ACEI danas

ACEI today

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Učinci angiotenzina II

KRVNE ŽILE	▪ vazokonstrikcija
SRCE	▪ inotropni i kronotropni učinak ▪ koronarna vazokonstrikcija
NBŽ	▪ lučenje aldosterona i adrenalina
MOZAK	▪ lučenje vazopresina ▪ stimulacija centra žeđi ▪ povećana simpatička aktivnost
BUBREG	▪ vazokonstrikcija (E>A) ▪ kontrakcija mezang. stanica ▪ reapsorp. Na u proks. tubulu ↑ ▪ sekrecija K u dist. tubulu ↑ ▪ lučenje renina ↓
TROMBOCITI	▪ stimulacija adhezije i agregacije

ENDOTELNE STANICE	▪ inaktivacija NO (inhibicija eNOS) ▪ ekspresija oxLDL receptora
SIMPATIČKI SUSTAV	▪ povećanje periferne noradrenergičke neurotransmisije ▪ lučenje kateholamina iz srži NBŽ
FIBRINOLIZA	▪ ekspresija PAI-1 ↑
UPALA	▪ aktivacija i migracija makrofaga ▪ ekspresija adhezijskih molekula ↑(VCAM, ICAM, P-selektin) citokina (IL-6), kemotaktičnih proteina (MCP-1)
TROFIČKI UČINCI	▪ hipertrofija kardiocita ▪ stimulacija VSMC ▪ stimulacija proto-onkogena i MAPK-a ▪ stvaranje faktora rasta ↑ (TGF-ß1, PDGF, IGF-1, bFGF) ▪ sinteza proteina ECM ↑ (fibronektin, kolagen I i III, laminin ß1-ß2)
ATEROSKLEROZA	▪ peroksidacija lipida, stvaranje superoksida, stimulacija NADH/NADPH

Angiotensin II Effects

BLOOD VESSELS	▪ vasoconstriction
HEART	▪ Inotropic and chronotropic effects ▪ coronary vasokonstriction
SUPRARENAL GLAND	▪ secretion of aldosterone and adrenaline
BRAIN	▪ secretion of vasopressin ▪ stimulating the thirst center ▪ increased sympathetic activity
KIDNEY	▪ vasoconstriction (E>A) ▪ Contraction of mesangial cells ▪ re-absorption Na into prox. tubule ↑ ▪ secretion K into dist. tubule ↑ ▪ secretion of renin ↓
THROMBOCYTES	▪ stimulation of adhesion and aggregation

ENDOTHELIN CELLS	▪ NO inactivation (eNOS inhibition) ▪ expression oxLDL receptors
SYMPATHETIC SYSTEM	▪ Increasing peripheral noradrenergic neurotransmission ▪ Secretion of catecholamine from core of suprarenal gland
FIBRINOLYSIS	▪ Expression PAI-1 ↑
INFLAMMATION	▪ Activation and migration of macrophage ▪ Expression of adhesive molecules ↑(VCAM, ICAM, P-selectine) cytokine (IL-6), chemotactic proteins (MCP-1)
TROPHIC EFFECTS	▪ Cardiocyte hypertrophy ▪ Stimulation of VSMC ▪ Stimulation of proto-onogen i MAPK-a ▪ Creation of growth factor ↑ (TGF-ß1, PDGF, IGF-1, bFGF) ▪ Protein synthesis ECM ↑ (fibronectin, collagen I and III, laminin ß1-ß2)
ATHEROSCLEROSIS	▪ Lipid peroxidase, creation of superoxide, stimulation of NADH/NADPH

Farmakologija ACE inhibitora

- Mogu biti podjeljeni s obzirom na različitu **apsorpciju**, **vezanje o bjelančevine plazme i o tkiva**, **poluživot** i način dostupnosti lijeka – **svi lijekovi ove klase slično snižavaju arterijski tlak**
- Osim kaptoprila i lizinoprila svi su prolijekovi
- Strukturno su različiti; razlikuju se po sulfhidrilnom, fosfirilnom ili karboksilnom postraničnom lancu
- lipofilnost

Pharmacology of ACE Inhibitors

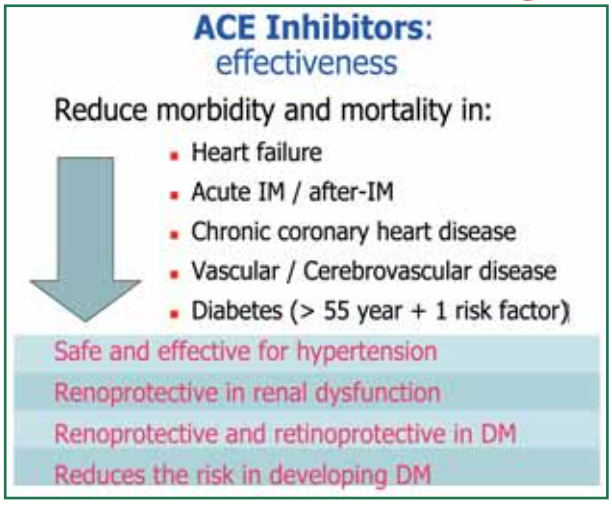
- Can be divided according to various **absorption**, **linking of proteing plasma and body cells**, **half-life** and type of access to medication– **all medication of this class reduce blood pressure in a similar manner**
- Besides captopril and lisinopril, all are prodrugs
- Structurally are various; differ according to sulfhydryl, phosphoryl or carboxyl latheral chain
- lypophility

Mehanizam djelovanja ACE inhibitora

- **Neurohumoralni učinci**: ACE – pluripotentna serinska proteaza (konverzija AG I u AG II; degradira bradikinin – BK stimulira produkciju NO)
- **"Angiotenzinski bijeg"** kod dugotrajne upotrebe ACE inhibitora
- NSAID mogu umanjiti učinkovitost ACEI
- ACEI umanjuju refleksni odgovor SNS

Mechanism in ACE inhibitor action

- **Neurohumoral effects**: ACE – pluripotent serine protease (conversion AG I to AG II; degrades bradykinin – BK stimulates production of NO)
- **"Angiotensin escape"** for long-term use of ACE inhibitors
- NSAID can reduce the effectiveness of ACEI
- ACEI reduces the reflex response of SNS



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