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Research article

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Drugs effect on renal damage or GFR

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ABSTRACT

Kidney is the one of most important organ in our body for excretion or elimination or filtration. It excrete waste material, nitrogenous waste some drugs etc. In these study, we study different types of drugs are involved in the renal damage such as NSAIDS ,antibiotics ,diuretics , antiviral, antiepileptic etc. these drugs mainly effects on the GFR .Due to increase of exposure of these drugs cause some renal disease or renal damage.

Keywords: Renal GFR, Drugs, Acute interstitial nephritis, CKD, Analgesic nephropathy, Prostaglandins

INTRODUCTION

KIDNEY

It is major excretory organ in the body .These are appear in reddish brown in colour& bean shaped structure. Each kidney of adult human measures 10-12cm in length, 5-7cm width, 2-3cm in thickness of with an average weight of 120-170gms.

On an average kidneys are filtered the amount of blood is 1100-1200ml/min and it is known to be GLOMERULAR FILTRATION RATE.

The normal GFR per minute- 1.1-1.2lit.

The normal GFR per day -180lit.

Abnormal ranges in the GFR is indicates to renal damage or kidney failure. Some drugs are acts on renal filtration it alters the GFR rate.

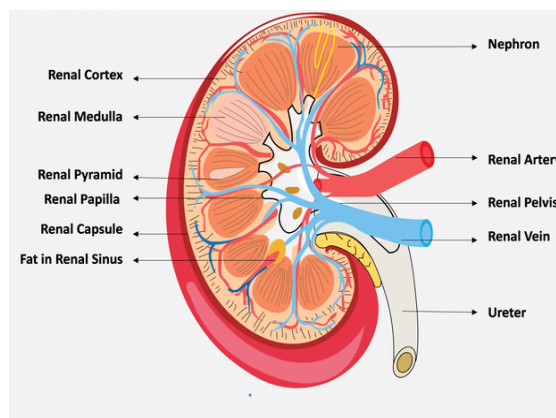


Fig 1: Internal anatomy of kidney

Some drugs are involved in damaging of the renal functions:

S.NO	CLASS OF DRUGS	EXAMPLE
1	NSAIDS	Ibuprofen
2	ANTIBIOTICS	Aminoglycosides
3	DIURETICS	Furosemide
4	ANTI HYPER LIPIDEMICS	Fibrates, statins
5	PROTAN PUMP INHIBITORS	Pantaprazole
6	ANTIDIABETICS	Sulfonylurease
7	ANTIVIRAL DRUGS	Acyclovir
8	ANTIEPILEPTIC	Phenytoin gabapentin
9	COX -2 INHIBITORS	Celecoxib
10	BIPOLAR DISEASE DRUG	Lithium

1) PAINKILLERS

Long-term expose to certain painkillers can damage the small filtering blood vessels in the kidney .This is called ANALGESIC NEPHROPATHY. It leads to chronic kidney problems.

IBUPROFEN

MECHANISM OF ACTION -1

Long-term [or] Heavy use of ibuprofen can cause chronic kidney disease is chronic interstitial nephritis.¹ Ibuprofen and other NSAIDS block a process in the body called the COX-Pathway. The COX-Pathway is involved in creating pain and swelling. But it is also involved in helping blood to flow to the kidney. Blocking the COX-Pathway can narrow blood vessels leading to the kidneys, it lead to less oxygen reaches the kidneys. And that can cause Acute kidney injury. Acute kidney injury can happen with any NSAIDS including ibuprofen.² The risk for kidney damage is higher for adults over 60 and people who leave CKD. Ibuprofen is harder on the kidneys than acetaminophen. Acetaminophen does not have the same effect on the COX-Pathway as ibuprofen. Exposure of NSAIDS is associated with higher risk for an incident estimated glomerular filtration rate [eGFR] below 60% and an eGFR decline of 30% [OR] Greater. Adverse renal effect from NSAIDS are caused by two distinct pathological studies.

A) AKI from NSAIDS:

- i) NSAIDS decreases the renal blood flow, it leads to decreases the prostaglandins, which regulate the vasodilation at glomerular level.
- ii) NSAIDS distinct the compensatory vasodilation response of renal prostaglandins to vasoconstrictor hormones released by the body.³
- iii) Inhibition of renal prostaglandins results in acute deterioration of renal function after ingestion of NSAIDS.

B) AKI IS ACUTE INTERSTITIAL NEPHRITIS:

- i) Presence of an inflammatory cell infiltrate in the interstitium of renal .
- ii) AIN is caused by an immunological reaction after NSAIDS exposure of about a week.

MECHANISM OF ACTION -2

Ibuprofen inhibits COX pathway, it decreases the prostaglandins(PGs) synthesis. Especially decreases the PGE2 & PGI2. It cause vasodilation in renal then it decreases GFR and ERPF (Effective renal plasma flow).

2) DIURETICS

MECHANISM OF ACTION

Diuretics may be hampered because of reduced renal blood flow.

Loop diuretics decreases the effective circulating volume through vasodilation or diuresis and may cause a decrease in renal blood flow and GFR.⁴

Loop diuretics acidify the urine and there by actually increase the aggregation of TAMM-HORSFALL protein in the tubules, thus worsening tubular blockage .they may cause electrolyte abnormalities and metabolic alkalosis.⁵

3) ANTIBIOTICS

EX: AMINOGLYCOSIDES – Protein inhibitory antibiotics

MECHANISM OF ACTION

Most severe side effect of aminoglycosides is nephrotoxicity .it can cause renal tubular dysfunction and increase in serum creatinine

Larger the number of constituent NH₂ group on aminoglycosides molecule are more chances for it's inherent nephrotoxic potential .

Nephrotoxicity results in the increase serum creatinine levels(>1.5mg/dl).

It is caused by the inhibition of an intracellular lysosomal phospholipase -A₂ in renal brush-border.

It leads to lysosomal distention ,rupture and release of acid hydrolases and the free aminoglycoside into the cytosol. This free drug binds to other cellular organelles .

4). BIPOLAR DISEASE DRUG

EX-Lithium

MECHANISM OF ACTION-1

Lithium is handled by kidney in much the same way as sodium .

Most of the filtered lithium ions are reabsorbed in PCT (proximal convoluted tubule), when sodium ions are restricted , a larger fraction of filtered sodium ions are reabsorbed so is as lithium ions.

A major biochemical action of lithium in the kidney is competition with magnesium , there by inhibiting magnesium – dependent G-proteins that activates vasopressin -sensitive adeny cyclase .

Lithium nephrotoxicity can be divided into three main categories.

- I) Nephrogenic diabetes insipidus (NDI)
- II) Acute intoxication
- III) Chronic renal disease

Lithium inhibits the action of vasopressin (ADH) leads to decreased urine osmolality and increased urine volume

(polyurea). Reduced GFR may some times occurs at early stages after initiation of lithium therapy.

S.NO	DRUG	EFFECT
1.	ANTIHYPER LIPEDEMICS	Atorvastatin reduction in proteinuria and glomerular sclerosis with out influencing lipid levels or renal function this leads to decreased (TGF-beta bgr) transforming growth factor -beta bgr gene expression and less glomerular and tubulointerstitial macrophage accumulation. Statin therapy slows the decline GFR
2.	PROTON PUMP INHIBITOR	It may triggers the acute interstitial nephritis ,prolong use of PPIs may increase the risk of CKD,ESRD (END STAGE RENAL DISEASE)increase the risk of estimated GFR, and increase the serum creatinine levels . Pantaprazole may cause the interstitial inflammation and eosiniphil infiltration in kidney. Lansoprazole aggravated the tubular damage and further increased the elevated levels of the serum creatinine. ⁶
3.	ANTIVIRAL DRUGS	These drugs may cause direct renal tubular toxicity . Acyclovir may also cause the crystal nephropathy by the formation of crystal deposition in the kidney may promote the development of renal failure. Renal injury associated with antiviral drugs involved in the diverse processes having effect on the renal transporters as well as renal tubular cells. ⁷
4.	ANTI EPILEPTICS	Renal tubular acidosis and urolithiasis were reported with acetazolamide and topiramate. ⁸ Renal glomerular and tubular markers increases they are Urinary N-Acetyl-beta-glucosamimidase(NAG) to urinary creatinine, urinary malondialdehyde to creatinine. Gabapentin mostly excreted by the kidney, the plasma levels of gabapentin increases it leads to decrease renal clearance.
5.	COX -2 INHIBITORS	They can cause acute decline in renal function and GFR. COX-2 Is constitutively expressed in renal tissues of all species. Rofecoxib and celecoxib procedure qualitative changes in urinary prostaglandin excretion , GFR. ⁹
6.	ANTIDIABETICS	Pharmacokinetics of antidiabetic drugs may be altered, once the GFR is <60ml/min. Risk of hypo glycemia associated with sulfonyl urea and glinide therapy is further increased in the presence of renal impairment.

CONCLUSION

These type of drugs are followed based on prescription if any miss use and wrong administration and may chance of increasing the toxicity to the body and alter the renal functioning.

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