What is distal tubular renal acidosis (dRTA)?

Distal renal tubular acidosis is a rare kidney disorder that occurs when the kidneys are unable to effectively remove the buildup of circulating acids in the blood—a condition called acidosis—which leads to a metabolic imbalance. dRTA is a serious disorder, especially for pediatric patients.

dRTA can be either genetically inherited or acquired. The inherited form of dRTA is most common among infants and children, while the acquired form is more common in adults. Inherited dRTA is caused when one of three genes responsible for managing the pH levels of blood in our body undergoes a change and is passed from parent(s) to child. Acquired dRTA is due to autoimmune disorders like Sjögren's syndrome, systemic lupus erythematosus (SLE), and rheumatoid arthritis, or to certain medications, such as anti-inflammatory drugs.

It's difficult to determine the exact incidence of the disorder, which was first described in the 1930s. To date, it is estimated that about 30,000 patients in Europe and 20,000 patients in the United States suffer from dRTA.

What are the signs and symptom of dRTA?

The principal sign for the presence of dRTA is a hypokalemic (decreased blood potassium) and hyperchloremic (elevated chloride ions in the blood) acidosis, which is revealed by a severe drop in the blood alkaline reserve (a decrease in HCO3-, or bicarbonatemia, concentration) associated with an inability to acidify the urine.

Symptoms can begin in infants or as late as adulthood and can vary depending on the specific gene change, the level of acidosis, the age of the individual, and even how advanced the disease is. Severe manifestations of the disease occur primarily in pediatric patients, especially infants. Early signs and symptoms in babies include nausea and vomiting, dehydration, extreme tiredness, feeding issues and problems with weight gain (also known as failure to thrive).

Because phosphate, and consequently calcium, can be leached from the bones in patients living with dRTA, the disease can lead to mineral imbalances and bone disorders. Children can develop rickets, a condition in which the bones become too soft and do not harden or calcify as normal. Children often also experience stunting of growth and may not reach their full adult height potential.

Mineral imbalances caused by dRTA can also lead to the formation of kidney stones and other kidney deposits. Kidney deposits can trigger the risk of chronic kidney disease (CKD) increases and the filtering ability of the kidneys is hampered. Because dRTA can also decrease levels of potassium in the blood (hypokalemia), severe muscle weakness, shortness of breath, and abnormal heart rhythm can result. In extreme cases of hypokalemia, severe cardiac arrhythmias, paralysis and even death can occur. Patients with dRTA can also experience significant digestive disorders, such as anorexia, vomiting, diarrhea and constipation. These symptoms are typically due to metabolic acidosis, but hypokalemia can cause a decrease in gastrointestinal motility.

Additionally, dRTA can lead to difficulty with hearing caused by changes in the inner ear. This can progress to deafness in some individuals.

How is dRTA diagnosed and treated?

dRTA is diagnosed using a combination of a physical exam to detect signs and symptoms consistent with the disease, tests to determine acid and mineral levels in the urine and blood, and genetic testing. Doctors may check for other diseases that can cause dRTA, such as Sjögren's syndrome, systemic lupus erythematosus (SLE), and rheumatoid arthritis. Medications will also be reviewed for drugs that might cause or worsen dRTA.

Currently, there is no published clinical guidance for treating patients with dRTA. The main treatment involves alkali agents, which are used to neutralize excess acid in the blood. Alkali agents can include sodium bicarbonate, potassium bicarbonate, sodium citrate or potassium citrate. Compared to adults, pediatric patients are generally treated with higher doses relative to their weight because their bicarbonate needs are greater than adults.

Reducing acid levels can also help correct imbalances of other electrolytes, such as potassium, phosphorus, and potassium. Correcting these imbalances may help reduce the risk of bone disease and help prevent kidney stones; however, a treatment's efficacy can depend on different factors, such as a person's age, stage of disease, overall health, medication adherence, and whether or not there are other diseases present.

Since dRTA often results in hypokalemia, treatment requires potassium supplementation. This may be administered as a component of the alkalizing salt or as supplementary medication in the form of potassium chloride.

These products usually require repeated dosing per day and have a poor tolerance profile and palatability. Because maintaining overnight treatment is of particular importance, compliance is low in pediatric patients, due to their increased sleep needs. As a result, patients may experience poor control of homeostasis over 24 hours, which is vital to preventing long-term complications. Side effects of these treatments can also include abdominal pain.

Thus, a need exists for therapeutic treatments that re-establish normal homeostasis over a 24-hour period, maintain complete 24-hour dosing including during sleep periods, and have the potential to improve patient compliance over currently available formulations. This is why Advicenne has developed an innovative product in an oral pharmaceutical form, appropriate for children and adults, a global treatment which maintains a sustained-release of various agents along the entire intestinal tract over 12 hours for a twice-a-day administration, thus maximizing absorption of the agents, re-establishing homeostasis, and avoiding abdominal pain.