Drugs for Managing Heart Failure

Note: The doctor read most of the related slides in the lecture, the sheet is mostly about extra notes and clarifications.

Loop diuretics

Loop diuretics are used when there is heart failure with edema. Remember loop diuretics cause hypokalemia, hypomagnesaemia, hyponatremia and also cause hypovolemia; as it works on the ascending loop of henle causing inhibition of electrolytes reabsorption by 25%

Loop diuretics should be started at low doses accompanied with monitoring of all electrolytes (potassium, sodium and magnesium).

It is not allowed to combine gentamicin (used a lot by hospital to treat nosocomial infections) with furosemide as this increases ototoxicity.

If we have a patient with sulfur allergy we can't give him furosemide or Bumetanide, give him Ethacrynic acid.

Spironolactone, (used in stage 3 of heart failure)

Opposite to the thaizide and lasix (Furosemide) on their effect on potassium

Used for two reasons:

1) As a modulator to the hypokalemia that results from other diuretics.

2) Reducing the rate of remodeling of the heart muscles (related to its activity on renin-angiotensin pathway, and aldosterone and its effects on the heart)

Remember ACEI has a similar activity to spironolactone on potassium and in reducing the remodeling of heart muscles.

Spironolactone is given in advanced heart failure patients (a patient who is on diuretic, ACEI, beta-blockers and still has symptoms)

We are not allowed to combine spironolactone with ARB with ACEI as it causes severe potassium retention.

Spironolactone as a diuretic is not as strong as loop diuretics, it has an effect on blood pressure but not a strong one.

Spironolactone can cause endocrine abnormalities, one of these abnormalities is gynaecomastia (appearance of female characteristics on males), Eplerenone can be substituted for spironolactone in those patients.

Females are more LIKELY TO GET MENTAL confusion than males

Digoxin (used in stage 4 of heart failure)

It is an inotropic agent.

Although the symptoms of heart failure would be greatly reduced but the age of mortality does not really change.

The problem of heart failure is due to the low contractility of the heart, and not due to the low heart rate.

MOA : Digoxin will get attached to sodium-potassium ATP pump and inhibit its work, so there would be accumulation of sodium inside the cell, as a result the electrochemical gradient of sodium from outside to inside the cell will be reduced, so the sodium-calcium pump that rely on the influx of sodium down its electrochemical gradient won't be working, so the calcium ions will get trapped inside the cell and their concentration will increase, which will cause a stronger contraction of the muscle, in addition, calcium ions tend to get stored more in the sarcoplasmic reticulum so this will result in more calcium release from SR when an action potential happens.

Digoxin is the only effective orally taken inotropic medicine. Dobutamine is beta-1 agonist that has a positive inotropic effect on the heart and is not taken orally.

Digoxin has a narrow therapeutic index, effective dose is 0.125 mg and highest dose allowed is 0.25 mg

Here is a case, we have a patient on furosemide that as we know causes hypokalemia, do you think that the effect of digoxin will increase or decrease?

It will increase, as digoxin and potassium bind on the same part on the potassium-sodium pump, so if we have low potassium concentration, it is going to be easier for the digoxin to bind to the pump (competitive antagonism) that will cause an increase in its activity and as a result its toxicity.

Digoxin has a long half-life so it tends to accumulate in the body, which is dangerous and may cause toxicity.

Signs of digoxin toxicity include:

Starts as GI symptoms: anorexia, nausea, vomiting and diarrhea. Then the CNS is affected; Vision changes (it is called yellow and green holes, the patient will start seeing yellow and green circles), fatigue and headache. The last sign is the cardiac effects that include: premature ventricular contraction, ventricular tachycardia and fibrillation, arrhythmias and atrial tachycardia.

Digoxin is a complex drug that has a lot of drug-drug interactions, mostly with antiarrhythmic drugs. There are interactions that affect the distribution (replacing digoxin from tissue protein binding sites) this will cause an increase in digoxin concentration, and others that affect elimination.

Macrolides and tetracycline antibiotics should be avoided because they elevate digoxin serum concentration, and enhance the risk for digoxin toxicity through CYP3A4 inhibition that decreases digoxin metabolism. Although there is no direct connection between digoxin metabolism and CYP3A4, but it seems that those drugs lower the metabolism of the whole body.

I am not sure that you have to know this but the Dr mentioned this in the lecture: Warfarin also has a lot of drug-drug interactions, if you have a meal full of potassium (vitamin K is a major antagonist for warfarin), you will inhibit warfarin. Also, cyp2b12 enzyme which works on warfarin metabolism is inhibited by بابونج و مرمية. Most cases of drug toxicity are from warfarin.