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ORIGINAL ARTICLE

Proinflammatory and anti-inflammatory cytokine profile in pediatric patients with irritable bowel syndrome☆,☆☆

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KEYWORDS
Irritable bowel syndrome;
Pediatrics;
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Abstract
Background and objectives: There is evidence that patients with irritable bowel syndrome (IBS) have a low degree of inflammation in the intestinal mucosa. The aim of the study was to evaluate theprofile of pro- and anti-inflammatory cytokinesin plasmain Mexican pediatric patients with IBS.
Patients and methods: Fifteen patients with IBS according to Rome III criteria for childhood and 15 healthy children, matched by age and sex, were included in the study. Plasma levels of tumoral necrosis factor alpha (TNF-α), interleukins 10 and 12 (IL-10, IL-12) and transforming growth factor beta (TGF-β) were quantified and compared between groups.
Results: Plasma levels of IL-10 were lower in patients with IBS (86.07 + 21.3 pg/mL vs. 118.71 + 58.62 pg/mL: *P*=.045) and IL-12 levels were higher in patients with IBS compared to the control group of healthy children (1,204.2 ± 585.9 pg/mL vs. 655.04 ± 557.80 pg/mL; *P*=.011). The IL-10/IL-12 index was lower in patients with IBS (0.097 ± 0.07 vs. 0.295 ± 0.336; *P*=.025). Plasma concentration of TGF-β was higher in patients with IBS (545.67 ± 337.69 pg/mL vs. 208.48 ± 142.21 pg/mL; *P*=.001). There was no difference in plasma levels of TNF-α between groups.

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Conclusions: This study suggests that children with IBS have a state of altered immune regulation. This is consistent with the theory of low-grade inflammatory state in these patients. Further studies are needed to elucidate the role played by these cytokines, specifically TGF-β in the pathogenesis of IBS.

PALABRAS CLAVE
Síndrome de intestino irritable;
Pediatría;
Citocinas;
Factor de crecimiento transformante beta

Perfil de citocinas proinflamatorias y antiinflamatorias en pacientes pediátricos con síndrome de intestino irritable

Resumen
Antecedentes y objetivos: Existe evidencia de un grado bajo de inflamación a nivel de la mucosa intestinal en pacientes con síndrome de intestino irritable (SII). El objetivo del estudio fue evaluar el perfil de citocinas proinflamatorias y antinflamatorias en plasma en pacientes pediátricos mexicanos con SII.
Pacientes y métodos: Quince pacientes con SII de acuerdo con los criterios de Roma III para pacientes pediátricos y 15 niños sanos, pareados por edad y sexo fueron incluidos en el estudio. Se cuantificaron en plasma y se compararon el factor de necrosis tumoral alfa (TNF-α), las interleucinas 10 y 12 (IL-10, IL-12) y el factor de crecimiento transformante beta (TGF-β).
Resultados: Los niveles plasmáticos de IL-10 fueron menores en los pacientes con SII (86.07 + 21.3 pg/mL vs. 118.71 + 58.62 pg/mL; p = 0.045) y los niveles de IL-12 mayores en los pacientes con SII en comparación con el grupo control de niños sanos (1,204.2 ± 585.9 pg/mL vs. 655.04 ± 557.80 pg/mL; p = 0.011). El índice IL-10/IL-12 fue menor en los pacientes con SII (0.097 ± 0.07 vs. 0.295 ± 0.336; p = 0.025). La concentración en plasma de TGF-β fue mayor en los pacientes con SII (545.67 ± 337.69 pg/mL vs. 208.48 ± 142.21 pg/mL; p = 0.001). No hubo diferencia en los niveles plasmáticos de TNF-α entre ambos grupos.
Conclusiones: Este estudio indica que los niños con SII presentan un estado de alteración de la regulación inmune. Aún está pendiente por dilucidar el papel que juegan estas citocinas, específicamente la TGF-β, en la patogénesis del SII.

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder that is defined by the Rome III criteria for pediatric patients as the sensation of abdominal discomfort or pain that has presented at least once a week in the 2 months prior to diagnosis and is associated with 2 of the following characteristics at least 25% of the time: *a)* it improves with a bowel movement, *b)* onset is associated with changes in bowel movement frequency, and *c)* onset is associated with change in the form (appearance) of the bowel movements. There is no evidence of an inflammatory, anatomic, metabolic, or neoplastic process accompanying these characteristics and they should also be present at least once a week in the 2 months before diagnosis.[1] Between 22-45% of the pediatric patients from 4 to 18 years of age that are seen at tertiary care clinics are diagnosed with IBS. Multiple mechanisms are involved in its pathophysiology. One of the first studied is visceral hypersensitivity, a consequence of an alteration in the brain-bowel axis that most likely is modulated by genetic factors that regulate the local inflammatory and immunologic responses to different processes such as infections, intestinal trauma, or allergy. These, in turn, cause intestinal motility disorders that clinically manifest as diarrhea or constipation, associated or not, with abdominal pain.[2–5] However, psychologic and inflammatory factors, as well as motility alterations also come into play in relation to its pathophysiology.

An infectious event can apparently precipitate IBS development in individuals with a psychosocial and genetic susceptibility, probably by conditioning a mild grade of intestinal mucosa inflammation that leads to immune system activation.[4,6–8] Recent studies support the hypothesis of immune activation in adults with this syndrome: infiltration of immune cells into the intestinal mucosa of IBS patients[9–11] and a greater expression of proinflammatory cytokines, such as interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-α, and IL-12, with low levels of IL-10.[12–16] Polymorphisms of a single nucleotide in the genes that encode for TNF-α and IL-10 have been reported in adult IBS patients, compared with healthy controls.[12,17,18] Hua et al. recently found that IL-10 levels were lower in pediatric IBS patients when compared with healthy controls; they found no differences in the levels of TNFα and IL-6, both proinflammatory cytokines, but