The Renal System

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Topics for Discussion

• Function
• Anatomy
• Physiology
• Pharmacology
• Pathophysiology
Renal Function

- Removal of waste products - urea and uric acid
- Maintenance of fluids & electrolytes
- Acid-base balance
- Endocrine functions:
  1. Blood pressure – Renin-angiotensin-aldosterone system
  2. Haemoglobin – Erythropoeitin
  3. Calcium & phosphate – Vitamin D activation
Renal Anatomy
Renal Anatomy

- Each kidney has outer cortex and inner medulla.
- Urine is formed within functional subunits known as nephrons.
- Each nephron contains a glomerulus, consisting of a tuft of capillaries with an afferent and efferent arteriole.
- The glomerulus is surrounded by epithelium of the Bowman’s capsule.
- Glomerulus and Bowman’s capsule form renal corpuscle.
Renal Anatomy

- This initial filtrate is then modified by a variety of secretory and reabsorptive processes as it passes through:
  1. **Proximal convoluted tubule**
  2. **Loop of Henle**
  3. **Distal convoluted tubule**
  4. **Collecting duct**

- The glomeruli and convoluted tubules lie within outer cortex and loop of Henle and collecting duct extend into medullary region.

- End product, urine, is delivered via **renal pelvis** to **ureter**.
Regulation of Fluids & Electrolytes

- Fluid balance is the concept of homeostasis, that the amount of fluid lost is equal to the amount taken in.
- For the normal function of the body it is vital that fluid balance is maintained.
- **Euvolaemia** is the state of normal body fluid volume.
- The major source of fluid loss is urine.
- Fluid loss is regulated in the kidney hormonally. Largely through **RAAS** and **ADH**.
Hormonal Regulation

Renin-angiotensin-aldosterone system

**Renin**
- Secreted from **juxtaglomerular apparatus** – macula densa
- Secreted in response to renal hypoperfusion
- Conversion of angiotensinogen to angiotensin I
- **Direct Effects**
  - Vasodilatation of afferent arteriole
  - Direct Na⁺ loss

**Angiotensin II**
- Very potent vasoconstrictor of peripheral & efferent arterioles
- Stimulates aldosterone secretion

**Aldosterone**
- End product of RAA axis
- Produced by adrenal cortex
- Acts on DCT causing reabsorption of Na⁺ & water
- Increases ECF → increases blood pressure

Increases ECF → increases blood pressure
Hormonal Regulation
Antidiuretic hormone

- Secreted from posterior pituitary
- Secretion is ↑ if:
  1. ↑ osmolality (ECF)
  2. ↓ volume
  3. ↓ atrial pressure
- Promotes water reabsorption in the distal convoluted tubule and collecting duct
- Also known as vasopressin – a direct vasoconstrictor
Regulation of Fluids & Electrolytes

- Na\(^+\) in particular is the major driving force of fluid shifts in the body – it maintains ECF volume.
- Therefore it is hugely important to maintain an appropriate Na\(^+\) balance.
- 99% of Na\(^+\) filtered in the glomerulus is reabsorbed.
- Transport proteins in the renal tubule mediate Na\(^+\) reabsorption.
- Na\(^+\) concentration gradient along the tubule allows sodium to move into tubule cells. The gradient is maintained by the Na\(^+\)/K\(^+\) ATPase pump.
- Again maintenance is controlled hormonally, largely by aldosterone counteracted by Atrial Natriuretic Peptide.
Acid Base Regulation

• H⁺ levels are regulated through two buffering systems:
  – Chemical buffers – binds to H⁺ e.g. Bicarbonate buffering system
  – Physiological buffer – controls excretion of acids or bases (kidneys) or volatile acids (lungs)

• Bicarbonate buffering system:
  – CO₂ + H₂O ↔ H₂CO₃ ↔ H⁺ + HCO₃⁻

• The kidney acts as a physiological buffer:
  – When pH is low excess H⁺ ions are secreted in the tubules via the Na⁺/H⁺ exchanger and more bicarbonate is reabsorbed.
  – When pH is high less bicarbonate is reabsorbed.
Assessment of Renal Function

Measurement of plasma [urea] and [creatinine]

Measurement of GFR

Creat. Clearance = UV/P

U = urinary [creatinine]
V = urinary output in 24 hours
P = plasma [creatinine]
GFR

• Normal values are:
  • ♂ 90-110 ml/min
  • ♀ 80-125 ml/min
• In clinical practice an estimated GFR (eGFR) is provided based on:
  1. Plasma [creatinine]
  2. Age
  3. Gender
  4. Ethnicity
Renal Pharmacology

Proximal Convoluted Tubule
- Glucose, bicarbonate, amino acids reabsorbed
- 2/3 of sodium reabsorbed

Collecting Duct
- Stimulation of aldosterone receptors → Na⁺ reabsorption & K⁺ secretion

Descending Loop of Henle
- Permeable only to water

Distal Convoluted Tubule
- 10% of NaCl reabsorbed
- Ca²⁺ excretion is regulated by PTH

Ascending Loop of Henle
- Impermeable to water
- Active reabsorption of Na⁺, K⁺ and Cl⁻ mediated by Na-K-2Cl co-transporter
Sites of Diuretic Effect

Mode of Action
Inhibits Na-K-2Cl co-transporter in thick ascending limb of loop of Henle.
↓ reabsorption of Na\(^+\), K\(^+\) & Cl\(^-\)
Diuresis – increased urine output

Indications
Pulmonary oedema due to LV failure
Chronic heart failure
Resistant hypertension

Contra-indications
Antihypertensives
NSAIDs
Aminoglycosides
Thiazide diuretics

Adverse Effects
Electrolyte
- Hyponatraemia, hypokalaemia, hypocalcaemia
Metabolic
- Hyperglycaemia, hyperuricaemia

Loop Diuretics
Furosemide, Bumetanide
Mode of Action
Inhibits the reabsorption of Na\(^+\) & Cl\(^-\) in the cortical diluting segment of DCT.
Enhances Ca\(^{2+}\) reabsorption in the distal tubule.
Natriuresis and ↓blood volume and pressure.

Indications
Hypertension
Mild to moderate heart failure

Interactions
Other antihypertensives
Antidiabetic drugs
NSAIDs
Other drugs causing hyponatraemia

Adverse Effects
Hyperuricaemia, hyperglycaemia
Hypokalaemia, hyponatraemia, hypomagnesaemia
Postural hypotension, impotence

Thiazide Diuretics
Bendroflumethiazide
**Mode of Action**

- Aldosterone-dependent potassium sparing diuretics.
- Inhibits $\text{Na}^+ / \text{K}^+$ exchange in distal tubule and collecting duct.
- Promotes $\text{K}^+$ retention and $\text{Na}^+$ and water loss.
- Hypotensive effect.

**Indications**

- Oedema in CCF
- Ascites
- Primary hyperaldosteronism
- Nephrotic syndrome

**Contra-indications**

- Severe renal impairment
- Addison’s disease

**Adverse Effects**

- Hyperkalaemia
- Acute kidney injury
- Gynaecomastia, impotence and testicular atrophy with *spironolactone*
Urinary Tract Infections

Lower UTI – **Cystitis**
Frequency, dysuria, urgency, suprapubic pain, haematuria

Upper UTI – **Pyelonephritis**
High fever, rigors, vomiting, loin pain

**Organisms**
- *E. coli*
- *Staphylococcus saprophyticus*
- *Proteus mirabilis*

**Trimethoprim**
Bacterial dihydrofolate reductase inhibitor
Limits bacterial reproduction

**Nitrofurantoin**
Inhibits bacterial enzymes involved in carbohydrate metabolism and cell wall synthesis
Acute Kidney Injury

Reduce in GFR resulting in rise in urea and creatinine
Reduced urinary output

Pre-renal
- Acute reduction in renal perfusion
- Hypovolaemic shock, acute cardiac failure, obstruction of renal vasculature
- Compensatory mechanisms result in increased urine osmolality, increased urine specific gravity, reduced urine [Na⁺]
- Rx - Fluid resuscitation to restore renal perfusion

Renal
- Renal parenchymatous disease / acute tubular necrosis often from ischaemic damage
- Reduced Na⁺ and water reabsorption, reduced tubular K⁺ secretion, reduced tubular H⁺ secretion, reduced GFR
- Rx - Limit Na⁺, K⁺ fluid and protein intake. D
- Dialysis as needed until renal function recovers

Post-renal
- Urinary tract obstruction by abnormalities in lumen, wall or outside wall of urinary tract
- Rx - Relieve obstruction e.g. urinary catheter, treat underlying cause, prevent/ treat infections, common in urinary tract obstruction with stasis
Chronic Kidney Disease

Causes

1. Congenital / inherited e.g. ADPKD
2. Glomerular disease – primary glomerulonephritis, secondary to diabetes
3. Vascular disease
4. Urinary tract obstruction

- 70% cases caused by diabetes, hypertension and atherosclerosis.
Chronic Kidney Disease

Complications

- **Reduced GFR**
  - Fluid retention – tissue oedema and heart failure
  - Reduced metabolite excretion – uraemia, increased lipids, increased plasma urate and [creatinine]

- **Reduced tubular function**
  - Reduced fluid reabsorption causing polyuria
  - Reduced K+ secretion resulting in hyperkalaemia
  - Reduced acid secretion resulting in metabolic acidosis

- **Anaemia**
  - Reduced erythropoietin production – normocytic normochromic anaemia

- **Renal bone disease**
  - Reduced vitamin D activation leads to decreased Ca2+ absorption from GIT
  - Plasma phosphate elevated due to reduced renal excretion and reduced calcium
  - Reduced levels of vitamin D and reduced calcium stimulate parathormone secretion → secondary hyperparathyroidism

- **Cardiovascular complications**
  - Activation of RAAS – increases PR → hypertension
  - Fluid retention leading to heart failure
  - Increased cholesterol → atherosclerosis

- **Skin disease**
  - Pruritis caused by nitrogenous waste compounds
Chronic Kidney Disease

Management

Renoprotection

- Maintain normal BP and restrict proteinuria
- Reducing angiotensin II activity – **ACE inhibitors**
- Reducing BP – **diuretics and calcium channel blockers**
- Manage other pathogenic conditions e.g. smoking, diabetes

Treat complications

- Anaemia - **EPO**
- Hyperlipidaemia - **statins**
- Hyperkalaemia – **restrict intake**
- Acidosis – **oral bicarbonate**
- Hyperphosphataemia – **phosphate binders**
- Ostemomalacia & secondary hyperparathyroidism – **activated vit D analogues**

Haemodialysis

- Deals with waste products and fluid/electrolyte overload

Renal **transplantation** is the complete solution
All the best in the upcoming exams!
Questions?

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