Case study on a patient with heart failure

Mr. SB, 60-year-old male is a retiree and was admitted to the hospital accompanied by his daughter. He is 100kg at a height of 180cm so his calculated body mass index (BMI) was 30. 9 indicating that he was overweight. When admitted, patient was complained of shortness of breath for 2 weeks and was worsening on the day of admission. Besides, he also experienced orthopnea, fatigue, paroxysmal nocturnal dyspnea and leg swelling up to his thigh. Mr. SB was admitted to the hospital for to the same problem last year.

Mr. SB had known case of heart failure since 3 years ago and he had also diagnosed with hypertension for 5 years. Before admitted to the hospital, patient was taking frusemide 40mg, aspirin 150mg, metoprolol 50mg, amlodipine 10mg, and simvastatin 40mg for his hypertension and heart failure. Patient does not allergic to any medication and he does not take any traditional medicines at home. His family history revealed that his father had died of ischemic heart disease 4 years ago while his brother has hypertension. As for his social history, he smokes 2-3 cigarettes a day for 35 years and the calculated smoking pack years was 5 pack years. Besides, Mr. SB also drinks occasionally.

On examination, Mr. SB was found to be alert and conscious but he was having pedal oedema up to his knee. Besides, the patient was noted with bibasal crepitations with no rhonchi. His body temperature was normal. However, his blood pressure was found to be elevated upon admission with a record of 159/100 mmHg with an irregular pulse rate at 85beats/min. His echocardiogram showed that he had left ventricle hypertrophy while chest X-ray was conducted and revealed that the patient had cardiomegaly.

Lab investigations such as full blood count, liver function test, urea and electrolyte test and cardiac enzyme were done upon admission. His creatinine concentration was found to be 143µmol/L. Therefore, the calculated creatinine clearance was 68. 8ml/min. Besides, there was also blood found in the urine and the echocardiography showed that the patient has sinus tachycardia. In addition, ECG test was performed on day 1 and the result indicated that there was a T-wave inversion. The patient's INR was 1. 04 which was lower than normal while APTT was found to be slightly higher (59. 4 seconds). Mr. SB's random blood glucose was found to be normal during his hospitalization.

Mr. SB was diagnosed with congestive cardiac failure (CCF) with fluid overload. The patient also suffered from hypertension. The management plan included intraveneous frusemide 40mg twice daily, aspirin 150mg once daily, simvastatin 40mg once at night and ramipril 2. 5mg once a day. Besides, patient was asked to restrict his fluid intake to 500ml per day and oxygen therapy was given to patient at high flow using a face mask when patient experiencing shortness of breath.

As for his clinical progression, on day 1, the patient was complained of shortness of breath, leg swelling and orthopnea. Enchocardiogram showed that he had cardiomegaly. Treatment of CCF was given. Throughout the stay in the hospital, Mr. SB had responded well to the heart failure therapy as there was no more complaint of chest pain or shortness of breath on day 13 and his pedal oedema had gradually improved. However, patient's blood pressure throughout day 1 to 9 was fluctuating between the range of 102/67-160/100 mmHg and therefore, hypertension treatment was given and blood

pressure on day 10 onwards had been seen fell within the normal range. Furthermore, Mr. SB’s renal function became progressively worse from 143µmol/L on admission to 175µmol/L on day 11 and the calculated creatinine clearance on day 11 was 56. 2ml/min.

2. Pharmacological Basis of Drug Therapy

2. 1 Disease Summary

Congestive cardiac failure (CCF) is a complex syndrome that is usually caused by the inability of heart to pump sufficient blood to meet metabolic needs of body during exercise. It is more commonly known as heart failure38 and it can affect either left or right ventricle or both39. The risk factors predisposing one to heart failure are obesity, high blood pressure, diabetes, and smoking. Heart failure is commonly characterized by typical signs of fluid retention with symptoms of breathlessness, fatigue, paroxysmal nocturnal dyspnoea, and reduced exercise tolerance39.

CCF is a common disease which affects approximately 1-2% of the general population in developed countries1. Prevalence increases with age especially those aged above 75 years where the prevalence of CCF could be as high as 10%2. In addition, men are prone to getting heart failure as compared to women1. Each year, there are about 1-5 new cases of CCF per 1, 000 population and it also increased with age40. In United Kingdom, the incidence of CCF is about 0. 02 cases per 1000 per annum between the ages of 25-34. However, the incidence increased to 11. 6 cases in those above 86 years old1. The prognosis for CHF is relatively poor. Approximately 40% of individuals with CCF die within a year after diagnosis3.

There are many causes of CHF but the most common underlying causes are heart attack, coronary heart disease, and high blood pressure. Others such as cardiomyopathy, valvular heart disease and diabetes may also precipitate heart failure4. An early diagnosis of CHF is often based on the signs and symptoms which the patient is experiencing5. Other tests are needed to confirm or rule out the diagnosis. These include chest X-ray examination, physical examination, electrocardiograph (ECG), echocardiography and exercise testing.

The severity of heart failure can be classified according to the New York Heart Association (NYHA) classification system. This system consists of four classes which relate patient's symptoms to physical activities and quality of life.

Table 1: New York Heart Association (NYHA) Classification5.

Class	Patient Symptoms
I (Mild)	No symptoms with ordinary physical activity (walking and climbing stairs)
II (Mild)	Slight limitation of activity with dyspnoea to severe exertions (climbing stairs or walking uphill)
III (Moderate)	

Marked limitation of activity. Less than ordinary activity causes dypsnoea. (restricting walking distance and limiting climbing to one flight of stairs)

IV (Severe)

Severe disability, dyspnoea at rest. (unable to carry on physical activity without discomfort)

2. 2 Drug pharmacology in treatment of congestive cardiac failure

Chronic cardiac failure should be treated immediately once it is diagnosed. The goal of treatment is to improve patient's quality of life by alleviating the symptoms, improving exercise tolerance, preventing the progression of myocardial damage as well as reducing hospital admission and mortality.

Angiotensin-converting enzyme inhibitors (ACEis)

ACE inhibitors are considered as first line therapy in patients with CCF5. They bind to and inhibit angiotensin converting enzyme which subsequently inhibit the action of angiotensin I. As a consequence, the production of angiotensin II is prevented. Angiotensin II is a potent vasoconstrictor which has a direct action on kidney to stimulate the secretion of aldosterone and antidiuretic hormone (ADH). This will cause sodium and water retention. Hence, ACE inhibitors improve cardiac function and relieve symptoms of oedema by promoting sodium and water excretion41. Besides, they also increase the concentration of a potent vasodilator, bradykinin. This results in a fall in blood pressure as bradykinin is associated with the release of nitric oxide and prostacyclin. However, high levels of bradykinin also responsible for the main adverse effect of ACE inhibitors, dry cough42. Other common side

effects include hyperkalaemia, profound hypotension and gastrointestinal disturbances15. ACE inhibitors are contraindicated in patients with renal impairment even though some studies have shown that they have renal protective properties43. Example of ACE inhibitors are captopril, enalapril, and ramipril. The starting dose for ACEis should be low and the dose should be increased gradually to target doses5.

Beta blockers

Beta blockers used to be contraindicated in patients with CCF as it may worsen the condition of the heart due to its negative inotropic effect. Nowadays, beta blockers should be considered in all patients with heart failure unless contraindicated5 as they have been shown to reduce the mortality, hospitalization and the progression of heart failure7. Beta blockers should be introduced following treatment with ACE inhibitor once the patient’s condition is stable7. Only bisoprolol, carvedilol, and nebivolol are currently licensed to be used in the treatment of heart failure in UK8. Both nebivolol and bisoprolol are cardioselective where they act on beta1 receptors. On the other hand, carvedilol is a non-selective beta blocker9, 10. The mode of action of beta blockers in heart failure is poorly understood but the proposed mechanisms include antiarrhythmic action, anti-ischaemic action, and attenuation of cathecholamine toxicity as well as reduced cardiac modelling through blockade of sympathetic influences on the heart9. Besides, carvedilol has an additional antioxidant property which may be thought to slow down the process of atherogenesis by inhibiting the oxygen-free radicals11, 12. The starting dose should be low as high doses may worsen the condition of heart failure7. Over time, the dose of beta blocker

should be gradually titrated upward if the patient is well tolerated until target dose is reached5.

Diuretics

Diuretics are often used to relief the congestive symptoms and fluid retention7. Hence, they should be used in heart failure patients with the symptom of oedema7. Frusemide, a loop diuretic is the most commonly used agent in heart failure. It is considered as the first choice of drug for the long-term treatment of CCF with the advantages of improves cardiac function, exercise tolerance, as well as symptoms of breathlessness and oedema13. The main site of action is at the thick ascending limb of the loop of Henle. Furosemide acts at the Cl- binding site of Na+/K+/2Cl- co-transport and as a result, sodium reabsorption is inhibited. This promotes the excretion of sodium up to 20-25% as well as enhances water clearance13. Consequently, it reduces the blood volume thus reducing the preload on the heart. As a result, ventricular ejection is improved and the heart is able to pump more efficiently14. The most common side effect is hypokalaemia. Hence, it is important that patient’s potassium level and the renal function are closely monitored.

Aldosterone Antagonists

Patients with moderate to severe heart failure should be considered for the treatment of aldosterone antagonists such as spironolactone15. It is a potassium sparing diuretic where its action is mainly on the renin-angiotensin-aldosterone (RAA) system18. Spironolactone prevents the synthesis of basolateral Na+/K+-ATPase pump protein by acting as a competitive inhibitor at the aldosterone receptor site in the distal convoluted

tubules. As mentioned earlier, aldosterone promotes sodium and water retention and the use of spironolactone therefore inhibits sodium and water reabsorption while retains potassium. As a result, spironolactone reduces the workload of the heart and the heart is therefore able to work more efficiently18. It is often use in conjunction with other agents such as diuretic in the management of CCF44. Nevertheless, spironolactone may cause hyperkalaemia, particularly in patients with renal impairment due to the inhibition of potassium excretion. Hence, the patient's potassium level and the renal function should be closely monitored.

3. Evidence for treatment of the condition(s)

Angiotensin-Converting Enzyme Inhibitors (ACEis)

ACE inhibitor, ramipril prescribed for my patient Mr. SB was proven to be the mainstay therapy in the management of CCF. NICE and SIGN guidelines recommended that ACE inhibitor therapy should be started once the patient is diagnosed with CCF before beta blocker is initiated5, 32. It should be prescribed to the patients with heart failure due to left ventricular dysfunction as studies have demonstrated that ACE inhibitors alleviate symptoms and reduce rehospitalisation as well as slow down the progression of the disease in all NYHA classes5, 33. The benefits of ACE inhibitor in CCF can be seen based on the systemic review of 5 randomised, controlled trials which involve a total of 12763 patients. Results shown that in comparison to placebo group, long term treatment with ACE inhibitors were shown to have statistically significant reduction in mortality rate (23. 0% vs 26. 8%; p <0. 0001) as well as rehospitalisation for heart failure (13. 7% vs 18. 9%; p <0. 0001). Benefits of ACE inhibitor were evident right after the initiation of

therapy. The advantages were not affected by age, gender and other classes of drugs such as diuretics, aspirin and beta blockers36.

Other studies such as CONSENSU34, and SOLVD35 were also found that ACE inhibitirs are beneficial in the treatment of heart failure. CONSENSUS trial reported a significant reduction in term of the mortality rate during the 6-month follow up (44% vs 26%) in NYHA class IV patients while SOLVD also shown an improvement in the survival rate in the active treatment group with the absolute risk reduction of 4. 5%. At present, all the ACE inhibitors are licensed to be prescribed for the treatment of heart failure. However, there are limited evidence to support whether all the ACE inhibitors show the similar effect in reducing the mortality and hospitalisation among patients with heart failure. In a study that involved a total of 43 316 heart failure patients, ramipril was found to be superior over captopril and enalapril as both drugs were associated with 10-15% higher mortality rate as compared to ramipril37.

Other than that, ramipril is also proven to be beneficial in Mr. SB’s hypertension as studies have found that ACE inhibitors also have an antihypertensive effect. One of the adverse effects associated with ACE inhibitor is dry cough. However, it is not very common for patients to experience the side effects of ACE inhibitors such as cough and hypotension as studies shown that the withdrawal rate is similar between the treatment and placebo groups31. This support the use of ACE inhibitor for the management of CCF and hypertension in this patient as it can delay the deterioration of heart failure and also reduce the patient’s high blood pressure.

Beta blockers

Bisoprolol 1. 25 mg was initiated during Mr. SB’s stay in the hospital. Beta blockers were shown to significantly improve survival rate and reduce admission to the hospital8. The benefits of beta blockers in chronic cardiac failure were shown in the outcome from the Cardiac Insufficiency Bisoprolol Study (CIBIS), a randomised, double-blind, placebo-controlled trial which studied the effects of bisoprolol against placebo. When compared to the placebo group, bisoprolol showed a reduction in the rate of mortality with the risk reduction of 0. 8% in a 23-month period of the study. Nevertheless, the differences between the treatment and placebo groups were not statistically significant but the trial had demonstrated that bisoprolol did improve the mortality rate as well as decrease the frequency of admission to the hospital in all classes of heart failure. Besides, it is well tolerated with fewer side effects.

Five years later, CIBIS-II trial was conducted with greater number of patients (n= 2647) and the dose of bisoprolol was forcefully titrated to the maximum tolerated dose (10mg/day). The trial was terminated early due to the statistically significant improvement in total cardiovascular mortality (34%), sudden death (44%) and hospital admission (20%)22.

Beta blocker is therefore recommended by NICE and SIGN guidelines as the first line therapy in the treatment of CCF and only bisoprolol, carvedilol and nebivolol are the licensed beta blockers available for the treatment of heart failure. If the patient is already on a beta blocker before being diagnosed with CCF, the current beta blocker can be continued or changed it to another licensed beta blocker22. Based on the evidence available, the use of

bisoprolol in this patient is appropriate. However, it is important to monitor the patient’s heart rate, blood pressure and clinical status in order to make sure that beta blocker does not worsen the condition of the patient.

Diuretics

M. SB was given intraveneous furosemide 40 mg upon admission to the hospital. During his stay in the hospital, the dose of furosemide was increased to 60 mg and then replaced with tablet furosemide 60 mg on day 10. Diuretics are shown to be powerful agents used to alleviate the symptoms of fluid retention and breathlessness in patients with symptomatic heart failure13. However, evidence that support the use of diuretic in CCF was very limited. A Cochrane systematic review of small randomised controlled trials found that diuretic shows benefits in improving survival rate and reduce hospitalisation when it was compared with placebo24. In addition, there was a 75% reduction (p= 0. 03; number needed to treat (NNT) = 12) in the mortality as well as improved the exercise tolerance by 63% (p= 0. 007) based on the outcome from the meta-analysis. For every 1000 patients, about 80 deaths can be avoided in patients treated with diuretics24. All these studies conducted were rather small and the duration was short. Therefore, large and long-term placebo-controlled trials would be needed in order to further confirm the long-term benefits of diuretics in CCF patients. However, the available data did prove that diuretics are able to improve the exercise capacity and reduced mortality rate in patients with CCF25. For these reasons, the use of furosemide in this patient is justified.

Adosterone Antagonists

There is evidence that addition of aldosterone receptor antagonist such as spironolactone to the standard therapy significantly reduce the risk of morbidity and mortality among patients with heart failure. In a single large randomised controlled trial, Randomised Aldactone Evaluation Study (RALES) conducted in 1996 which studied the effect of aldosterone receptor antagonists in patients with severe heart failure, spironolactone with the dose of 25 mg daily in combination with an ACE inhibitor and a loop diuretic were shown to confer a 30% reduction in the all-cause mortality when it was compared to the placebo group with $p < 0.001$. It was also shown to reduce sudden death from cardiac-related causes and rehospitalisation for cardiac reasons by 31% and 30% respectively. In addition, there was an improvement in the NYHA classification in patients treated with spironolactone27. However, one of the major side effects of taking spironolactone is hyperkalaemia. Therefore, low dose of spironolactone (usually 25mg daily) should only be prescribed to patients who have severe heart failure (NYHA class III and IV) with left ventricular dysfunction. In addition, they should have a normal serum potassium level and renal function to begin with. Serum potassium level should be regularly monitored after the initiation of therapy30. The dose of spironolactone prescribed for Mr. SB was appropriate as the dosage given was as recommended in studies with the support of evidence. Furthermore, patient’s potassium concentration was closely monitored and it was found that there was no sign of hyperkalaemia.

Antiplatelet

During his stay in the hospital, Mr. SB also prescribed with aspirin 150 mg as an antiplatelet therapy. In a meta-analysis of four randomised controlled trials, aspirin had been proven to be effective in the primary prevention of coronary heart disease. Aspirin was able to significantly reduce myocardial infarction risk by 30% and total cardiovascular events by 15%. The benefits were largest in patients with coronary event risk greater than or equal to 1. 5% per year. Nevertheless, the use of aspirin was shown to be associated with a significant increased in the risk of major bleeding. The studies also shown that there was a 69% (95%CI, 38% – 107%) increased in the bleeding complications in aspirin treated group but the side effects are far outweighing by the benefits of the drugs46. Only low dose of aspirin (75mg-150mg) was given to the patients for the primary prevention of heart disease as the side effects of this drug are dose-related47. It is appropriate to prescribe aspirin to Mr. SB. However, the dose of aspirin should be reviewed. Since both 75mg and 150mg of aspirin were proven to be equally effective, the starting dose for this patient should be 75mg in order to reduce the dose-related side effects.

Conclusion

In conclusion, the management of patient’s CCF was found to be in line with the guidelines available as well as supported by evidences found from the studies. In addition, the condition of patients did improve during his stay in the hospital. However, the dose of aspirin 150mg should be reviewed and reduced to 75mg instead based on the recommendation from British National Formulary. It is also crucial to monitor Mr. SB’s renal profile and

electrolytes in order to detect or reduced the side effects associated with some of the drug regimen such as furosemide and beta blockers. The patient should also be counselled on lifestyle management to reduce the development of fluid overload. These include reduce the salt intake to 6g per day as well as restrict the fluid intake. Patient should also be advised to monitor the body weight regularly and inform GP if weight gain is more than 1. 5kg in 2 days.

Pharmaceutical Care Issues

Action

Output

Management of congestive cardiac failure

Ensure that the patient was treated according to the recommended guidelines such as NICE and SIGN guideline.

Ensure doses given were appropriate by referring to British National Formulary.

Guidelines checked. First line therapy: ACE inhibitor, beta blocker and diuretic were prescribed.

Doses checked and were shown to be appropriate.

Dosage of simvastatin

Comfirm the dose is appropriate.

Patient’s cholesterol and liver function test should be conducted every 3 months in order to ensure that the dose of simvastatin remains appropriate.

Patient should be advised on the risk of myopathy- report any unexplained muscle pain, tenderness or weakness.

Avoid grapefruit juice as it may increased the level of statin and leads to side effects

Dose check is comfirmed and appropriate.

Side effects of statin were not experienced by the patient.

Patient was informed and understood the interaction.

Drug interaction between beta blocker and calcium channel blocker

Combined use may enhance hypotensive effect.

Prescriber was aware regarding this issue and blood pressure of the patient had been carefully monitored

Patient also had been told to monitor signs and symptoms of hypotension such as dizziness and weakness.

Side effects of drugs

Spironolactone may cause hyperkalaemia

Frusemide may cause hypokalaemia

Monitor the patient’s potassium level regularly.

Patient’s potassium level was found to be low on day 8.

Potassium chloride was given on day 9 and the potassium level was gradually increased to normal range.

Risk of hyperkalaemia with potassium chloride

Potassium chloride should not be given as long-term treatment because one of the side effects of spironolactone is hyperkalaemia

It should only be used when the potassium level is slow

Hence, it should be stopped once the level of potassium has been normalised.

Not taken

Smoking cessation to reduce cardiovascular death

Advise of importance of quitting.

Assess interest and assist in quitting

Not taken

Dose of aspirin

According to BNF 57, the starting dose for aspirin in prevention of coronary heart disease should be 75mg

Suggest change the dose from 150mg to 75mg

Not taken

Lifestyle management

Advice the patient to reduce salt intake (6g/day) as well as restrict fluid intake

Encourage to weigh themself daily.

Inform the GP if the weight gain is more han 1. 5-2kg in 2 days.

Patient was informed and understood.