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ORIGINAL ARTICLE

Apoptotic effect as biomarker of disease, severity and follow-up in interstitial cystitis☆

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KEYWORDS
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Abstract

Objective: To determine whether the apoptotic effect test could serve as a biomarker of severity in bladder pain syndrome/interstitial cystitis.

Material and methods: A prospective study was conducted between January 2010 and January 2015, which included 57 patients diagnosed with interstitial cystitis and 49 diagnosed with chronic pelvic pain of gynecological origin. The urine was exposed to cell cultures, and the urine's capacity for inducing apoptosis in the cultures was analyzed. A statistical analysis was then conducted to assess whether the apoptotic effect was associated with the symptoms.

Results: After performing an analysis of the association between the degree of apoptotic effect and the symptoms of patients with interstitial cystitis, we observed a significant increase in the mean percentages of apoptosis as the degree of symptom severity increased. After analyzing the association between the apoptotic effect and symptoms, we obtained a positive correlation in the patients with interstitial cystitis and a lack of correlation in the patients with chronic pelvic pain of gynecological origin. The rates of apoptosis increased progressively in the patients with interstitial cystitis as the symptoms increased, while the patients with chronic pelvic pain of gynecological origin remained stable.

Conclusions: The apoptotic effect of the urine of patients with interstitial cystitis could be a marker of disease, thus differentiating patients with interstitial cystitis from patients with chronic pelvic pain. The effect could also provide an objective measure of symptom severity.

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PALABRAS CLAVE
Biomarcador;
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Diagnóstico

Efecto apoptótico como biomarcador de enfermedad, severidad y seguimiento en la cistitis intersticial

Resumen

Objetivo: Estudiar si el test de efecto apoptótico podría servir como biomarcador de severidad en el síndrome de dolor vesical/cistitis intersticial.

Material y métodos: Se realizó un estudio prospectivo entre enero de 2010 y enero de 2015, se incluyeron 57 pacientes diagnosticadas de cistitis intersticial y 49 de dolor pélvico crónico de origen ginecológico. Se expuso la orina a cultivos celulares y se analizó su capacidad para inducir apoptosis en ellos. Posteriormente se llevó acabó un análisis estadístico para valorar si el efecto apoptótico se asociaba con la sintomatología.

Resultados: Al realizar un análisis de la asociación entre el grado del efecto apoptótico y la sintomatología de las pacientes con cistitis intersticial, se observó un aumento significativo de los porcentajes medios de apoptosis a medida que aumenta el grado de severidad sintomatológica. Al analizar la asociación entre el efecto apoptótico y la sintomatología, se obtuvo una correlación positiva en los pacientes con cistitis intersticial y una ausencia de correlación en los pacientes con dolor pélvico crónico de origen ginecológico. Los porcentajes de apoptosis aumentan de manera progresiva en las pacientes con cistitis intersticial a medida que presentan mayor sintomatología mientras que los pacientes con dolor pélvico crónico de origen ginecológico permanecen estables.

Conclusiones: El efecto apoptótico de la orina de pacientes con cistitis intersticial podría ser un marcador de enfermedad, permitiendo diferenciar las pacientes afectas de cistitis intersticial de pacientes con dolor pélvico crónico y además poder tener una medida objetiva del grado de severidad de los síntomas.

Introduction

Bladder pain syndrome or interstitial cystitis (BPS/IC) is a chronic disease that produces disabling pain (pressure, discomfort), which is perceived as related to the urinary bladder and is associated with symptoms of the lower urinary tract. The diagnosis is made by exclusion, ruling out infection and other causes that justify the pain.[1,2] IC remains a diagnostic challenge and the need for a biomarker that identifies patients and its severity would be of great help in clinical practice. In 1999, the National Institute of Health defined that a disease biomarker is a characteristic that is measured and evaluated objectively as an indicator of normal or pathological biological processes or pharmacological responses to a therapeutic intervention. In urology, PSA is the most used; however, no biomarker of disease has been identified for IC.[3]

It is known that not all women with BPS/IC have the same intensity of symptoms, and that the same treatment does not work for all of them.[4] Due to the great variability of symptoms and different response to the treatment, it is interesting to investigate a biomarker of disease that makes it possible to differentiate the different degrees of severity of BPS/IC.

The objective of this work is to study if the apoptotic effect test could serve as a biomarker of severity in the BPS/IC.

Material and method

Between January 2007 and January 2011, 106 female patients were studied; 57 diagnosed with BPS/IC, and 49 diagnosed with gynecological chronic pelvic pain (GCPP).

The inclusion criteria for IC patients were: women older than 18 and diagnosed according to the criteria of the National Institute of Diabetes and Digestive and Kidney Diseases (symptoms of pain and/or urinary urgency and cystoscopic demonstration of glomerulations and/or presence of Hunner's ulcer). All of them with a de novo diagnosis and without having received any treatment. All the patients self-filled the genito-urinary pain index questionnaire (GUPI), in order to objectively quantify the symptoms.[5]

The study of the apoptotic effect of urine on cell cultures was carried out at the Instituto de Investigación Príncipe Felipe in Valencia in the Department of Cytomics. The urine of patients with IC and of patients with SDPG was exposed to cultures of neoplastic cells and their ability to induce apoptosis in them was analyzed, following the protocol explained below. The cell lines were seeded with multichannel pipette in 96-well culture plates at a density of 50,000 cells per well. After 24 h of culture in incubator at 37 °C and 5% CO_2, the culture medium of the plates was removed and replaced with 180–200 μL fresh culture medium. The wells were treated with 0–20 nL of neutralized urine sample from control subjects or patients with IC.