HYPERTENSION AND HYPOKALEMIA

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INTRODUCTION
Hypertension and Hypokalemia are two distinct clinical entities, whenever present in a single clinical setting of an individual, may or may not be related to each other. However it is mandatory for a treating physician to search for this clinical correlation. Detection of the underlying cause not only guides the treatment protocol but also dictates further steps for prevention of hypertension & hypokalemia, prevention for life threatening conditions like arrhythmias, sudden cardiac death, respiratory failure etc. & provides the insights for prognosis. Simple reason like diuretic induced hypokalemia for the treatment of hypertension may be overshadowed with complicated genetic disorders, channelopathies or endocrine disorders which need prolonged biochemical & genetic workup. Therefore careful & vigilant approach is warranted in this clinical setting.

POTASSIUM HOMEOSTASIS
• Approximately 98 % of total body stores are intracellular
• Normal Serum [K+] ranges from 3.5 – 5 mmol/ L
• Insulin, aldosterone, catecholamine & acid base status influence movement of [K+] into the cells.
• K+ excretion is regulated at the distal nephron.
• K+ excretion is related to (Urine flow rate)

The marked discrepancy between intracellular & extracellular content of potassium is illustrated Fig. 1. Total body potassium content in healthy adult is approx 50mEq/ kg, so a 70 kg adult will have 3500 mEq as 2% of total amount is in extracellular fluid, therefore ECF contain 70 mEq K+. As plasma
accounts for approx 20% of ECF volume, the potassium content of plasma is about 15 mEq which is about 0.4% of total body potassium. This suggests that plasma potassium is an insensitive marker of changes in total body potassium stores.

**Serum level of K+ is regulated by-**

- Uptake of K+ into cells by altering activity of Na – K- ATP’s pump in the cell membrane.
- Renal excretion – mainly controlled by aldosterone.

**DEFINITION OF HYPOKALEMIA**

Hypokalemia has been defined as Serum [K+] is < 3.5 mEq/ L. Severe hypokalemia where Serum [K+] = < 2.5 mEq / L (Figs. 3 and 4).

**HYPERTENSION**

Hypertension, more specifically systemic arterial hypertension is defined as the elevation of blood pressure (BP) to such a level that place patients at increased risk of target organ damage in several vascular beds including the retina, brain, heart, kidneys and large condict arteries. In demographic studies the level has been observed above 120/80mHg. Hypertension has been staged as High normal stage I & II, Hypertensive crisis, isolated systolic HTN according to level of elevation of BP, rapidity of development of HTN, threat to vascular bed, etc.

**PREVALENCE**

Recent studies have reported a high prevalence of hypertension in both urban & rural areas, in India

In urban area the prevalence varies from 30 - 45 % in different regions, which is consistent with the findings with other developing countries in Asia where prevalence is 50% Epidemiological studies report that currently 70% of hypertension in India is Stage I (140 – 159 / 90 – 99 mmHg.) & rest of are Stage II.

Prevalence of resistant hypertension in India is unknown.

Fig. 2 : Relationship between the Serum potassium concentration & changes in total body potassium content.

![Fig. 2: Relationship between the Serum potassium concentration & changes in total body potassium content.](image)

**Fig. 3: Mechanism of hypokalemia**

![Fig. 3: Mechanism of hypokalemia](image)
Table 1: Causes of K⁺ depletion

<table>
<thead>
<tr>
<th>Extrarenal (Urine K⁺ &lt; 20mmol/day)</th>
<th>Renal (Urine K⁺ &gt; 20mmol/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inadequate intake</td>
<td>Renal tubular acidosis</td>
</tr>
<tr>
<td>Copious perspiration</td>
<td>Diabetic ketoacidosis</td>
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<tr>
<td>Gastrointestinal losses</td>
<td>Chloride depletion</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Vomiting/gastric suction</td>
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<tr>
<td>Laxative abuse</td>
<td>Diuretics</td>
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<tr>
<td>Villous adenoma</td>
<td>Bartter’s syndrome</td>
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<td></td>
<td>Gitelman’s syndrome</td>
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<tr>
<td></td>
<td>Mineralocorticoid excess states</td>
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<td></td>
<td>Liddle’s syndrome</td>
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<tr>
<td></td>
<td>Glucocorticoid excess</td>
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<tr>
<td></td>
<td>Magnesium depletion</td>
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<tr>
<td></td>
<td>Antibiotic therapy</td>
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<tr>
<td></td>
<td>Leukaemia</td>
</tr>
<tr>
<td></td>
<td>Interstitial nephritis – immune related</td>
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<tr>
<td></td>
<td>Diuretic conditions</td>
</tr>
</tbody>
</table>

Endocrine cause –
- Primary hyperaldosteronism
- Secondary hyperaldosteronism
- Cushing Syndrome
- Congenital adrenogenital syndrome

What is the relation between Hypertension & Hypokalemia?
Hypertension & hypokalemia are two distinct clinical syndromes which may or may not be associated. Relation between these two clinical syndromes can be established as follows.

1. Aetiology of hypertension is associated with hypokalemia.
2. Treatment of HTN may lead to hypokalemia
Aetiology of HTN associated with hypokalemia.

Among all the causes of HTN, the following are related to hypokalemia.
Hypertension and Hypokalemia

Table 2: Mineralocorticoid Excess States

<table>
<thead>
<tr>
<th>Low aldosterone</th>
<th>High aldosterone</th>
<th>Normal cortisol</th>
<th>Low aldosterone and PRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary hyperaldosteronism</td>
<td>Renovascular disease</td>
<td>Exogenous mineralocorticoid</td>
<td>Adrenogenital syndrome</td>
</tr>
<tr>
<td>Glucocorticoid-remediable Aldosteronism (GRA)</td>
<td>Main renal arteries</td>
<td>11β-HSD deficiency</td>
<td>17α-Hydroxylase deficiency</td>
</tr>
<tr>
<td>Aldosteronism (GRA)</td>
<td>Small vessels</td>
<td>Congenital</td>
<td>11β-Hydroxylase deficiency</td>
</tr>
<tr>
<td>Renin secretory tumour</td>
<td></td>
<td>Liquorice</td>
<td>Carbenoxolone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liddle’s syndrome</td>
<td>MR activation mutation.</td>
</tr>
</tbody>
</table>

**Clinical Presentation**

1. Clinical presentation may be related to both of hypertension & hypokalemia. Features of K⁺ depletion vary greatly & their severity depends in part on the degree of hypokalemia. Symptoms seldom occur unless the plasma [K⁺] is < 3 mEq/L.

2. Fatigue, myalgia, muscular weakness or cramps of lower extremities are common. Constipation or paralytic ileus occurs when smooth muscle function is affected. More severe hypokalemia may lead to complete paralysis, hypoventilation or rhabdomyolysis.

3. K⁺ depletion is associated with increased risks of arrhythmias leading to palpitation or Syncope.

4. Polydipsia & Polyuria may result for hypokalemia induced NDI.

5. Possible causes of transcellular shift should be sought, such as use of bronchodilators in COPD. Diuretic & laxative abuse & recurrent vomiting should be excluded.

6. Sign of hypovolemia or hypervolemia, hypotension/ hypertension provides the clue to the aetiology.

7. ECG changes of hypokalemia do not correlate well with the plasma [K⁺]. Early changes may include flattening or inversion of T waves a prominent U wave (more than 1 mm in height) S.T.segment depression and a prolonged Q u interval. Severe K⁺ depletion may result in a prolonged PR interval, decreased voltage and widening of QRS complex.

We approach these patients by check there Urinary K⁺ excretion & look for TTKG (transstubular potassium gradient)

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TTKG = \frac{(\text{Urinary K⁺/plasma K⁺})}{\text{Urinary osm/plasma osm}}
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**Increased loss**

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24 hrs UK, TTKG

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UK > 30mEq/day, TTKG >7

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Renal loss

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Check BP

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**PRIMARY HYPERALDOSTERONISM**

**Definition:** - Diastolic hypertension without oedema, decreased renin & increased aldosterone secretion

Aetiology
1. Aldosterone producing adrenal adenoam (Conn’s syndrome) 75%
2. Adrenal hyperplasia (25%)

**CLINICAL FEATURES:**

_Hypertension_
- Polyuria – polydipsia - nocturia
- Fatigue – weakness – paresthesia
- Headache
- Severe case – Tetany – Intermittent paralysis

_Investigations:_
- Urea & electrolytes – hypokalemia, mild hypernatremia, hypomagnesaemia
- High 24 hrs or plasma aldosterone + low random plasma renin.
- CT or MRI (to differentiate adenoma from hyperplasma)

_Treatment:_
- Medical –
  - Spironolactone (aldosterone antagonist or Amiloride.)
  - ACEI might be added for better control of BP
- Surgical –
  - Removal of adenoma

**SECONDARY HYPERALDOSTERONISM**

**Definition:**- Increase in the level of aldosterone in response to activation of renin-angiotensin system.

_Renovascular hypertension:_ This is hypertension secondary to Renovascular disease.

It is suspected if:-
- Negative family history of HTN
- Spontaneous hypokalemia
- Sudden onset of exacerbation of HTN.
- Difficult to control with antihypertensive therapy.

Pathophysiology: - There is decreased in renal perfusion in one or both kidneys leading to increased renin release & subsequent Angiotension II production.

It is two types –
- Atherosclerotic plaque – prox ⅓ rd of renal artery involved, usually male> 55 years.
- Fibromuscular hyperplasia – distal ⅔ rd of renal artery involved usually in young females.

**CUSHING SYNDROME**

**Definition:**- Clinical syndrome results from chronic Glucocorticoid excess.

Aetiology – ACTH dependant
- ACTH secreting pituitary adenoma (Cushing’s disease 80 %)
- Ectopic ACTH secreting tumor (SCLC)

ACTH independant –
- Long term use of exogenous Glucocorticoid
- Primary adrenocortical Tumor.

**TREATMENT:**

_Pituitary_ – Transphenoidal resection

Irridiation only 50 % Effective

_Adrenal_ – Adenoma – Unilateral adrenalectomy

Carcinoma – palliative

_Ectopic ACTH_ –

Chemotherapy, Radiation

Ketoeonazole, Metyrapone.

**LABORATORY TESTS FOR EVALUATION OF HYPERTENSION**

**BASIC TEST FOR INITIAL EVALUATION**

1. Always included
Hypertension and Hypokalemia

1. Urine for protein, blood, and glucose
2. Microscopic urinalysis
3. Hematocrit
4. Serum potassium
5. Serum creatinine and/or blood urea nitrogen.
6. Fasting glucose
7. Total cholesterol
8. Electrocardiogram

2. Usually included, depending on cost and other factors
   a. Thyroid-stimulating hormone
   b. White blood cell count
   c. HDL and LDL cholesterol and triglycerides
   d. Serum calcium and phosphate
   e. Chest x-ray; limited echocardiogram.

SPECIAL STUDIES FOR SECONDARY HYPERTENSION

2. Pheochromocytoma: 24-h urine assay for creatinine, metanephrines, and catecholamines.
3. Cushing’s syndrome: overnight dexamethasone suppression test or 24-h urine cortisol and creatinine.

MANAGEMENT

Treatment of hypertension & hypokalemia includes the following:
1. To identify the cause & treat the cause.
2. Treatment of hypertension & prevention of hypokalemia.
3. Treatment of hypokalemia

Treatment of hypertension & prevention of hypokalemia

a. Life style modification.
   i. Avoid use of diuretics.
   ii. ACEI/ARB preferred.
   iii. Potassium sparing diuretics may be prescribed carefully to avoid hyperkalemia

Treatment of Hypokalemia

Therapeutic goals:
1. Prevent life threatening complication (Arrhythmias, Respiratory failure.)
2. Correct K+ deficit.

Assessment of K+ deficit:

If the hypokalemia is due to potassium depletion (where transcellular shift e.g. alkalosis is excluded)-

Every 1mmEq/L [K+] depletion = 10% Reduction of total body K+ store.
[Total body K+ content = 50mEq/KG]
For a 60 kg person, total body K+ store = 60 x 50 = 3000 mEq.
Therefore,
1 mEq/L [K+] depletion = 3000 x 10% = 300 mEq = Total K+ deficit.

Oral therapy:

i. It is generally safer to correct hypokalemia via oral route. KCl is usually preparation of choice for hypokalemia + Metabolic alkalosis.

ii. Potassium bicarbonate & citrate tend to alkalize the blood, may be useful in correcting hypokalemia associated with chronic diarrhea or RTA.

iii. Potassium phosphate may be preferred for DKA.

IV therapy: Imminently life threatening hypokalemia (unable to take KCl orally.)

Concentration of K+ administration –

≤40 mEq/L in peripheral vein
≤100 mEq/L in central vein.

K+ solutions are hyperosmotic, therefore should be diluted with NS always (Dextrose should be avoided to prevent transcellular shift of K+).

Rate of infusion ≤ 20mEq/hour.

Hypomagnesemia should be sought in all hypokalemic patients and corrected to allow effective K+ repletion.

CONCLUSION

Hypertension & hypokalemia are distinct clinical Syndromes which can be correlated clinically & biochemically. Both the conditions are widely prevalent among different groups of
patients. Prevention and treatment of these clinical states depends on proper history taking & examination, clinical suspects, laboratory investigations & its adequate proper management. Though these two conditions are mild in most of the instances these can be life threatening & should be managed aggressively & adequately in ICU setup.

REFERENCES: