

DRUGS AND KIDNEY

Though they constitute less than 1% of the total body mass, the kidneys receive approximately 20% of the total cardiac output out of which 90% is distributed to the renal cortex. Hence the renal tubules and interstitium are maximally exposed and vulnerable to toxin and drug-induced injury. Early and prompt recognition of drug induced renal injury is crucial since it can be easily curtailed and even reversed by stopping the intake of the offending drug.

The list of drugs with adverse effects on the kidney is exhaustive. However we would restrict only to a few, but very harmful ones. Drug induced renal injury can be broadly classified into two categories:

- 1) Glomerular disease
- 2) Tubulo-interstitial disease

DRUG-INDUCED GLOMERULOPATHIES	DRUGS AND INTERSTITIAL NEPHRITIS
MINIMAL CHANGE DISEASE NSAIDs, Rifampin, Ampicillin, Interferon α	ANTIBIOTICS β lactams, Sulphas, Quinolones, Vancomycin, Erythromycin, Rifampicin, Ethambutol, Acyclovir
MEMBRANOUS NEPHROPATHY Penicillamine, Gold, Captopril, Mercury, Chlormethiazole	NSAIDs & COX-2 INHIBITORS
FOCAL SEGMENTAL GLOMERULOSCLEROSIS Heroin	DIURETICS Thiazides, Frusemide, Triamterene
PROLIFERATIVE GN WITH VASCULITIS Allopurinol, Penicillin, Sulfonamides, Thiazides, i.v. Amphetamines	ANTI-CONVULSANTS Phenytoin, Carbamazepine, Valproate
PAUCI-IMMUNE NECROTIZING GLOMERULONEPHRITIS Ciprofloxacin, Hydrallazine	MISCELLANEOUS Captopril, H2 Receptor blockers, Omeprazole, Allopurinol, Indinavir

NSAIDs & KIDNEY

Pain killers have been the major cause of acute and chronic renal injury since time immemorial. When used over long periods (even short term use may cause ARF) they cause irreversible renal damage, which can progress to CRF. The dreaded offenders are propionic acid derivatives like ibuprofen, naproxen, etc.

In NSAID induced renal injury, nephrotic syndrome and ARF frequently coexist due to a combination of acute interstitial nephritis and a glomerular lesion similar to minimal change disease. Membranous nephropathy may occur as an idiosyncratic reaction.

NSAID induced tubulointerstitial nephritis is common in elderly people, perhaps because of the higher incidence of arthritic disorders and the subsequent abuse of pain-killers. Acute allergic interstitial nephritis should not be confused with the acute vasomotor renal insufficiency, which can occur in patients with preexisting underperfusion of the kidney.

The luckier aspect of NSAID induced injury is that stopping the drug usually results in complete reversal of renal dysfunction, at least in early stages.

Often simple clinical disease scenarios are drastically affected by the use of NSAIDs. For example a very common presentation is that of a controlled stable hypertensive going to a dentist, is advised 5 days of NSAIDs, following which he develops sudden worsening of hypertension (due to sodium retention). This

patient may also suddenly present with flash pulmonary edema (due to fluid retention) or (less commonly) with sudden, severe hyperkalemia which may even lead to sudden cardiac death.

THE EFFECT OF ANTIBIOTICS

Cases of antibiotic induced renal injury are usually observed in the hospital setting during treatment of serious infections. The onset is within several days to weeks of initiation of antibiotic therapy. It manifests as rash, eosinophilia and eosinophiluria, as well as sterile pyuria, hematuria, and modest proteinuria (usually <1 g/day). Unlike in NSAID-induced allergic interstitial nephritis, nephrotic range proteinuria is very rare. If a renal biopsy is performed, eosinophils can be seen as a component of the interstitial nephritis. Occasionally, ill-defined granulomas are seen.

Amongst antibiotics, **RIFAMPIN** is unique in that the interstitial nephritis generally occurs when the antibiotic is reintroduced after an interval. Furthermore, the interstitial nephritis associated with it does not manifest with eosinophilia. In some cases, rifampin-associated interstitial nephritis has been reported to show casts containing immunoglobulin light chains in tubular lumens without any evidence of myeloma in the patient. Flu like symptoms, flank pain, hypertension, and oliguric acute renal failure are common. In some patients, circulating anti-rifampin antibodies and IgG deposits along the tubular basement membranes have been reported.

CONTRAST INDUCED NEPHROPATHY

Another important cause of ARF is acute allergic response to i.v. contrasts used in various radio-diagnostic procedures. They cause intra-renal vasoconstriction resulting in acute ischemic pre-renal ARF. This effect is dose related & is characterized by acute onset within 24–48 hrs, peak in 3–5 days and resolution by a week. It is common in CKD patients, diabetics, CCF patients, hypovoleemics, patients with Multiple myeloma, etc.

The solution is reduction in the use of non ionic dyes. Gadolinium or CO₂ contrasts are much safer. The use of saline infusion / Soda bicarbonate is beneficial. N-Acetylcysteine has been shown to play a protective role, but effects are poorly documented.

ACE INHIBITORS & ANGIOTENSIN RECEPTOR BLOCKERS

After the exhaustive list of drugs causing adverse effects on the kidneys, it would only be fair enough to mention about the family of drugs having beneficial effects. ACE inhibitors and Angiotensin receptor blockers play this role.

ACE inhibitors slow the progression of CKD, reduce proteinuria and stabilize & improve kidney function besides exerting beneficial effects on the heart, which indirectly contribute, by improving the blood supply and thus the afferent arteriolar blood pressure. The only contraindication to their use is the presence of bilateral renal artery stenosis.

ARBs reduce proteinuria, the time required for doubling of creatinine and also the time to dialysis.

The prophylactic use of ACE inhibitors in Type-II Diabetes Mellitus preserved kidney function for over 6 years in normotensives without microalbuminuria

- Levi et al : Annals of Internal Medicine 1998

Dual blockade may offer additional renal and CVS protection in Type – I Diabetes with Diabetic Nephropathy

- Parving H.H. JASN 2003

Thus combined use of ACEIs + ARBs is the key to controlling the progression of renal disease.

To conclude the article we would like to share a list of nephrotoxic drugs to be avoided and corresponding safe drugs to be used in existing kidney disease patients and also as a preventive measure because your prescription can make a difference.....

CATEGORY	DRUGS TO BE AVOIDED IN RENAL FAILURE	DRUGS SAFE IN RENAL FAILURE
PAIN KILLERS	NSAIDs- Brufen, Indomethacin, Piroxicam, Diclofenac, Nimesulide Ointments- Volini gel, Pirox gel, Dicloran gel, Nise gel COX2 inhibitors- Celecoxib, Rofecoxib, , Valdecoxib, Aceclofenac Aspirin (unless used in heart or brain disease), Analgin, Novalgin, Baralgin	Paracetamol 650mg (Crocin, Lanol ER) Morphine, Tramazac, Fortwin, Proxyvon / Spasmoproxyvon, Ultracet
ANTIBIOTICS	Aminoglycosides- Gentamycin, Amikacin, Netilmicin, Streptomycin Cephalosporins - Cephaloridine, Cefazoline Tobramycin, Septran, Sulfas, Tetracyclines except Doxycycline	Penicillins- Penicillin-G, Ampicillin, Amoxycillin Cephalosporins- Cephalexin, Cephadroxil, Cefotaxime, Cefipime, Ceftazidime, Cefuroxime Quinolones- Ciprofloxacin, Norfloxacin, Levofloxacin Erythromycin, Doxycycline
DIURETICS	Acetazolamide (Diamox), Spironolactone	Frusemide, Torsamide (Dytor), Thiazides
ANTIDIABETICS	Metformin, Pioglitazone	All other classes of drugs are safe
OTHERS	Proctoclysis enema, Eno salt	Simple enema, Neotomic enema, Glycrine syringe enema

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