Role of fixed combination therapy in multiple risk patients:

Telmisartan HCTZ

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A (rather) simple choice
- one of 5 drug classes (with 1-4 doses)
- ≈ 20 possibilities

However...

- 2/3 of patients will need >1 drug
- Combination therapy
  - ↓ complexity of choice
  - ↑ patient compliance
Monotherapy titration

- Adverse effects are dose-dependent
- Proper effects of most drugs in monotherapy come with higher dose

Monotherapy titration

benefit

adverse effects

Combination therapy

- no dose increase → less adverse effects
- better effect

Combination

Combination therapy

Combination

benefit

adverse effects

Monotherapy titration vs combination therapy

- 10.968 patients in 42 studies
- Antihypertensive effect:
  - Doubling dose: ↑ 20% effect
  - Combination therapy: ↑ 100% effect

Monotherapy titration vs combination therapy

Ratio of observed to expected incremental blood pressure-lowering effects of adding a drug or doubling the dose according to the class of drug

Are adverse effects common / important?

- review of 354 studies
- administering ½ of standard dose reduces the incidence of adverse effects by:
  - CCB: ↓ 81% (peripheral edema)
  - thiazids: ↓ 80% (hypokalaemia)
  - BB: ↓ 27% (bradycardia / fatigue)

Law et al, BMJ 2003
Advantages of FIXED combinations

- How many options for patients requiring 3 medications?
- Based on pure mathematics (only for the “strong” 5!):
  - 6 different CCB; 16 possible starting doses
  - 5 different diuretics; 8 possible starting doses
  - 5 different BB; 11 possible starting doses
  - 7 different ACEI; 16 possible starting doses
  - 6 different ARB; 11 possible starting doses

- Three prescription scenarios and number of possibilities:
  - 1 dose / drug ~ 3000
  - Lowest and middle dose / drug; sequence not important ~ 35.000
  - Lowest and middle dose / drug; sequence IS important > 200.000!

Dresser et al, Curr Opin Cardiol 2010
Simple algorithms with fixed combinations

Initial therapy with a low-dose ACE/diuretic or ARB/diuretic combination

**IS BLOOD PRESSURE CONTROLLED?**

- **Yes**
  - Continue with current therapy

- **No**
  - Up-titration of combination therapy successively to the highest dose
    
    - **Yes**
      - Continue with current therapy
    
    - **No**
      - Add calcium channel blocker and up-titrate
        
        - **Yes**
          - Continue with current therapy
        
        - **No**
          - Add an α-blocker, β-blocker or spironolactone

STITCH study, Hypertension 2009
Efficacy in BP lowering vs valsartan is continuously higher during 24-hour period
Significantly stronger in last 6 hours period
**Telmisartan HCT in 24 h efficacy**

- Significant differences in BP lowering vs valsartan
- Each mmHg brings multi-fold benefits
Conclusion

In high-risk, overweight/obese patients with hypertension and type 2 diabetes,

- T/HCTZ provides significantly greater BP lowering versus V/HCTZ
- throughout the 24-hour dosing interval,
- particularly during the hazardous early morning hours.
Figure 1. Study design. E=entry; R=randomization; T=telmisartan; HCTZ=hydrochlorothiazide; A=amlodipine; ABPM=ambulatory blood pressure monitoring.
Telmisartan HCT in ISH

- Efficacy in BP reduction higher during 24 h vs amlodipin
- Sinergistic effect of 2 agents with different mode of action

*Neldam S et al, The American Journal of Geriatric Cardiology 2006; VI:4;3151-160*
Patient adherence to therapy is crucial!
• The significantly superior SBP reductions with T+H during the morning and daytime periods, provided a significantly ($p<0.0001$) larger mean reduction with T+H for the 24-hour period as a whole.

• The greater reductions in BP seen in our study with T+H compared with A+H are likely due to differences between the mechanism of action of telmisartan and HCTZ.

• CCBs, on the other hand, have intrinsic natriuretic properties and are thus less likely to provide additive benefits from combination with HCTZ.

• Therefore, patients with isolated SH may benefit from initial treatment with Telmisartan+H combination therapy.
Let’s make ours and patient’s life simpler and easier!
Thank you