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REVIEW ARTICLE **OPEN ACCESS**

Dyskalemia and the risk of arrhythmia in kidney disease

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ABSTRACT

Potassium is the most well-known intracellular cation and assumes a huge job in nerve and muscle cell movement. Potassium aggravations or dyskalemia are generally visited in clinical practice. Hypokalemia and hyperkalemia are not unserious electrolyte issue, especially in patients with a renal ailment. Long haul guideline of potassium homeostasis is for the most part performed by renal discharge of potassium with changes in dietary admission. Infection claims kidney illness, may upset the limit of the kidneys to offset potassium ingestion with potassium discharge, which may prompt dyskalemia. Cardiovascular patients since k+ is an essential element that directs heart repolarization. Hypokalemic conditions impacts affect myocardial stubborn periods and the hazard for arrhythmia caused. Hypokalemia is portrayed as a plasma k+ focus underneath 3.5 meq/l. Potassium particle conductivity in heart myocytes is legitimately connected to the plasma k+ fixation. Hypokalemia hence diminishes k+ conductivity and adds to a more extended time of repolarization of the heart activity potential, hyperkalemia is portrayed as a grouping of plasma k+ more prominent than 5 meq/l. Hyperkalemia actuates an improved k+ conductivity of cardiovascular myocytes. Since repolarization is the capacity of the k+ current, the principal event of hyperkalemia is quick repolarization. Improved k+ conductivity regularly permits the danger of resting layer potential increasingly negative, to a point to which Na+ channels begin to get inactivated. Hyperkalemia and hypokalemia in kidney infection can cause impacts from the enactment of disabled driving forces, unpredictable actuation of the motivation requires diminished ordinary automaticity, sporadic automaticity and activity animated after depolarization. Both such pathways have been appeared to include brokenness of the arrhythmias into ventricular fibrillation prompting demise.

Keywords: hyperkalemia, hypokalemia, serum potassium, kidney disease, arrhythmia, cardiovascular risk

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INTRODUCTION

Potassium is the intracellular cation which is the key determinant of the myocardial resting membrane potential. Serious hypokalemia or hyperkalemia cases are predisposed to atrial and ventricular arrhythmias and can be death. [1, 2]. In those with kidney disease, the chance of hyperkalemia increases. [3, 4]Adaptations to normalize potassium levels involve elevated distal tubular potassium secretion, enhanced potassium shift into the intracellular compartment and increased intestinal excretion [5, 6, 7, 8]. Individuals with kidney disease are often at risk of hypokalemia, including the high incidence of volume overload and diuretic use, which may enhance the hazard of hypokalemia with arrhythmias. [9]Although the possibility of serious dyskalemia with arrhythmias is recognized, what is unknown is the rate that causes an actual danger. Potassium rates in the strong standard or moderate spectrum of hyperkalemia predict more severe episodes of hyperkalemia.[10,11,12].There is a U- shaped association in certain research of potassium levels with the cardiovascular or renal outcome of significant incidence at relatively mild rates of dyskalemia.[13,14,15, 16,17]. People with hypokalemia or hyperkalemia prefer to have stronger chronic conditions and to be consuming more potassium-influencing drugs. It may reason for part of the improved dyskalemia related mortality or dyskalemia maycontribute to the elevated risk of arrhythmias. The usage of agents to inhibit the renin-angiotensin pathway in heart failure and kidney disease remains a restricting factor for hyperkalemia. This is attributed to the increased chance of hyperkalemia [18].

SERUM POTASSIUM

The estimation of serum K^+ is not necessarily uniform but readily achieved. However, the standard range for K^+ levels between laboratories is also extremely variable; the lower limit fluctuates between 3.5 and 3.8 mmol/L and the upper limit between 5.0 and 5.5 mmol/L [19]. Interpretation of the value obtained from the laboratory includes a strict analysis of the situations from which the sample was generated and interpretation. Blood samples collected using inappropriate procedures can often induce pseudohyperkalemia. Prolonged usage of a tourniquet over a venipuncture site or prolonged twitching of the fist can induce tissue hypoxia and K^+ leaching from the tissue into plasma K^+ values indicate a circadian rhythm (average range-to-trough variation of 0.60mmol / L and the lowest night values) [20, 21]. Which even postprandial decreases due to insulin release in response to carbohydrate loads ingested. Those are essential factors when determining K^+ status in patients treated with diuretic agents one of the most frequent inpatient electrolyte disorders found in clinical practice is a lower serum K^+ value. Too several hospitalized patients are observed to be a hypokalemic condition (defined by a K^+<3.6 mmol/L serum) at several periods during hospitalization [22]. Most of these patients have K^+ serum levels falling between 3.0 and 3.5 mmol/L in anywhere. The reported hypokalemia is always evanescent due to transcellular K^+ shifts which appear to be readily reversible. Hypokalemia is most generally concerned with renal defects, on an outpatient basis. These renal deficits usually occur from either chronic or acute kidney disorders that may be linked to the condition of the disease or treatment. Under such situations, the frequency of hypokalemia detected associates similar to the severity of the total body deficits [23].

KIDNEY DISEASE

Patients with kidney disease also take some of these drugs, can cause electrolyte and fluid disruption. Diuretics may induce significant changes in the equilibrium of body potassium. Patients needing renal replacement therapy, particularly hemodialysis, may undergo significant fluid, electrolyte, and acid-base balance changes at the time of treatment. In these patients, the state of overall body water is better determined by changes in body weight [24].

TYPES OF KIDNEY DISEASE

ACUTE KIDNEY DISEASE

Hyperkalemia is a typical complication of acute kidney injury where the damage affects the distal nephron and spreads into the collecting duct, allowing the cells responsible for K^+ secretion to injure directly [25]. This damage can lead from acute tubular necrosis due to ischemia or toxins, or from inflammation as in acute nephritis of the tubulointerstitial (a type of diseases are characterized by acute or chronic inflammation of the renal tubules and interstitium).Hyperkalemia is an early finding of acute urinary obstruction, as elevated tubular pressure disrupts the distal nephron's high-resistance structure, resulting in the lack of electrical driving force for K^+ secretion.Sudden decreases in the glomerular filtration rate in patients with severe kidney damage are a restricting factor for K^+ secretion. Decreased distal distribution of salt and water in patients with oligoanuria also leads to a decreased distal K^+ secretion.[26,27] The toxicity of hyperkalemia in patients with Acute Kidney Injury grows with moderate raises in the plasma K^+ content since the raise is sudden. Like what arises with Chronic Kidney Disease, there is insufficient opportunity to establish adaptation pathways at the molecular level to reduce toxicity. Hyperkalemia is further aggravated by endogenous release of K+ into the extracellular space owing to tissue breakdown as in rhabdomyolysis (is the breakdown of damaged skeletal muscle) or at settings of elevated catabolism or cell change due to acidemia [28].

CHRONIC KIDNEY DISEASE

Chronic kidney disease is distinguished by a decrease of nephron mass and a decline in the amount of K^+ secretion ducts produced. The chronic nature of this pathway allows for an adaptive response in the remaining nephrons, allowing an increase in the amount of K^+ excreted per unit GFR (fractional excretion of K^+). It is attributed to improved K^+ secretory potential arising from structural improvements occurring in the distal nephron and key collecting duct cells [29].]Such modifications are close to those observed in normal subjects in reaction to chronic K^+ loading and involve proliferation and basolateral membrane folding, cellular hypertrophy, and increased mitochondrial number [30]. Amplification of the basolateral surface is followed by decreased Na^+- K^+-ATPase pump intensity and pump activity. These structural modifications arise from the enhanced operation of the K^+ plasma and/or mineralocorticoid. Loss of kidney mass in the remaining nephrons often improves drainage and Na^+ transfer to the distal nephron. Plasma K^+ concentration in chronic kidney disease rises below 5.5 mEq / L before the GFR falls below 15 ml/min except in the case of oliguria (is defined as a urine output that is less than 400 mL or 500 mL per 24h in adults), high-K^+ diet, decreased tissue degradation or diminished aldosterone secretion or reactivity [31]. To order to preserve K^+ homeostasis, excessive losses of working kidney mass includes a rapidly steeper increase in the K^+ concentration of steady-state plasma. Given such physiological

improvements, patients with chronic kidney disease remain at risk of hyperkalemia; this is because the capacity to further enhance K+ secretion is highly limited and that the rise in K^+ plasma is larger and lasts longer with an exogenous load relative to regular subjects. [32]

POTASSIUM DISTURBANCES IN PATIENTS WITH KIDNEY DISEASE

Severe renal disorder induces potassium retention renal failure acidosis will lead to potassium shifting out of the cells (In acute acidosis K, 0.5 mmol per pH drop of 0.1 may rise) of this purpose, ventilated patients will be treated whether they become hyperkalemia, to ensure that they do not induce respiratory acidosis.[33] While chronic hyperkalemia is best treated than acute hyperkalemia, levels of potassium > 6.5 mmol it can be linked with significant problems such as hypotension, fatigue and ventricular dysrhythmias. Potassium levels >6.5 mmol/l or ECG-associated hyperkalemia (P wave flattening, T wave tenting, and QRS widening) should be treated. [34]The aim of treating hyperkalemia would be to decrease potassium plasma levels; first, by increasing potassium intracellular movement and secondly, by enhancing potassium excretion. Relatively poorly established will experience hypokalemia (K <3.5). This is also linked, for example, to the treatment of diuretics. Potassium is lost in people with renal tubular acidosis, in replacement for hydrogen ions. Potassium supplementation therapy should be conducted carefully in patients with serious renal failure, as life-threatening hyperkalemia may occur [35].

ELECTROPHYSIOLOGICAL EFFECTS OF POTASSIUM DISORDERS

The proportion of concentrations of Intracellular and extracellular potassium is critical for the resting membrane potential and for inducing action potentials in the heart and other excitable tissues. Approximately 98 % of total body potassium is distributed as an intracellular cation, although only a limited portion is extracellular with plasma levels that are commonly specifically maintained between 3.5 and 5.0 mmol/L [36]. Potassium causative agents influence electrophysiological properties and facilitate arrhythmia through the interplay between K+, Na+ and Ca2 + and the control of the exchange between Na^+K^+ ATPase and Na^+Ca2^+. Hypokalemia induces resting membrane hyperpolarization, prevents Na^+K^+ ATPase, and suppresses the conductance of K+ channels. It in effect results in prolongation of the action potential duration (APD), decreased reserve for repolarization, early after depolarization (EAD), delayed after depolarization (DAD), and automaticity. EAD-mediated arrhythmias include point Torsadesde and polymorphic ventricular tachycardia, which may degenerate into ventricular fibrillation. Many clinical evidence indicated a potential link between atrial fibrillation and hypokalemia [37, 38]. An experimental study found that hypokalemia decreases the automaticity of the sinoatrial nodes and causes stimulated activation and burst to fire in the pulmonary veins, which could play a role in atrial fibrillation genesis [39]. Systemic hyperkalemia increases the conductance of K^+ channels, shortens action potential duration, and causes post repolarization refractoriness, resulting in enhanced reserve for repolarization. The resting membrane potential depolarizes, which biphasic manner changes the conduction velocity (CV). Firstly conduction velocity accelerates but also progressively becomes slower when hyperkalemia develops. Moreover, hyperkalemia enhances the restitution of conduction velocity, i.e. the dependency of the conduction velocity of a propagating wave on the previous diastolic interval. Arrhythmias arising from hyperkalemia involve asystole, heart block and ventricular tachycardia / ventricular fibrillation, where multiple pathways can cause reentry. The severity of the hyperkalemia required to cause arrhythmias differs considerably between humans. The sinus node and sinoatrial conduction are usually less sensitive to hyperkalemia than the atrioventricular (AV) node and intranodal escape pacemakers.[40] Interstitial hyperkalemia describes a rise in interstitial [K^+] in tissue with regular [K^+] in the systemic circulation. Interstitial [K+] rises swiftly after acute coronary occlusion in the central ischemic region. Action potential duration shortens and the resting membrane potential depolarizes resulting in currents of systolic and diastolic injuries flowing through the boundary region, which can re-exciting no ischemic recovered tissue to produce further re-entry systems. Also, reentry of phase 2 can originate from the subepicardium [2]. Altogether, these modifications set the stage for both triggers and substrates capable of causing acute myocardial ischemia in ventricular ectopia, ventricular tachycardia, and ventricular fibrillation [40, 41].

POTASSIUM DISTURBANCES AND RISK OF CARDIOVASCULAR DISEASE

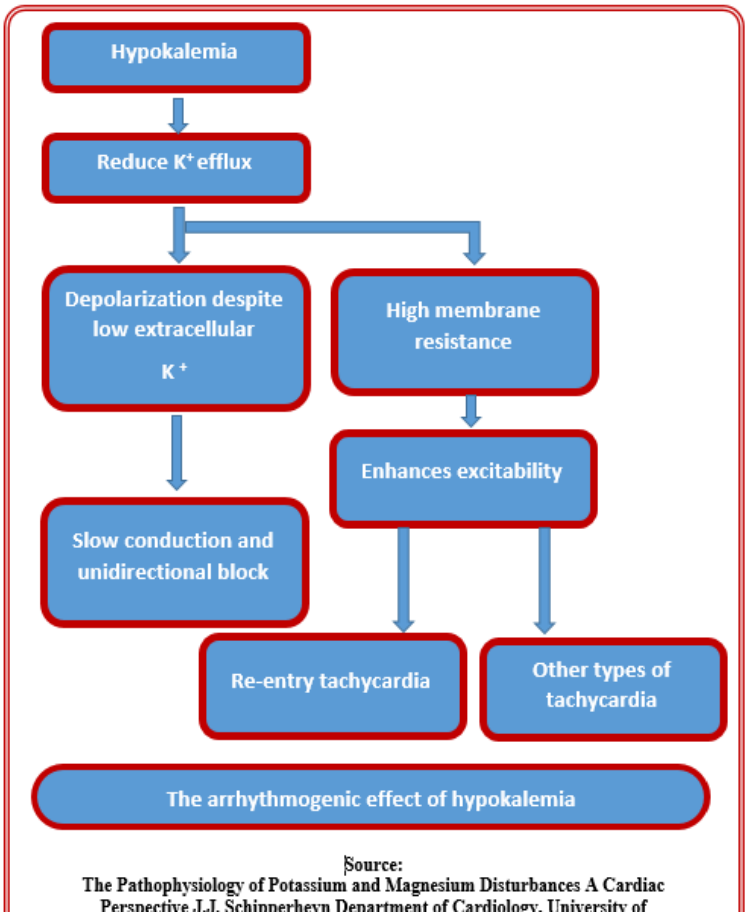
HYPOKALEMIA:

Lower levels of potassium in the extracellular space cause the resting membrane potential to Hyperpolarization. This Hyperpolarization is induced by the impact on the resting membrane potential of the altered potassium gradient, as described by the Goldman equation. As an effect, the depolarization of the membrane requires a greater-than-normal stimulation to activate an action potential. Because of the less-than-complete recovery from sodium channel inactivation, hypokalemia induces arrhythmia in the

heart, rendering a possible intervention stimulus less probable. Furthermore, the decreased extracellular potassium (paradoxically) prevents I_{Kr} potassium current activity, and slows ventricular repolarization. This delayed repolarization may stimulate reentrant arrhythmias [42]. Hypokalemia symptoms are results of actions on the muscle resting membrane potential (MRP) and on the acid-base status [43]. Low plasma K+ in the muscles results in a hyperpolarized myocyte, which tends to be more refractory to excitation. This causes fatigue, myalgia and weakness, most pronounced in the large proximal skeletal muscles, such as the hip and thigh muscles. Worsening hypokalemia results in weakening of the respiratory muscle, and eventually severe muscle dysfunction, like paralytic ileus. [44] In cardiac myocytes the conductance of potassium ions is closely linked to the concentration of plasma K^+ [45]. Hypokalemia thus reduces K+ conductance and causes to a prolonged phase of repolarization of the cardiac action potential, reflected in the electrocardiogram (ECG) as a prolonged QT (or QU) interval. Other improvements to the ECG include flattening or inversion of the T wave, a strong depression in the U-wave and ST-segment. Patients undergoing digital therapy are prone to increased toxicity in hypokalemia situation because digital and potassium impede binding on each other at the Na+/K+/ATPase pump [46, 47].

ARRHYTHMIAS EFFECT

Hypokalemia is getting more complex effects. Reducing extracellular K^+ levels reduces the cell membrane's K^+ permeability, thus limiting the cell's potassium loss. As a result, if the extracellular K^+ concentration is further lowered the membrane potential will no longer increase. Instead of hyperpolarization, one observes depolarization at low concentrations of K^+, as one would assume. Membrane resistance in hypokalemia is enhanced, and the stabilizing impact of an improvement in K_+ conductance insufficiently matches the excitatory influence of increases in Na+ or Ca^{++} conductance. Low K^+ enhances excitability, whatever its cause, and also slightly depolarizes the cell. Extremely low K^+ will depolarize the cell to partly inactivate Na channels, thus raising the risk of tachycardia re-entry from sensitive areas of the heart.



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The Pathophysiology of Potassium and Magnesium Disturbances A Cardiac Perspective J.J. Schipperheyn Department of Cardiology, University of

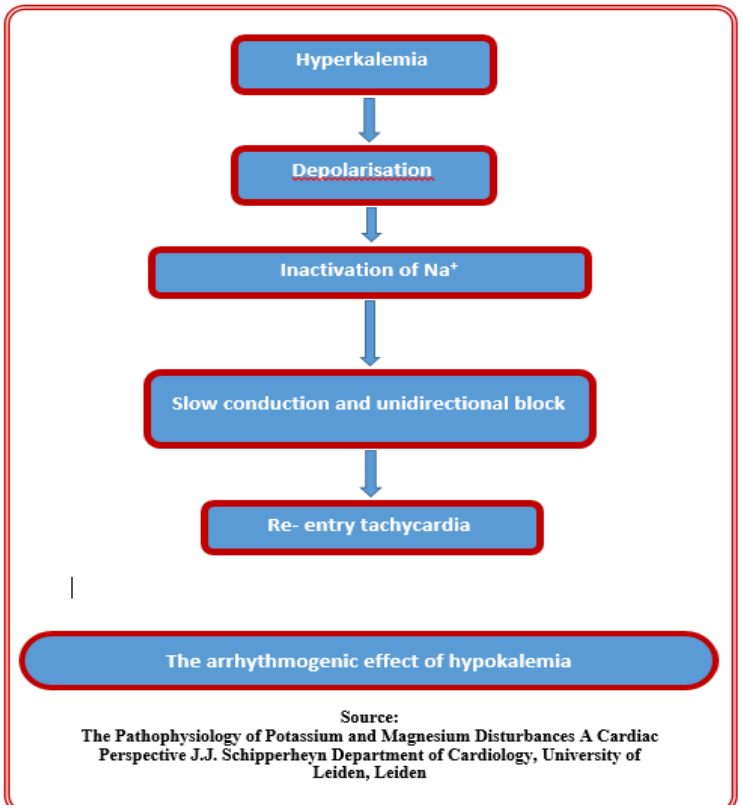
HYPERKALEMIA:

Hyperkalemia occurs when potassium is produced excessively or ineffectively dispose of Ineffective removal may be hormonal (in the failure of aldosterone) or induced by kidney conditions that impair the

excretion [48]. Enhanced extracellular potassium levels occur in cell membrane potentials being depolarized owing to a rise in potassium's equilibrium potential. Such depolarization activates several voltage-gated sodium channels, which often also raises the inactivation. Because depolarization is slow due to change in concentration, it never produces an action potential by itself; rather it results in accommodation. Depolarization inactivates sodium channels above a certain level of potassium, opening potassium channels, making the cells refractory. Which contributes to neuromuscular, cardiac, and gastrointestinal organ systems being affected. Of special interest is cardiac conduction dysfunction, which may induce ventricular fibrillation, abnormally slow heart rhythms, or asystole [49]. Such as for hypokalemia, the symptoms of hyperkalemia also have to do with results from neuromuscular and acid-base. Enhanced concentration of the extracellular fluid K^+ forces K^+ through the cells' ever-open leaky potassium channels, leading to a mild depolarization. A continuous phase of depolarization effects excitability, and again exhaustion and weakness are the results. When extreme, pulmonary muscle dysfunction may be a life-threatening condition. Hyperkalemia induces elevated K^+ conductance in cardiac myocytes [50]. Because repolarization is the function of the K^+ present, the first manifestation of hyperkalemia is rapid repolarization, reflected on the (ECG) as a sharp, peaked T wave. Increased K^+ conduct also causes the Resting Membrane Potential(RMP) more negative to a level at which Na^+ channels start to become inactivated [51]. An atrioventricular nodal block can also be caused by hyperkalemia [1] Reflected as a prolonged PR and ventricular rhythm with wide QRS complexes [52]. P wave intensity is decreasing owing to an 'electrical paralysis' of the atria, which may not be observable. With hyperkalemia progressively extreme, the widened QRS tends to merge with the peaked T wave, generating a typical sine wave pattern [46]. Cardiac arrhythmia gradually deteriorates into ventricular fibrillation or asystole which leads to death.

ARRHYTHMIAS EFEECT

Cardiac muscle cells are highly permeable to K^+ at diastole and less to Na^+ and Ca^{++} at this. The diastolic membrane potential plotted against the extracellular K^+ concentration logarithm is strongly controlled by a straight-line relationship. As expected in the equation Nernst with K^+ concentrations over 3.5 mmol/L, whether the K^+ concentration is increased, the membrane de-polarizes about 17mV. It is well established that concentrations of K^+ over 7.5 to 8 mmol/L depolarize cardiac muscle cells to such an extent that Na+ channels get inactivated and it is difficult to transmit impulses. Serious hyperkalemia over 8 mmol/L of K+ concentrations quickly leads to cardiac arrest or ventricular fibrillation. Slightly reduced levels of K+ only slow down the conduction but this increases the risk of tachycardia re-entry in an ischemic or partially damaged myocardium



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DISCUSSION

Increases in potassium levels are a significant pathophysiologic problem in patients with kidney disease. This is simple to understand in most situations because progressive deterioration in renal function is associated with impairment of diuresis. Any condition that may induce acute or chronic kidney disease that reduces the glomerular filtration rate (GFR) may establish a fluid homeostasis disturbance for the patient And may contribute to serious, often life-threatening problems such as hypokalemia or hypokalemia in various degrees, with the possibility in extreme rhythm abnormalities presence Potassium is the predominant intracellular cation and is the main determinant of the myocardial resting membrane capacity. Atrial and ventricular arrhythmias, which may be deadly, are predisposed to people with extreme hypokalemia or hyperkalemia. For people with kidney failure the chance of hyperkalemia increases. With slowly decreasing renal activity, potassium continues to increase and achieve a current, somewhat higher, steady-state, while usually still within the normal range. Adaptations to normalize potassium levels include enhanced distal potassium tubular secretion, decreased potassium change into the intracellular space, and increased bowel excretion. Due to the high prevalence of fluid pressure and diuretic use, people with kidney disease are also at risk for hypokalemia. Also, diuretics can cause hypomagnesaemia, which may worsen the risk of hypokalemia arrhythmias. Although the possibility of serious dyskalemia arrhythmias is recognized, what is unknown is the level that creates an immediate danger. Potassium levels within the range of higher normal or moderate hyperkalemia indicate more serious incidents of hyperkalemia. Across the reports, there is a U-shaped association between potassium levels and cardiovascular or renal complications with significant risk at relatively mild dyskalemia stages. Individuals with hypokalemia or hyperkalemia appear to be more comorbid and have renal failure impacting potassium rates. This can account for some of the elevated dyskalemia-related mortality or dyskalemia that result in an increased risk of arrhythmias. For those with renal insufficiency, the risk of cardiovascular disease is high, suggesting most of these people may be on kidney failure, which is likely to change their potassium rates.

CONCLUSION

Potassium plays an important part in establishing electrical regulation of the myocardial. When establishing myocardial ischemia, the Na-K ATPase pump is triggered by adrenergic activation, which reduces plasma potassium rates. It is related to ventricular arrhythmias. Changes in potassium levels are a significant pathophysiologic problem in the treatment of patients with a kidney disorder. It is important to understand in most situations since significant impairment in renal activity is associated with the failure of the diuresis. Some dysfunction that may induce kidney disease that reduces the glomerular filtration rate may identify an imbalance in the fluid homeostasis of the individual which may contribute to serious problems, often life-threatening, such as hypokalemia or differing degrees of hypokalemia, with the possibility of extreme rhythm disorders. The main function of the kidney is to regulate fluid and homeostasis of electrolytes. The kidney also plays a key function in homeostasis of potassium for the number of people that suffer from severe renal disease, including kidney disease. Renal failure of kidney disease can itself cause fluid disruption and homeostasis of electrolytes loss of proper renal function can result in significant fluid and potassium balance shifts. Assessment of the volume level may be necessary for patients with renal failure as both hypokalemia and hyperkalemia are at high risk. Electrophysiological impact of potassium disturbances ratio of intracellular and extracellular potassium concentrations is important to the resting membrane potential and the activation of the action potential in the heart and other excitable tissues. Reducing the extracellular K^+ levels decreases the K^+ permeability of the cell membrane, thereby limiting the potassium loss of the cell. As a consequence, the membrane potential would no longer improve if the extracellular K^+ concentration is further reduced. Instead of hyperpolarization, the possibility of re-entry of tachycardia from vulnerable regions of the heart is thereby decreased. Hyperkalemia results when unnecessary or ineffectual storage of potassium is created. Ineffective elimination may be hormonal (aldosterone failure) or caused by disorders in the kidneys that affect the excretion. Related to an improvement in the equilibrium potential of potassium, elevated extracellular potassium levels result in cell membrane potentials being depolarized.Which leads to the specifically impaired neuromuscular and cardiac organ systems is cardiac conduction failure, which may cause ventricular fibrillation, abnormally slow heart rhythms The failure of renal function can result in potassium retention with significant systemic and cardiovascular effects like cardiorespiratory harm and cardiac collapse The possibility of potassium disorder in kidney disease-related arrhythmia is very high, so avoidance should be of importance by alteration of cardiovascular risk factors. A bad prognosis is correlated with supraventricular arrhythmia, primarily as a result of underlying cardiac failure.

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