THE EFFECT OF CALCIUM GLYCEROPHOSPHATE (PRELIEF®) ON EPITHELIAL REGENERATION USING NMP22 AS A QUANTITATIVE EVALUATION IN THE TREATMENT OF INTERSTITIAL CYSTITIS (IC)

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NMP22 Abstract

THE EFFECT OF CALCIUM GLYCEROPHOSPHATE (PRELIEF®) ON EPITHELIAL REGENERATION USING NMP22 AS A QUANTITATIVE EVALUATION IN THE TREATMENT OF INTERSTITIAL CYSTITIS (IC)

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Introduction: IC includes a major portion of the "painful bladder" disease complex. The etiology of IC remains unknown, but is likely multifactorial. Treatment of IC is symptomatic and most patients are treated with either systemic or intravesical therapies. Monitoring the efficacy of treatment has been difficult due to the subjective nature of reporting symptoms such as dysuria, frequency, and nocturia, etc. The Multimodal NMP22® Test Kit (Multistix, Inc.) is an FDA-approved quantitative assay for bladder cell damage using a monoclonal antibody against transitional epithelial cell protein in voided urine, and may also serve as a useful indicator of urothelial cell-inflammation.

Study Objective: To determine the utility of measuring NMP22 during the evaluation and treatment of IC.

Materials and Methods: 5 patients (4 females, 1 male) previously diagnosed with IC were followed prospectively for 12-24 months (mean 22) during which time NMP22 levels and IC symptoms were measured.

Results: Three patients were acute symptomatic (IC) and 2 were symptomatic. The 2 asymptomatic patients had been taking calcium gluconate (Rodellar, Hofmann-La Roche) and the 3 symptomatic patients had not. All patients were given a urine analysis, urine-culture and sensitivity at each visit. Patients were also given the IC Symptom Diary and NMP22 readings were taken on 3 occasions in addition to the void NMP22 Test. NMP22 values for the 3 IC patients were higher (mean 67) than the 2 asymptomatic patients (mean 38). All patients showed an increase in NMP22 levels measured by study 1 and study 2. In the 3 IC patients, levels were higher in NMP22 3 days after the last IC flare point of the baseline study, This suggests an increase in NMP22 values in IC patients and symptoms.

Conclusions: NMP22 may be a useful marker for the cellular inflammation that causes symptoms of IC. Patients with frequent bladder infections and extensive inflammation showed increased NMP22 values, suggesting a decrease in cellular defense. Patient's also reduced subjective symptoms in all of the IC patients evaluated. The use of PreLief! for the effective treatment of IC should therefore be confirmed in a full clinical trial.

Purpose

To prospectively measure urinary NMP22 levels in the 5 patients whose work-up has identified them as having interstitial cystitis. During a period from 2001-2004 these patients continued to have urinary NMP22 evaluated during medical management.

A SINGLE-BLEND, BANANOSIZED, CONTROLLED STUDY WITH TOPICAL CALCIUM GLYCEROPHOSPHATE IN PATIENTS WITH COMPROMISED EPIDERMAL CELL REWALN AND MODERATELY SEVERE DRY SKIN

Lipids, Cells and Tissues, VOL. 17, LIPIDOSIS, 2003, pp. 37-46

Effect of CDP on Equilibrated Blue Cell Membrane

Conclusions

NMP22 is an excellent, FDA-approved test for bladder cancer detection, and changes in its levels indicate changes in the IC symptoms reported by this group of patients. The monitoring of NMP22 levels may therefore provide additional information regarding the efficacy of therapy. Quantitative urine analysis of NMP22 may be useful in consistently assessing symptom improvement with symptomatic improvement in IC patients. These measurements may also allow for close observation of the status of bladder mucosa and help detect potential developing neoplasia.

The use of PreLief! either alone or in conjunction with Eltrombopag, as shown in this pilot study, appears to be capable of ameliorating symptoms associated with interstitial Cystitis. The ability of PreLief! to relieve symptoms of interstitial cystitis should therefore be evaluated in a prospective, placebo-controlled study.

Speculation

The epithelial observations by Leyden and Gove are intriguing. A similar response is implied in the bladder of IC patients who are under PreLief! therapy when utilizing the NMP22 urinary marker to evaluate the state of epithelial differentiation. Other researchers have shown that patients with interstitial Cystitis have an increased antiproliferative factor (APF), a tanning agent, produced by bladder epithelial cells. CDP (PreLief!) has been shown to effect epithelial cell growth, either by direct stimulation, or through another mechanism affecting cellular proliferation. In the present study we have documented beneficial effects of CDP in five IC patients. We are currently measuring the potential to ameliorate this benefit using CDP urinary marker, a measure of cellular distress. We propose therefore that the reduced NMP22 levels and IC symptoms, the subjects showed had reduced parameters recorded at each of the visits indicated.

Subjects using PreLief! were asked to take 300 mg twice daily. Subjective symptoms were evaluated using validated IC questionnaires.