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Antihypertensive drugs of pregnancy:

Usage of normal drugs of chronic HTN is controversial in pregnancy, because after few weeks or second trimester, there is decrease in the blood pressure of the pregnant lady, so no need to used them. However, after short period, pressure starts to rise again.

HTN of pregnancy is serious and must be controlled, because without monitoring it can develop into pre-eclampsia and finally to eclampsia.

Pre-eclampsia: sustained increase in blood pressure with proteinuria, must be managed, sometimes may require induced labor.

eclampsia: after pre-eclampsia , characterized by tonic chronic seizures , management is difficult .

in cases of sever (emergent) HTN in pregnancy : hydralazine is the first line drug , then labetalol , then nifedipine (with caution) ,
Note: nitroprusside leads to hypotension and pregnancy is more related to hypotension so pregnant ladies are more susceptible to develop it , and if hypotension occurs , it decreases perfusion of the baby and lead to more edema in the mother so we don't use this drug.

In mothers with chronic HTN: if she "plans" to get pregnant, she has to stop ordinary drugs: (ACE i) and ARBs (lasortan) (teratogenic) . note that they are stopped as she intends to be pregnant.

-ACEi:
Totally contraindicated in second and third trimester because of fetal renal damage
In the first semester: was not contraindicated in the past, however, they discovered that it causes teratogenicity.
ACE I contraindicated in first trimester because of malformations, in the second and third because of renal abnormalities.

-B blockers: contraindicated in early and mid trimesters, however, can be

taken at lately at pregnancy, why? Because they affect the development of the heart of the baby in the first and second trimesters , however in he third , there is no real effect.
-both propranolol and atenolol can be used , but atenolol is better.

-prazosin (alpha1 blocker) is contraindicated in pregnancy.

-ARBS totally contraindicated because of teratogenicity

Note : ACEi and ARBs are also contraindicated in lactation

Drug of choice in the treatment of chronic HTN in pregnancy is methyldopa, it can cause dizziness , if occurs , we use second line therapy which is labetalol, or calcium channel blockers (nifidipine)
Note: verapamil and diltiazem are contraindicated (they affect conductivity of the heart of the baby).

Management of pre-eclampsia: magnesium sulfate is used. Although magnesium decreases the pressure by small amounts, we use it because this substance is naturally present in our bodies so it is safer. After a week if not reduced we move to another drug like methyldopa.

There is a scale that can show the level of contraindication of drugs during pregnancy.
There are four groups: A, B, C, D

D: Totally contraindicated: ACEi , ARBs , prazosin (teratogenicity)
C: some teratogenicity, caused teratogenicity during trials in animals (if used we have to be very cautious)
B: no teratogenicity in human or animals.
A: completely safe drugs

Most important to be ware of is groups c and d.

Now back to Heart Failure:

Normally, the body try to compensate for decreased perfusion caused by heart failure by two mechanisms : sympathetic nervous system and the activity of angiotensin converting enzyme and drugs used try to control

these two processes.

CHF is a problem that we face usually in old-age people , world wide we have twenty million cases of CHF , about six millions in USA which has the highest rate mainly because of good management , so people can live with CHF for longer time.

One of the major characteristics of CHF patients, that they require recurrent hospital admission, and that lead us to the concept of management because this disease is non treatable, which means more pressure on the national economy.

Slide #6:

In HF, our goal is management of the diseases .
HF is a degenerative disease and usually ends with death after 10 to 15 years its beginning, or more by transplantation.

1-elevate the symptoms: most important symptoms are dyspnea and edema.
Edema is caused by water retention by renin angiotensin system.
If we give a treatment and caused the reduction of these symptoms , then we the patient is responding to this treatment .

2-slow diseases progression:by controlling remolding process, the much the hypertrophy the weaker the heart becomes .

3-improve survival: related to digoxin

--HF classification: (this is a kind of pathology , but we have to know it , to understand how we deal with different patients)

class one: no limitation in the function of the heart in any activity, patient has no problems but he has HF.

class two : mild limitation of activity , patient is comfortable at rest or mild exercise , problems only in severe exertion .

class three : marked limitation at any activty , only comfortable at rest , problems appear at any activity (most common).

class four: any physical activity bring symptoms and even at rest , total heart failure

this classification is important for following the progression of patient and to know severity of symptoms.

Note : 80-90% of HF patients are of the left sided type.

Slide #7 :

In cases associated with edema , we give high doses of diuretics(loop diuritics), we don't use hydrochlorothiazide because it is week .

Remember side effects of side effects : hypokalemia , hypomagnesaemia ,hypocalcaemia, hyperurecemia .

Note: Even with proper treatment , there is progression in HF , so patients ends up in using all of these drugs.

Slide #8:

It is the first line drug in all classes of HF whether we have symptoms or not .

work on both processes that cause remodeling:

1-inhibiting renin-angiotensin system and so aldosterone production

2- there is a link between aldosterone and noradrenaline released from the adrenal gland , and by inhibiting aldosterone synthesis , we decreases the sympathetic activity.

So we decrease hypertrophy and vasoconstriction and blood volume and water retention.

it will decrease symptoms(decreases water retention) remolding

Also increased amounts of angiotensin have an effect on the heart causing remolding.

In the past : inotropic agents were the first line drugs , but nowadays it is

the ACEi
when we used to start with digoxin the patient will live for 2-3 years followed by complete heart failure , however with ACEi they live for 10-15 years.
Slide #10:

When we use ACEi and B-blockers and still we have symptoms(edema and dyspnea) , we can benefit from the activity of Candesartan(ARB) which can be added to them.

ARBs: they inhibit activity of angiotensin II produced by ways other than renin angiotensin system.

The idea in HF that we use drugs in a guide line one by one

Both ARBs and ACEi cause hyperkalemia that is balanced by diuretics.

if we don't use diuretics we have to monitor hyperkalemia. Hyperkalemia by ACEI is week, because its effects is on ductal tubules, and reabsorption of potassium from there is not that much and also because of indirect inhibition of aldosterone effect, so it is not important to have diuretics to balance hyperkalemia, how ever we have to monitor it.

ARBS has the same uses of ACEi and used together usually to potentiate the effect

Note : ACEi with candesartan is not used in HTN.

Slide #11:

B blockers were contraindicated until 2000 because it has negative inotropic and chronotropic activity, after that it became a milestone in treatment HF, resulted from preventing remodeling .

It is important in remolding: by
1- b blockers have effect on renin release so on angiotensin II (this is not significant because they are used usually with ACEi that has the same job)
2- Blocking continuous sympathetic activity (causing apoptosis necrosis fibrosis leading to remolding) (main mechanism)

-bisprolol and carvidolol are always in HF and they are the only allowed B blockers to be used in HF

-Nebivolol is a new drug

-We don't know the effect of propranolol and atenolol in HF because no trials was made for them, so if you give it to your patients, this will be under your own risk.

-Remember: Deltiazem and verapamil are contraindicated in HF because of their effect on the activity on the heart.

Slide #13:

In the short term usage (first to second week) of B blockers, it may cause worsening of the HF(increased symptoms), because of decreased contractility of the heart, so we give these drugs depending on the concept of titration, which means starting at a certain dose and increasing it gradually depending on the outcome.

**Doctor here opened another set of slides that we are not given yet, so I tried to wright what I understood, you can go back to these slides when we get them.

If we start with a high dose of B blockers in HF we destroy the patient completely,
So we give them by titration, and see how much patient tolerate this treatment, also this is used in HTN but it less significant because we need less dose and effect on blood pressure appears in lower doses

In HTN we start with 50 mg/daily and we increase the dose weekly because we cannot know the effect before one week of that dose. In HTN doses above 100 will not produce further effect.

In HF we use the lowest dose with sub therapeutic effect (25 mg) and we monitor the patient, it may worse HF, then we increase weekly until we reach our desirable effect (decreased edema, dyspnea), we can reach up to 200mg/day.

In Angina we start with 50. Dosing is highest in angina we can reach 200-300 mg and thus loosing selectivity.

Good Luck :D