

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

CrossMark

The diagnostic value of hepcidin to predict the presence and severity of appendicitis in children

Margarita Kaiser, MD, Magdalena Schroeckenfuchs, MD,
Christoph Castellani, MD,* Gert Warncke, MD, Holger Till, MD,
and Georg Singer, MD

Department of Paediatric and Adolescent Surgery, Medical University of Graz, Graz, Austria

ARTICLE INFO

Article history:

Received 13 July 2017

Received in revised form

26 September 2017

Accepted 12 October 2017

Available online 2 November 2017

Keywords:

Appendicitis

Children

Hepcidin

Simple

Complicated

Predictive value

ABSTRACT

Background: The aim of this study was to determine the diagnostic capacity of hepcidin in pediatric acute appendicitis and its accuracy as a predictor of the severity of appendicitis. **Materials and methods:** In children with appendicitis ($n = 39$), leukocytes, platelet count, and the serum levels of C-reactive protein (CRP) and hepcidin were compared to a control group ($n = 25$) of patients with unspecific abdominal pain. Additionally, parameters were compared between children with simple ($n = 17$) and complicated appendicitis ($n = 22$). Receiver operation characteristic analyses of the different parameters were performed and the areas under the curve (AUCs) calculated.

Results: Leukocytes and serum hepcidin levels were significantly higher in children with acute appendicitis versus control group (13.7 ± 5.7 versus 9.8 ± 3.9 G/L, $P = 0.005$ and 31.3 ± 21.7 versus 20.4 ± 14 ng/mL, $P = 0.039$). AUCs for hepcidin, leukocytes, and CRP were 0.654, 0.711, and 0.619, respectively. Complicated appendicitis was associated with significantly higher hepcidin concentrations compared to simple appendicitis (38.5 ± 17.6 ng/mL versus 21.6 ± 23.4 ng/mL, $P < 0.001$). A combination of leukocytes, CRP, and hepcidin had the highest AUC (0.914) to predict complicated appendicitis.

Conclusions: Increased serum levels of hepcidin were found in children with appendicitis compared to controls. While hepcidin was useful to identify patients with complicated appendicitis as it does not seem appropriate to distinguish between simple appendicitis and other causes for acute abdominal pain.

© 2017 Elsevier Inc. All rights reserved.

Introduction

Acute appendicitis (AA) is one of the most common causes for admission to pediatric surgical emergency departments in children and adolescents.^{1–3} The lifetime risk of developing AA is approximately 8%, and a peak incidence in the early teenage years has been reported.⁴ Even for experienced pediatric surgeons, the diagnosis of AA still remains challenging. A plethora of differential diagnoses including gastroenteritis,

ovarian pathologies, cecal or Meckel diverticulitis, and constipation may mimic the signs of AA. Consequently, misdiagnosis rates of 28% to 57% have been described in children younger than 12 years.^{5,6}

The combination of high misdiagnosis rates and the diversity of clinical symptoms triggers ongoing research, evaluating the diagnostic accuracy of various laboratory parameters in children with appendicitis. Hepcidin, originally termed LEAP-1 (liver-expressed antimicrobial protein 1), was

* Corresponding author. Department of Paediatric and Adolescent Surgery, Medical University of Graz, Auenbruggerplatz 34, 8036 Graz, Austria. Tel.: +43/316/385-13762; fax: +43/316/385-13775.

E-mail address: christoph.castellani@medunigraz.at (C. Castellani).

0022-4804/\$ – see front matter © 2017 Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.jss.2017.10.021>

first described by Park *et al.*⁷ in 2000 and is a 25-amino acid peptide predominantly produced in the liver. Hepcidin is the main regulator of intestinal iron absorption and macrophage iron release. One of its key functions is to decrease the extracellular iron levels, thus reducing the iron availability for invading microorganisms.^{8,9} Increased serum levels of hepcidin were found in children with inflammatory states such as sepsis and inflammatory bowel disease.^{10,11} Therefore, hepcidin is classified as an acute-phase protein and a component of the innate immune system. Presently, the usefulness of serum hepcidin in predicting AA in children has not been addressed in the literature.

Therefore, the aim of this prospective single-center study was to determine the diagnostic capacity of serum hepcidin levels in pediatric patients with AA. Additionally, the accuracy of hepcidin as a predictor of the severity of appendicitis was assessed.

Material and methods

Following informed consent of children and/or legal guardian, a consecutive series of children ($n = 39$) with AA who underwent appendectomy over a 6-month period were included in this investigation (appendicitis group [AG]). Children admitted with unspecific abdominal pain who improved under conservative treatment and did not require surgical intervention served as controls ($n = 25$; control group; CG). Conservative treatment consisted of pain therapy with nonopioids, infusion of crystallines, and dietary build up from liquid to solid foods. None of the patients in the CG received antibiotic treatment. Diagnosis on discharge was gastroenteritis in 18 patients, constipation in four, and abdominal cramps based on food intolerances in three children.

Demographic data and preoperative serum parameters including total leukocyte and platelet count and C-reactive protein (CRP) were obtained. Serum levels of hepcidin were measured using a hepcidin-25 (bioactive) ELISA kit (Alpco, Windham, NH) according to the manufacturer's instructions. The diagnosis of appendicitis was verified by standard histopathological examinations.

Patients with AA were allocated to a noncomplicated (simple AA, $n = 17$) or a complicated group (perforation, abscess, localized, or generalized peritonitis, $n = 22$) as previously described in the literature.¹²

The study has been complied with all the relevant national regulations, institutional policies, and in accordance the tenets of the Helsinki Declaration and has been approved by the local ethics committee (EK 25-421 ex 12/13).

Statistical analysis

SPSS 22.0 (IBM Corp, Armonk, NY) was used for statistical calculations. Categorical variables are presented as frequencies and percentages, and continuous variables as means and standard deviations. The chi-squared test was used to compare categorical variables. Continuous variables were compared using the Mann–Whitney U test. Post hoc power analysis was conducted using G* Power 3.1.9.2 software (Heinrich Heine Universitaet, Duesseldorf, Germany).

Statistically, significant differences were assumed in case of P -values < 0.05 . Receiver operation characteristic (ROC) curves were used to determine the diagnostic accuracy of the laboratory parameters addressed in this investigation. Additionally, logistic regression analysis paired with ROC was performed to assess the capacity of laboratory parameter combinations. Areas under the curve (AUC) of the different parameters and their combinations were determined.

Results

Diagnostic accuracy of markers in patients with AA

A total of 64 patients were included in the study (39 AA and 25 CG). The demographic data of the patients are presented in Table 1. Gender distribution, age, weight, height, and body mass index showed no statistically significant differences between the groups. The length of hospital stay was significantly longer in the AG (5.9 ± 1.6 versus 3.6 ± 0.9 d; $P < 0.001$). Table 2 shows a comparison of total leukocyte and platelet counts, CRP, and serum levels of hepcidin. Statistically significant differences could be found for total leukocyte count and serum levels of hepcidin.

ROC curves and the AUCs for hepcidin, CRP, leukocyte and platelet count, and combinations are shown in Figure 1. As a single parameter, leukocytes had the highest diagnostic accuracy. Hepcidin had a similar diagnostic accuracy to CRP (Fig. 1A). The combination of leukocytes and CRP reached an AUC of 0.715 (Fig. 1B). The combination of leukocytes, platelets, CRP, and hepcidin reached only a slightly higher AUC (0.735).

Markers in simple and complicated appendicitis

Among the 39 children who underwent appendectomy (AG), 17 had simple and 22 had complicated appendicitis. Patients did not differ significantly in age, height, and body mass index (Table 3). However, patients of the simple AG had a significantly higher body weight compared with those of the complicated AG. The length of hospital stay did not significantly differ between these groups (5.7 ± 1.4 versus 6 ± 1.7 d; $P = 0.624$). Total leukocyte count, CRP, and hepcidin were significantly increased in children with complicated appendicitis (Table 4). Figure 2 displays ROC curves and AUC for hepcidin, CRP, leukocyte and platelet count, and combinations with regard to the severity of appendicitis. Comparable AUCs were found for leukocytes and hepcidin (Fig. 2A).

Table 1 – Demographic data of all patients ($n = 64$).

	AG ($n = 39$)	CG ($n = 25$)	P value
Gender (m/f)	14/25	10/15	0.741
Age (years)	12.2 ± 3.1	12.8 ± 3.5	0.391
Weight (kg)	46.1 ± 13.7	51.3 ± 16.7	0.226
Height (cm)	155 ± 17	157 ± 16	0.715
BMI	18.7 ± 3	20 ± 3.5	0.147

Download English Version:

<https://daneshyari.com/en/article/8835812>

Download Persian Version:

<https://daneshyari.com/article/8835812>

[Daneshyari.com](https://daneshyari.com)