OPTIMAL MEDICAL THERAPY IN CHRONIC HEART FAILURE – AN AUDIT

Sajjad Hussain, Azhar Mahmood Kayani, Rubab Munir

Armed Forces Institute of Cardiology Rawalpindi

ABSTRACT

Objective: Systolic heart failure is a chronic condition with significant morbidity and mortality. Evidence based optimal medical therapy (OMT) has been shown to reduce mortality. Underuse of OMT due to multiple reasons has been a consistent problem. The study objective was to audit the use of OMT in patients with heart Failure.

Study Design: Descriptive study.

Place and Duration of study: This audit was carried out in AFIC-NIHD from April 2011- February 2012.

Material and Methods: Seventy consecutive stage D heart failure patients were included in the study. The patients were assessed clinically by a cardiologist and all previous documentations, referral letters, prescriptions, and purchase receipts were reviewed. To identify any other medication patients might have been taking (which did not appear on the prescriptions) patients were asked to identify common medicine packs. The patients underwent a detailed clinical evaluation including history, physical examination. Relevant investigations were done. ACCF/AHA (American College of Cardiology Foundation / American Heart Association) and ESC (European Society of Cardiology) guidelines for the diagnosis and treatment of acute and chronic heart failure were taken as standard of care.

Results: In our audit we found that a large proportion of patients who were at high risk as per the Seattle Heart Failure Model (SHFM) were not on OMT, only 4.3% of the patients were on beta blockers that have been shown to improve mortality in the large randomized clinical trials, 64.3% were not taking any beta blockers where as 55.7% were not on ACE inhibitors and adding the OMT greatly reduced their mortality risk.

Conclusions: We concluded that a large proportion of patients were not on OMT despite not having any contraindication to such therapy. This deprives them of significant survival benefit.

Keywords: Heart Failure, Optimal Medical therapy, Audit.

INTRODUCTION

Systolic heart failure is a chronic condition with significant morbidity and mortality, resulting in overall increased cost to any health care system because of increased clinical consultations, hospital admissions, pharmacological and device treatment[1]. Evidence based optimal medical therapy (OMT) has been shown to reduce mortality. Penetration of OMT in clinical practice has not been ideal.

Objective

We sought to conduct an audit about the use of OMT in stage D heart failure patients referred to AFIC – NIHD for heart transplant assessment.

METHODS

This descriptive study had been carried out at Armed Forces Institute of Cardiology- National institute of Heart Diseases from April 2011-February 2012. We prospectively collected data on 70 consecutive stage D heart failure patients. These patients had been referred to AFIC – NIHD for the management of advanced heart failure and assessment for the need of heart transplantation. They were assessed clinically by a cardiologist and all previous documentations, referral letters, prescriptions, and purchase receipts were reviewed. To identify any other medication patients might have been taking (which did not appear on the prescriptions) patients were asked to identify common medicine packs.

Standards of care

The following international guidelines were taken as the standard of care for the management of heart failure:

Correspondence: Maj Sajjad Hussain, Consultant Cardiologist and Physician, AFIC / NIHD, Rawalpindi.
Mobile: 0334-5228881
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1. AACF/ AHA guidelines for the diagnosis and management of heart failure in adults – 2009 focused update[2].
2. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008[3].

The patients underwent a detailed clinical evaluation including history and physical examination. The echocardiograms were repeated to document cardiac structure and function. The laboratory investigations performed included ECG, complete blood count, serum urea, serum creatinine, Na^+, K^+, bilirubin, ALT, alkaline phosphatase and BNP (Brain Nariuretic Pepide) levels at baseline and again at 4 weeks after starting OMT.

Optimal medical therapy was defined as a standard prescription as stated below:

1. Tab Lisinopril 2.5 mg once daily with dose doubling every one week as tolerated, target dose was 10 mg.

a. Indications to deviate from the above protocol were angioedema, deteriorating renal functions or hyperkalaemia.

2. Tablet Carvidalol 3.25 mg twice daily with the dose doubling every one week as tolerated, target dose was 25 mg twice daily.

a. Indications to deviate from the above protocol were 2nd or 3rd degree heart block, symptomatic bradycardia or clinical worsening of heart failure.

3. Tab Spironolactone 12.5 mg once daily with dose doubling every one week, target dose of 50 mg once daily.

a. Indications to deviate from the above protocol were hyperkalaemia or endocrine side effects.

4. Frusemide was given on a need basis depending upon fluid status of patient.

Data has been analysed using SPSS 17. Descriptive statistics were used to describe results. To study the change in renal biochemistry due to use of ACE inhibitors paired sample t-test and Wilcoxon signed rank test were applied where appropriate. p value 0.05 was considered as significant.

RESULTS

Total number of study population comprised of 70 stage D heart failure patients. Fifty (71%) patients were males and 20 (29%) were females. The mean age was 38.5 ± 13.13 years (range of 16-74 years). The mean ejection fraction calculated was 23 ± 9.46%. In our audit we found that a large proportion of patients who were at high risk as per the SHFM were not on OMT, and adding the OMT greatly reduced their mortality risk. A comprehensive distribution of OMT in patients is shown in table-1 through 3.

-blockers (BB)

The results (table-2) show that only 4.3% of the patients were on BB that have been shown to improve mortality in the large randomised clinical trials (bisoprolol, carvedilol, nebivolol, metoprolol CR/XL (controlled release/extended release). This indicates a poor penetration of BB into heart failure practice as 31.4% of patients were not on mortality reducing BB. To look into the common causes for non-prescription of BB we looked through the clinical history for contraindications to BB therapy and found that none of these patients had asthma or symptomatic peripheral vascular disease. This may have simply been by chance, but the patients still needed BB therapy. We looked at the ECGs of all the patients and found no evidence of a high grade AV block. The mean PR interval in this population was 174 ms (min 99 ms, max 289 ms).

We instituted beta blocker therapy in all these patients and on follow up we did not find any increase in heart block in these patients. No patients reported to us with symptomatic brady-arrhythmias.

Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin Receptor Blockers (ARB), Aldosterone antagonists (AA)

The prescription rate of ACEI was 44.3% and AA was 47.1%, this includes those on combination pills – e.g, spiromide) can at best be said to be modest. Only 5.7% of our patients were receiving ARBs. To look into the possibility of renal dysfunction limiting the use of these drugs we looked at the serum creatinine, potassium levels, and calculated creatinine clearance by the Cockgroft-Gault formula (table-4). It was clear to us that a very small number of patients actually were to be excluded from the prescription based on the serum K^+ or creatinine levels. We initiated the ACI and AA in all the patients after optimization of fluid balance and other heart failure therapy. The repeat values of the same variables at 4 weeks are shown in table-4. The mean serum potassium rose from 4.1 to 4.2 mmol/l (p=0.1). The serum creatinine levels had fallen from 1.1 to 0.9 mg/dl and were statistically significant (p=0.002). This clearly shows that the

Table-1: Prescription of drugs.

Drug class/ name	Prescription of drugs (n)	
	n (%) **Yes**	n (%) **No**
Beta blockers	25 (35.7)	45 (64.3)
ACE inhibitors	31 (44.3)	39 (55.7)
Angiotensin receptor blockers (ARBs)	4 (5.7)	66 (94.3)

Table-2: Different beta blockers prescribed to patients.

Drug class/ name	Patients prescribed drug n (%)
Trial proven beta blockers (Carvedilol, Bisoprolol, Metoprolol CR/XL*)	3 (4.3)
Beta blockers not trial proven for heart failure	22 (31.4)
Total patients on beta blockers	25 (35.7)

*None of the patients was taking Metoprolol CR/XL.

Table-3: Different aldosterone antagonists prescribed to patients.

Drug class/ name	Patients n (%)
Aldosterone antagonists (Spironolactone)	12 (17.1)
Combination of furosemide and spironolactone	21 (30)
Total patients receiving aldosterone antagonists in some form	33 (47.1)
Patients not on aldosterone antagonists	37 (52. 9)

Table-4: Renal profiles at baseline and at 4 weeks of patients prescribed *ACEI and **ARBs.

Renal profile at baseline					
Serum levels	**Min**	**Max**	**Mean**	**Median**	**Std. deviation (SD)**
Potassium (mmol/L)	3.8	6.4	4.27	4.1	0.44
Urea (mg/dL)	16	192	47.3	40	28.5
Creatinine (mg/dL)	0.6	2.8	1.11	1	0.42
Renal profile at 4 weeks					
Potassium (mmol/L)	3.8	5.0	4.26	4.2	0.26
Urea (mg/dL)	12	96	40	37	17
Creatinine (mg/dL)	0.6	2.2	0.99	0.96	0.27

*Angiotensin Converting Enzyme Inhibitors, **Angiotensin Receptor Blockers.

introduction of OMT actually improved renal perfusion. It is very clear that these patients had sufficient reserve to tolerate the ACEI and AA yet did not receive these therapies.

Digoxin

Our study showed that 75% of patients were receiving digoxin (with the same renal profile).

Drugs with a weak evidence base

A large number of patients were using trimetazidine, and a herbal medicine Tricardin, but were only on diuretics or digoxin as the alternative medications. Literature search did not reveal any significant randomised controlled trials for the use of Tricardin in heart failure.

DISCUSSION

Evidence based OMT in heart failure reduces morbidity and mortality. This has been emphasized in all international practice guidelines. Beta blockers, have been shown to improve symptoms reduce arrhythmic risk and mortality in multiple trials[4-8]. The beta blockers which have shown mortality benefit in heart failure so far include carvediolol, bisoprolol, and metoprolol XL. Prescribing metoprolol tartrate for mortality reduction is not supported by evidence based guidelines; it's use was tested in the MDC study[9]. Although there was a beneficial effect for the combined end point of morbidity and mortality, but this was primarily driven by the morbidity end point and there was no mortality benefit. ACE inhibitors have been shown to reduce mortality in major trials as well[10-13]. Similar benefits have been shown for angiotensin receptor blockers[14], and aldosterone antagonists (AA)[15-16]. While Digoxin does improve symptoms and exercise tolerance, and its withdrawal from the prescription can lead to worsening of symptoms, it has not been shown to confer any mortality benefit[17].

Despite concrete data to support the use of OMT in all stages of heart failure there is considerable variation in the prescription of these therapies in patients with heart failure. Heart failure audits in the last 2-3 years in the UK show that although the penetration of evidence based therapy for heart failure into clinical practice is on the rise, however it is not complete[18,19]. Multiple factors influence the prescription of beta blockers including concerns regarding advanced age, low EF, bradycardia, low BP[20] ; these may be the very people who stand to benefit from the OMT. Similarly ACE inhibitors[21] and AA[22] are known to be under prescribed due to concerns regarding renal function and sometimes for no discernible reason[21].

Our study found that a large proportion of patients had not been prescribed evidence based OMT for heart failure. We also showed the common beliefs and fears surrounding the prescription of BB, ACEI, ARB and AA can actually be alleviated by simple and careful clinical and lab monitoring of the patient, thus giving full benefit to the patient.

CONCLUSION

Evidence based OMT is not used in the patients who are likely to benefit from it the most. Given the proven mortality benefit by these medications their prescription needs to increase.

Action Plan

1. The benefits of OMT in heart failure need to be reiterated to the physicians and cardiologists.
2. Concerns for the safety of patients not supported by scientific data need to be addressed and allayed so that the prescription of these lifesaving, easily available medications can increase.
3. Dedicated heart failure services need to be set up. This is likely to ensure adequate clinical and lab follow up of these patients along with measures to ensure compliance.

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