

Galactose and the role of circulating permeability factors in FSGS

The cause of primary FSGS has remained a subject of intensive study over the last 30 years. While great strides have been made in our understanding of the biological mechanisms underlying this disease, the therapies used have not changed substantially. The mainstay of therapy continues to be long term use of harsh steroids and without response to this therapy the majority of patients can expect progression to kidney failure¹. While a transplant of the diseased kidney gives hope, when dealing with resistant FSGS, an estimated 30% of patients experience recurrence of the disease in their transplanted kidney. The rate increases significantly to over 75% of patients with repeat transplants².

The glomeruli, the tiny filters of the kidney, ensure that the useful substances that the body needs, such as proteins, are left in the blood while waste products are removed from the kidneys. In the case of FSGS there is damage to this filtering mechanism and proteins needed in the body leak into the urine³. Recurrence of FSGS following a transplant has provided support for the theory that circulating permeability factors may be a potential cause of primary FSGS. Permeability factors are so named because they are thought to increase the leakiness of glomeruli, resulting in the loss of proteins into the urine.

Researchers have been searching for the identity of the elusive permeability factor for years. Recently, Dr. Virginia Savin at the University of Wisconsin, through a series of experimental studies, has verified the presence of a molecule that she believes is the FSGS permeability factor. This factor is thought to be present in some patients with FSGS at increased levels and may be one of the key factors that lead to proteinuria and recurrence of disease after transplantation⁴.

Based on preliminary investigations performed on tissue samples, as well as anecdotal reports of treatment in patients with primary FSGS, a sugar, galactose, may bind to the FSGS permeability factor and reduce its levels in the blood⁴.

The effect of oral galactose was studied in a 30 year old man with kidney failure caused by recurrence of FSGS. The patient tested positively for the FSGS permeability factor and was given galactose to take orally (15grams dissolved in tap water twice a day for six weeks) while awaiting a kidney transplant. Blood was collected 1, 2 and 4 weeks into treatment, then again 4 weeks after discontinuing galactose. He showed progressively lower levels of the permeability



factor during the 4 weeks of ingestion and the level of the factor remained low 4 weeks after galactose was discontinued⁴. While there was decrease in the level of the permeability factor, the patient did not see a decrease in proteinuria possibly due to irreversible injury already done to the glomeruli.

A second case was documented in Montreal in which a 48 year old man was hospitalized with rapidly progressing kidney failure. The patient had failed traditional therapies including prednisone, cyclophosphamide, mycophenolate mofetil and cyclosporine. As a last resort, following a positive test for the FSGS permeability factor, he was started on oral galactose (10grams twice a day) in February of 2007. By September of 2007, his permeability had decreased dramatically and proteinuria had declined from 4.26grams/day to 0.56grams/day. Following this response, immunosuppressive medications were discontinued and at follow up 8 weeks later, his proteinuria remained at 0.57grams/day⁶.

While limited, these case studies raise the possibility that more extended treatment with galactose may be a safe and effective means of reducing the level of the FSGS permeability factor, leading to reduction in proteinuria, and possibly a delay in the progression to kidney failure.

NephCure is a sponsor of a study entitled, 'Effect of oral galactose on focal segmental glomerulosclerosis (FSGS) permeability factor,' by Dr. Howard Trachtman. This pilot study, involving 23 patients diagnosed with steroid resistant FSGS and a high level of the permeability factor, tests whether oral galactose reduces the FSGS permeability factor in patients with resistant FSGS. In the first 16 patients who completed the 28-day course of galactose, all had a reduction in the circulating level of the permeability factor. This proof of concept study was necessary to show that galactose could in fact reduce the suspected permeability factor in patients testing positively for it. The length of this study was not suitable to show a reduction in proteinuria. Extended treatment may be needed to lower proteinuria and protect the kidneys. While we are hopeful that galactose may be added to the potential arsenal of therapies used to treat NS and FSGS, larger clinical trials are necessary to elucidate the role and effect of galactose on this patient population.

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