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A REVIEW ON FANCONI SYNDROME: A WORST ENEMY

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ABSTRACT

Fanconi syndrome is a kidney tubule disorder in which visible substances that would normally be absorbed by the kidneys into the circulation are instead discharged in the urine. Basically, the body excretes excess glucose, bicarbonate, phosphate, uric acid, potassium, and certain amino acids. Damage to the cells of the renal tubules can produce this illness in a variety of ways. Due to genetic metabolic abnormalities, they might be endogenous or external poisons. The most prevalent cause of Fanconi syndrome in children is cystine storage disease, which is a hereditary illness caused by a recessive gene. In a more mature and mature age, Fanconi syndrome is usually not hereditary and may have a different cause. In some cases, vitamin D therapy also reduces dysfunction of other renal tubules by decreasing aminoaciduria and correcting chronic acidosis. This mini review aims to potrey the vital role that primary care plays in Fanconi Syndrome and to outline the main clinical treatment in this context.

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INTRODUCTION

A considerable development of pharmacological remedies for formerly fatal illnesses marked the dawn of modern medicine. Unfortunately, several of these medications might harm the kidneys. After the glomerulus, the PT is the initial part of the nephrectomy. Many medicines are eliminated by PT, which is why renal toxicity is so common [1], [2]. Fanconi syndrome is a kidney tubule condition in which some compounds that are typically taken into the circulation by the kidneys are instead expelled in the urine. Excess glucose, bicarbonate, phosphate (phosphorus salt), uric acid, potassium, and certain amino acids are among the compounds expelled from the body. [3].

Different types of Fanconi syndrome impact the proximal tube's functions differently and can lead to other issues. Type 2 or proximal tubular acidosis is caused by a loss of bicarbonate. Phosphate deficiency causes bone disease, rickets, and osteomalacia (even if you have adequate amounts of vitamin D and calcium). This is due to the fact that phosphate is required for bone formation in children and adult bone metabolism. [4], [5].

Hereditary disorders such as cystinosis, mitochondrial cytopathy, tyrosinemia, fructose intolerance, galactosemia, Wilson's disease, Dent's disease, and Roe's syndrome are among the various causes of FS. The most common cause of FS is drug toxicity, which is a significant clinical issue that can impede the development and administration of very effective medicines. The balance of related kidney illness is fast shifting from disease initiation to treatment initiations, because to the increased availability of extremely effective lifetime medicines in areas such as HIV treatment. [1], [4].

Clinical Features

Polyuria, Polydipsia, Dehydration, Hypophosphatemic rickets (in children) and osteomalacia (in adults), Growth failure, Acidosis, Hypokalemia, and Hyperchloremia are the clinical characteristics of proximal renal tubular acidosis. Hypophosphatemia / Hyperphosphaturia, Glycosuria, Proteinuria / aminoaciduria, and Hyperuricosuria are other symptoms of the Fanconi syndrome's extensive proximal tubular dysfunction. [6], [7]. A basic Etiology of Fanconi Syndrome is given in Table No. 1.

Table 1: Etiology of Fanconi Syndrome.

Sl. No.	Herediatory	Acquired	Reference
1.	Cystinosis	Vitamin D deficiency	
2.	Wilson disease	Heavy metal intoxication	
3.	Galactosemia	Various drugs (especially Tetracyclines)	
4.	Oculocerebrorenal syndrome	Renal transplantation	[8]–[10]
5.	Mitochondrial cytopathies	Multiple myelema	
6.	Tyrosinemia	Sarcoidosis	

Causes

Inherited

In children, cystinosis is the most common cause of Fanconi syndrome. Cystinosis is a lysosome accumulation disease marked by aberrant lysosome accumulation of the amino acid cystinine, which leads to the production of intracellular crystals in the body. [11]. CTNS (Cystinosin, Lysosomal Cystine Transporter) are a Protein Coding gene [12] encoding cystineosine, a special cystine transport chain in the lysosomal membrane. Like all amino acids, intracellular metabolism of cystine requires migration across cell membranes [13], [14]. The endocytic protein normally migrates into the cytoplasm after being broken into cystine in the lysosome. However, if the carrier protein is faulty, cystine accumulates in the lysosomes due to a mutation in the CTNS gene [15], [16]. With rising concentrations of cystine in tissue lysosomes, its solubility is quickly exceeded, and crystalline deposits accumulate in practically all organs and tissues [17] – [19]. Wilson's illness is a copper metabolism disorder caused by a genetic mutation. [3], [20].

Acquired

Reversible Fanconi syndrome, similar to that of stale tetracycline, is caused by damage to the proximal tubule caused by degraded products such as epitetracycline, anhydrous tetracycline, and epianehydrotetracycline [3], [20]–[22].

Diagnosis

Blood and urine tests, symptoms, and a test that reveals abnormalities in the blood, such as a high amount of acid, or in the urine, such as a high level of glucose, may cause a doctor to doubt Fanconi syndrome. When high quantities of glucose (despite normal blood glucose), phosphates, and amino acids are discovered in the urine, the diagnosis is confirmed. [20], [22].

Risk Factors

Toxicity of PT drugs is dose dependent in general. The concentration of medications impacted by PT cells is determined by their concentration in the blood, which is regulated by a number of factors, including the key risk factors for the development of FS. Despite these known risk factors, the frequency of nephrotoxicity from various medicines varies greatly among individuals, making it difficult to target specific subgroups for monitoring. Drug toxicity risk for medicines like tenofovir and cisplatin may be determined by major genetic polymorphisms of membrane transporters and other molecules that impact drug absorption or processing in PT cells [6]. It's crucial to keep in mind that drug [1]. More studies are required in this field for better palliative approach. Compartment displaying is broadly utilized and a matter of worry in restorative sciences [23].

Treatment

With the right medication, Fanconi syndrome can be managed. Sodium bicarbonate, potassium bicarbonate, sodium citrate, potassium citrate, and potassium supplements are all beneficial. [9]. Effective treatment can prevent and, in some cases, repair damaged kidney tissue and bones. Sodium bicarbonate can be used to neutralise high levels of acid in the blood (acidosis). Oral potassium supplements may be required for people with low blood potassium levels. Phosphate and vitamin D supplements are used to treat bone disorders. If a child develops kidney failure, a kidney transplant can save his or her life. [24], [25].

The risk of nephrotoxicity may not always rule out the use of a medication, especially if the benefits of treatment outweigh the dangers. The use of gentamicin in the treatment of severe gram-negative bacterial sepsis, for example, has saved countless lives. However, it is critical that doctors who use PT-toxic medications are aware of this impact and adequately monitor their patients. [26], [27]. In the case of serious poisoning, treatment must be stopped before the injury becomes serious and irreparable. Despite the identification of various risk factors for FS from medications, it is often unclear why some patients are toxic while others are not. Pharmacogenomics, on the other hand, may play a role, and more research is needed in this area. More research is needed to discover novel ways for developing less hazardous drug equivalents that avoid toxicity, heal injured tubules, and preserve therapeutic efficacy. As new medications become available, some will become more toxic to PT and thus more likely to produce FS. Therefore, it is important to learn from previous experience and conduct more comprehensive screening studies of nephrotoxicity in humans [1], [28]. Based on the information and knowledge, progress is possible and an individual should enrich knowledge of different subjects and the more people gain knowledge the more contribution can be expected to the upon this subject [29].

CONCLUSION

Fanconi syndrome may be a disorder of the kidney tubules during which certain substances normally absorbed into the bloodstream by the kidneys are released into the urine instead. The proximal tubule is that the first a part of the kidney tubule after the glomerulus where many drugs are excreted across the PT and it's the most typical site of toxicity within the kidney. The loss of phosphate leads to the bone diseases rickets and osteomalacia, because phosphate is important for bone development in children and even for ongoing bone Fanconi syndrome is a kidney tubule condition in which certain compounds that would usually be taken into the circulation by the kidneys are instead discharged into the urine. The proximal tubule is the first component of the kidney tubule following the glomerulus, and it's the most common location of toxicity within the kidney. Many medicines are excreted across the PT. Because phosphate is necessary for bone formation in children and even ongoing bone metabolism in adults, phosphate deficiency causes the bone disorders rickets and osteomalacia. metabolism in adults. The increasing availability of highly potent lifetime medicines in disciplines such as HIV medicine means that the balance of associated kidney diseases is quickly shifting from those caused by the disease to those induced by the pharmacological treatments. Polyuria, dehydration, polydipsia, hypophosphatemia rickets, acidosis, growth failure, hypokalaemia, and hyperchloremia are all symptoms of proximal renal tubular acidosis. However, cystine accumulates in lysosomes if the carrier protein is defective due to a mutation in the CTNS gene. A clinician may suspect Fanconi syndrome based on blood and urine tests, symptoms, and a blood test that reveals abnormalities. The amount of medication that PT cells are exposed to is determined by blood concentration, which is influenced by a number of factors that have been identified as major risk factors for developing FS. Drinking sodium bicarbonate can help to neutralise a high acid level in the blood. As new medications are developed, it is quite likely that some may be toxic to the PT and cause FS. As a result, it is critical that lessons from the past be learnt and that more complete nephrotoxicity screening tests in humans be conducted.

Future Scope

This study assesses Fanconi Syndrome, which is one of the most common disorders in today's society. With a hypokalemic metabolic acidosis associated with Vitamin - D resistant metabolic bone disease, proximal tubular reabsorption is impaired. So, in the near future, an overview will be created from this effort, which will assist researchers in obtaining knowledge on the challenge.

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CONFLICT OF INTEREST

Authors do not claim any conflict of interest.

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ABBREVIATION

FS – Fanconi Syndrome
PT – Proximal Tubule
HIV – Human Immunodeficiency Virus
CTNS – Cystinosin, Lysosomal Cystine Transporter gene

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