Medicine

Nephrology

5th year – lecture 6

الدكتور

محمد يونس العطبي

الاختصاص الدقيق بأمراض وزرع الكلى

اختصاص الطب الباطني

MBChB, FICMS (Medicine), FICMS (Nephrology), CABMS (Nephrology)

DRUGS AND THE KIDNEY

The kidney is susceptible to damage by drugs because it is the route of excretion of many water-soluble compounds, including drugs and their metabolites.

Mechanism of drugs induced renal dysfuctions:

Pre-renal: Impaired perfusion of the kidneys can result from drugs that cause:

- Hypovolaemia:
  (a) Potent loop diuretics such as furosemide, especially in elderly patients
  (b) Renal salt and water loss, such as from hypercalcaemia induced by vitamin D therapy.
- Decreased renal blood flow (e.g. ACE inhibitors particularly in the presence of renal artery stenosis).

Renal: Several mechanisms of drug-induced renal damage exist and may co-exist.

- **Acute tubular necrosis:** aminoglycosides (e.g. gentamicin, streptomycin), amphotericin B , paracetamol overdose , radiographic contrast media. The combination of aminoglycosides with furosemide is particularly nephrotoxic.
- **Acute interstitial nephritis** :This cell-mediated hypersensitivity nephritis occurs with many drugs, including penicillins, sulphonamides and NSAIDs .
- **Membranous glomerulonephritis**, e.g. penicillamine, gold

Post-renal

- **Retroperitoneal fibrosis** with urinary tract obstruction can result from the use of drugs (methysergide, ergot derived ergotamine , dopamine receptor agonists (cabergoline, bromocriptine, pergolide), methyldopa, hydralazine, beta-blockers (proctolol).
- **Tubular obstruction** (crystal formation) : Aciclovir , sulphonamides.

NSAIDs

- Sodium and water retention : because of reduction of prostaglandin production since **prostaglandins** play an important role in regulating renal blood flow.
- Acute kidney injury : due to Acute tubular necrosis resulting from hemodynamical effect of vasoconstriction via reduced prostaglandin production
- Acute interstitial nephritis :because of hypersensitivity reaction
- Hyperkalaemia : decreased renal excretion of K because of low renal renin and low aldosterone secretion .
- Papillary necrosis
- Nephrotic syndrome: because of membranous glomerulopathy or minimal change nephrotic disease.
- Analgesic nephropathy is now a rare complication of long term use.

ACE inhibitors /ARBs

- Physiology of Angiotensin II: Angiotensin II constricts both the afferent and efferent arterioles, preferentially efferent arteriole vasoconstriction.
- Impairment of angiotensin II mediated arteriole dilatation and fall in afferent arteriolar flow during renal hypoperfusion as in hypovolemia or bilateral renal artery stenosis, these hemodynamic changes can drop glomerular hydrostatic pressure to such a degree that the GFR will decrease.
- **Prevention and Management:** withdraw in renal hypoperfusion

Radiocontrast media

- High osmolarity, medullary vasoconstriction, lead to increase active transport in thick ascending loop of Henle thereby increasing O_2 demand ,lead to hemodynamical cause of AKI .
- The pathophysiology of contrast-induced nephropathy (CIN) is based on three interacting mechanisms: **medullary ischaemia**, **formation of reactive oxygen species and direct tubular cell toxicity**.
- **Prevention and Management:** Hydration (oral fluid or IV saline) with periprocedure N-Acetylcysteine (NAC) .