical trials conducted more than two decades ago and before modern heart failure therapy was available or on evidence from mainly observational studies .

Digoxin probably still has an excuse in patients with severe advanced systolic dysfunction who are unable to tolerate high doses of drugs due to limits in blood pressure, renal function. Digoxin should be used to reduce repeated hospitalizations and today's systolic heart failure patient is on average 10 years older than in the DIG study and a daily dose of 0.10 may be appropriate for a greater number of patients(13).The pharmaceutical industry has no interest in a new DIG study no matter how previous we may blame a number of shortcomings since digoxin it is a very cheap drug (12).

IV. LITERATURE

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