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Bone Disorder in Kidney Transplant Recipients: A Review

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Abstract :

A kidney transplant is the process of transferring a kidney organ from a normal person to a patient in the last stage of kidney disease. The condition of the new kidney should be monitored by measuring kidney function, in addition to other laboratory measurements every 3 months to preserve a person's life. After transplantation, the pathophysiology of the bones problem was caused by a complicated interaction of many factors. Using physical and clinical tests, this review examines the bone status of patients after renal transplantation. Clinical utility of bone turnover markers (osteocalcin, bone alkaline phosphatase ALP, Parathyroid hormone PTH,) specificity and sensitivity in predicting bone, structure and function loss. Parathyroid hormone decreasing 50% through 6 months after transplant the rate is still high in approximately 45% of kidney transplant recipients within two years post-transplant. 1,25-dihydroxy vitamin D3 levels associate with improve function of kidney. The calcium usually follows a biphasic pattern before and after kidney transplant low calcium level has been reported in around 5-15% of patients after 3 to 6 months transplantation. It is common for kidney transplant recipients to experience hypophosphatemia in the early stages of recovery from transplantation, occurring in 50% of cases. In conclusion during and after the transplantation surgery, the recipient suffered from osteomyelitis and osteoporosis. Therefore, it is necessary to follow up the bone status of the patient who relocate the kidney by determine their PTH, Vit D3 ,bAIP and serum minerals (i.e.Ca++ ,p,Mg++).

Keyword: transplantation, [1,25(OH)2D .

اضطراب العظام لدى متلقي زراعة الكلى: مراجعة

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مستخلص:

زرع الكلى هو عملية نقل عضو الكلى من شخص عادي إلى مريض في المرحلة الأخيرة من مرض الكلى. يجب مراقبة حالة الكلية الجديدة عن طريق قياس وظائف الكلى ، بالإضافة إلى القياسات المختبرية الأخرى كل 3 أشهر للحفاظ على حياة الشخص. بعد الزرع ، كانت الفيزيولوجيا المرضية لمشكلة العظام ناتجة عن تفاعل معقد بين العديد من العوامل. باستخدام الاختبارات الجسدية والسريرية ، تفحص هذه المراجعة حالة العظام للمرضى بعد زراعة الكلى. وتم دراسة علامات سريرية للعظام (اوستيوكالسين ، انزيم الفوسفاتاز القلوي ،هرمون جار الدرقية)حيث تبين انخفاض هرمون الغدة الجار درقية بنسبة ٪50 خلال 6 أشهر بعد الزرع ، ولا يزال المعدل مرتفعًا في حوالي ٪45 من متلقي زراعة الكلى في غضون عامين بعد الزرع. 1،25 – ديهيدروكسي فيتامين D3 ترتبط بتحسين وظائف الكلى. وسجل انخفاض مستوى الكالسيوم في حوالي 5 – 15 ٪ من المرضى بعد 3 إلى 6 أشهر من الزراعة في الختام ، أثناء وبعد جراحة الزرع ، كان المتلقي يعاني من التهاب العظم والنقي وهشاشة العظام. لذلك فمن الضروري متابعة حالة العظام للمريض الذي ينقل الكلية من خلال اجراء الفحوصات اللازمة.

1. Introduction

Kidney System: are two bean shape, reddish brown found in vertebrates, blood exits into the paired renal veins after they receive from the paired, the renal arteries. A tube called a ureter connects each kidney to the bladder whose function is to carry the expelled urine and throw it outside [1]. The nephrons are the structural functional unit of the kidneys; human kidneys contain around 1000000 nephrons for each adult. Nephrons carry out three fundamental physiological activities that enabling the kidneys to perform their functions: filtration, reabsorption, and secretion. Blood filtration, also referred to as glomerular filtration, the first process performed by the nephron, this occurs as blood passes through the glomerular capillaries' membrane and some plasma is filtered into the area's glomerular space, Since this filter is size-based and remain cells and the majority of proteins in the blood, but allows some of the smaller substances such as water, electrolytes (including sodium and potassium ions), acids and bases (such as hydrogen and bicarbonate ions), organic molecules, and metabolic wastes– to exit from the blood and enter the glomerular capsule. The next action the nephron takes is tubular reabsorption involves reclaiming substances from the filtrate, such as water, glucose, amino acids, and electrolytes, and returning them to the blood. The process of molecules being moved from a tubular capillary through the interstitial fluid in the opposite direction of reabsorption is known as secretion [2]. The kidneys release a different group of hormones, for example, citrulline, renin, and erythropoietin. Kidneys regulate blood pressure. Although the kidneys cannot directly sense blood, their role is to regulate blood pressure over the long term, which is largely dependent on them [3].

There are many causes of kidney disease; the acquisition of some causes is over the course of life, such as kidney stones or tumors, and diabetic nephropathy. There are also congenital diseases, such as polycystic kidney disease. When there is much less functional kidney tissue, one develops chronic kidney disease (CKD). The start of treatment is dialysis but the treatment of choice is kidney transplantation, when the glomerular filtration rate (GFR) is too low or if renal dysfunction leads to severe symptoms. The GFR shows how well the kidneys are filtering, in adults, the normal GFR number is usually more than 90. GFR declines with age, even in people without kidney disease [4].

Hemodialysis is a primary treatment that substitutes renal function; nonetheless, it can compromise healthy kidney function. Hemodialysis is when the bulk of kidney function is lost approximately 85 to 90 percentage of kidney "function, and a depending on GFR if less than 15 means kidney failure. The process of hemodialysis, through which the metabolic wastes

that cannot be removed by the affected kidneys are removed, as well as the excretion of excess water and sodium, and many chemical values are preserved inside the body [5].

2-Kidney Transplant

It is a process through which a kidney is transplanted from a person in a healthy condition to the patient at the end of kidney failure. Transplantation is done either from a deceased person or a living donor, depending on whether the organ is available from a donor. Kidney transplants from a donor with a genetic match or transplants with no genetic link have been described, how likely is it that a biological relationship exists between the donor and recipient? For the wound through a comprehensive medical report [5]. However, in order to prevent the recipients' bodies from rejecting the new kidney, kidney relocate patients should accept immunosuppressants (medicines that suppress the immune system) for the rest of their lives. [6] . Cellular or antibody-mediated rejection can occur after kidney transplantation, or both. Depending on how quickly after a transplant occurs, the antibody might be classified as acute, or chronic. If rejection is suspected, a kidney biopsy should be taken to rule out any potential problems. The transplanted kidney should be checked frequently to ensure its performance laboratory measures should be used like serum creatinine and other. For the rest of a person's life, this should be done at least every three months [7] .An estimated 95,479 kidney transplants were carried out in the world in 2018, with 36% coming from live donors. [8] .Joseph Murray, who received the Nobel Prize in Physiology or Medicine in 1990 for his work in organ transplantation, carried out the first successful kidney transplant in 1954[9].

3- Skeletal System

In the majority of vertebrate creatures, the skeleton is made up of stiff tissues called bones. The body's organs are shielded by bones, which also manufacture and store minerals and red and white blood cells. [9]

The major functions of the skeletal system are:-

Mineral storage: Minerals necessary for the organism, particularly calcium and phosphorus, are stored in bones. [10]

-Determined by the species, age, [11]

- Storage of fat: marrow, adipose tissue serves the reserve for the fatty acid storage [12].

-Acid-base balance: Bone absorbs or releases alkaline salts to buffer the blood against extreme pH shifts.

- Detoxification: Heavy metals and other foreign substances can be stored in bone tissues, which removes from the circulation, lessens theirs impact to other tissues. These, may thereafter be released gradually for excretion. [13],

- Fibroblast growth factor23, which inhibits phosphate reabsorption in kidneys, was released by the endo-

crine organ: bone to regulate phosphate metabolism.

- Calcium balance: An essential step in controlling calcium balance is the release of calcium that has been accumulated in bone during the osteoclasts' process of bone resorption. Resorption forcefully unfixes flowing calcium, bringing its steps up in the course; though bone creation effectively, fixes circulating calcium its solid form, remove it from the bloodstream. At places peculiar to a site, these processes coexist. (14)

3-1 Clinical significance of bones diseases

- Fractures: Fractures occur when a strong blow to the bone or continuous and prolonged trauma is done (15)
- Tumors: several types for the tumor that can affect bone. (16)
- **Cancer:** cancer can occur in all the bones in the body, and the bones are also a common place for other cancers to spread. Cancers that can appear in the bones are called "primary", although this type is rare. (17)
- Other painful conditions including the
- Osteomyelitis this is an infection of the bone or bone marrow, which can be caused by a bacterial infection.(18)
- Osteogenesis, imperfecta.(19)
- Osteochondritis, dissecans.(20)
- Ankylosing, spondylitis.(21)
- Skeletal, fluorosis.(22)

3-2 Bone status after Kidney Transplantation

In kidney transplant patients, bone and mineral abnormalities are common and are linked to a significant risk for the fracture, morbidity, and death. Following transplantation, a wide range of frequently overlapping bone illnesses, including osteoporosis and persistent low or high bone turnover disease has been found. The pathophysiology of post-transplant bone defect is due to a complex interaction of several factors, including renal osteodystrophy that is present before transplantation as well as bone loss resulting from several factors, including immunomodulators, and modifications In parathyroid chemical, vitamin D3, fibroblast development factor pivot 23, and changes in mineral digestion. (23)

3-3 Pathophysiology of Post, Transplant Bone Disease

Differentiating between these two frequently overlapping disorders is crucial for the care of post-transplant bone disease, which develops from underlying chronic kidney disease and mineral disease (CKD-MBD) as well as the development of osteoporosis in certain individuals. Because glucocorticoid medication reduces bone production, it was found that that the deficiency of bone mass in the early post-implantation time frame is rapid, which commonly affects all bones, especially the trabecular bone. In contrast, prior to implantation, bone loss is preferentially affected by cortical bone due to

high secondary hyperparathyroidism (SHPT). There are also other developments modulating the progression of bone disease after transplantation by a combination of post-transplant factors, including the constant utilization of immunosuppressive medications, the level of illicit match impairment, and dysregulation of mineral metabolism, remembering an increment for the degree of fibroblast development factor 23, Continuous SHPT and Vitamin D3 deficiency. The probability of hyperparathyroidism deteriorating or developing de novo increases with progressive renal function loss after transplantation. This is because active vitamin D insufficiency causes changes in bone histomorphometry that are comparable to those seen before transplantation. Since white dialysis patients are bound to have poor bone turnover than black patients, ethnicity may potentially influence the kind of renal osteodystrophy that develops following transplantation. The impact of several variables on the emergence of post-transplantation bone disease will be discussed in the sections that follow [24].

3-4 Changes in Mineral Metabolism Post-Transplantation

Its clinical utility for the serum indicators a bone turnover (alkaline phosphatase bALP , Parathyroid hormone PTH ,osteocalcin) in foreseeing bone loos or bone form and capability is currently constrained in terms of acceptable sensitivity and specificity.Due to increases in phosphorus, calcium, vit D3 levels linked to better kidney function, the parathyroid hormone drops by 50 % six months after transplant however remains raised in around 45 level of kidney transplant patients 2 years after relocate [26]. High PTH values are related with critical hip bone misfortune [27] although there is compelling observational evidence connecting high PTH levels to unfavourable results, the ideal post-transplant PTH level is still unclear. The post-transplant period shows a number of significant changes in mineral metabolism, however it's critical to note that the connections between graft/patient and mineral abnormalities are not always clear [28]. The serum calcium after kidney transplantation often exhibits a biphasic design, with an underlying decrease in calcium level in the initial not many weeks, likely as a result of the large decline in PTH observed after donation. Following this, blood calcium levels increase as a result of both chronic SHPT and increased 1,25(OH)2D production from the allograft. Around 5-15% of patients have experienced hypercalcemia following transplantation, which is most common three to six months later and is more common in those with high PTH levels [25, 32, 33]. Interstitial micro calcification and a worse long-term graft are linked to persistently elevated blood calcium and PTH levels. Half of incident kidney transplant patients experience hypophosphatemia in early post-transplant interval [25]. It normally resolves on its own and is caused by a

rise in PTH levels, an improvement on excretory kidney function, expansion in renal cylindrical aversion to PTH, fibroblast development factor 23. Significant changes in bone turnover have been linked to hypophosphatemia, including a decline in osteoblast activity and improper mineralization. Deficiency in 25-hydroxy Vit D3 (25-OHD) is seen in 30 % of kidney transplant recipients [29], Allograft function may return to normal, although 25-OHD levels frequently stay low. Hypocalcaemia and improper bone mineralization are caused by this ongoing 25-OHD deficit [30, 31].

4-Conclusions

According to this review`s data, it is necessary to follow up the bone status of the patient who relocate the kidney by determine their PTH, Vit D3 ,bAlP and serum minerals (i.e.Ca++ ,p,Mg++)

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