Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/pepo

Original research article/Artykuł oryginalny

A clinical characteristic of paediatric ulcerative colitis patients qualified for a Cyclosporin A therapy

Charakterystyka kliniczna dzieci z wrzodziejącym zapaleniem jelita grubego zakwalifikowanych do leczenia cyklosporyną A

Marcin Osiecki [1,*], Maciej Dądalski, Grzegorz Oracz, Jarosław Kierkuś

Klinika Gastroenterologii, Hepatologii, Zaburzeń Odżywiania i Pediatrii, Instytut "Pomnik-Centrum Zdrowia Dziecka", Al. Dzieci Polskich 20, 04-730 Warszawa, Poland

ARTICLE INFO

Article history:
Received: 13.03.2017
Accepted: 24.04.2017
Available online: xxx

Keywords:
- Inflammatory bowel disease
- Colectomy
- Immunosuppressive agents

Słowa kluczowe:
- nieswoiste zapalenie jelita
- kolektomia
- leki immunosupresyjne

ABSTRACT

Background: According to ECCO/ESPGHAN consensus for managing acute severe ulcerative colitis in children, Cyclosporin A remains a rescue therapy in acute steroid-refractory ulcerative colitis. **Aim:** To describe clinical features of children qualified for Cyclosporin A (CsA) treatment. **Material and methods:** It is a retrospective, single centre study. We describe a clinical characteristic of children who underwent CsA treatment in the course of ulcerative colitis (UC). **Results:** We evaluated 59 children's medical charts treated in our department with Cyclosporin A in the course of ulcerative colitis in years 2005–2015. There is a female predominance in the study (34/59). The median age at the diagnosis was 11.9 years, while the median age of the initiation of CsA 15 years. Ulcerative colitis had lasted on median 20 months when CsA was initiated. The median PUCAI score at the onset of CsA therapy was 50.00. Almost 80% of patients had a moderate/severe course. **Conclusion:** CsA was in our department the drug of choice in case of steroid refractory ulcerative colitis.

Introduction

It is established that a course of paediatric UC is more severe than in adults. Colitis proximal to the hepatic flexure is the most frequent phenotype [1]. An incidence of admission to the hospital due to severe flare is 1 per 100 000 children per year [2]. Acute severe ulcerative colitis (ASUC) is a life threatening event which is diagnosed when a patient receives more than 65 points according to the Paediatric Ulcerative Colitis Activity Index (PUCAI) [3]. Mortality in a course of UC has been reduced since steroids were introduced in 1955 [4]. Twenty eight percent of children with UC needs hospitalisation to have intravenous

* *Corresponding author at*: Tel.: +48 22 815 73 84; fax: +48 22 815 73 82.
E-mail address: m.osiecki@ipczd.pl (M. Osiecki).
[1] Kierownik Kliniki: prof. dr hab. n. med. M. Woynarowski.

Abbreviations: ECCO – European Crohn's and Colitis Organisation; ESPGHAN – European Society for Peadiatric Gastroenterology, Hepatology and Nutrition; CsA – Cyclosporin A; UC – ulcerative colitis; PUCAI – Paediatric Ulcerative Colitis Activity Index; ASUC – acute severe ulcerative colitis; INF – infliximab.

http://dx.doi.org/10.1016/j.pepo.2017.04.005
0031-3939/

steroids administered but only half of them do respond to the first line therapy [2]. In patients who do not improve on this treatment, in order to avoid rescue colectomy second line treatment is initiated. According to the consensus, therapies with Cyclosporin A, Tacrolimus, infliximab are available [5]. Cyclosporine A is an immunosuppressive cyclic peptide [6]. It primarily inhibits T-lymphocyte activation and proliferation through a calcineurin inhibition [7]. CsA was introduced in a steroid-refractory UC in 1994 by Lichtiger et al. [8]. Its main adverse events are paresthesias, hypomagnesemia, hypertension, minor nephrotoxicity and gingival hypertrophy [9]. To date 96 paediatric patients with UC receiving CsA have been reported [10–15]. Castro et al. determined that CsA allowed to avoid colectomy in 87% and 72% cases, in short-term and long-term observation respectively [15]. Socha et al. stated that CsA is less effective in maintaining remission and it does not allow to avoid colectomy in severe flares [12]. The main objective of this study was to describe clinical characteristic of children treated with Cyclosporin A.

Aim

Our goal was to describe clinical features of children qualified for CsA treatment.

Material and methods

We retrospectively assessed medical charts and electronic medical database of patients suffering from ulcerative colitis, who received CsA treatment in years 2005–2015 in the Children's Memorial Health Institute. Firstly we elicited patients who had CsA's level evaluated in the Gastroenterology Department. We received 1090 results belonging to 181 patients. Secondly, following ICD10 classification, we determined each patient's diagnosis. Diagnosis of ulcerative colitis was confirmed by review of clinical, endoscopic, histopathological data. Exclusion criteria were Crohn disease, Interleukin 10 receptor deficiency, inflammatory bowel disease, CsA initiation in course of a concomitant autoimmune hepatitis, primary sclerosing cholangitis, liver/kidney transplant, giant cell hepatitis, CsA initiation in other departments. Overall 59 patients were involved in the study. We assessed disease's history preceding CsA's therapy: the age at the time of diagnosis, the age at the time CsA's therapy onset, time between diagnosis and CsA's initiation. Q4 At the point of CsA's administration we evaluated: clinical disease activity (according to PUCAI), endoscopic severity, extension and medication. Moreover, we searched for patients who received biological treatment either before or after CsA initiation.

Results

There was a female predominance in the study (34/59). The median age of the diagnosis was 11.9 years (range: 1.3–17.2 years), while the median age of the initiation of CsA 15 years (range 1.6–18.9 years). The time between the age of a diagnosis and the CsA therapy's onset was 20.0 months (range 0–118 months). The median PUCAI score at the initiation of CsA therapy was 50.00. Overall 78.9% had a moderate/severe course. The most common endoscopic extension was left-sided colitis 39.2% (20/51). According to Mayo scale 82.4% of children had either 2 or 3 degree. At the time of CsA initiation patients received steroids, azathioprine, 5-aminosalicylic acid, 79.3%, 82.8%, 84.5% respectively. 18.6% of patients had received biological agents in the past, meanwhile 42.4% had biological agent administered after CsA cessation. 2 patients received anti TNF antibody before and after CsA therapy Table I.

Table I – Children's clinical characteristic qualified for Cyclosporin A treatment

Clinical characteristic	N = 59
Sex	
Female	34
Male	25
Age at the CSA's therapy onset (years)	15.0 (1.6–18.9)
Age at the UC's diagnosis (years)	11.9 (1.3–17.2)
UC's duration until CSA's therapy initiation (months)	20.00 (0–118.0)
Endoscopic extension	
E1	8 (15.7%)
E2	20 (39.2%)
E3	9 (17.7%)
E4	14 (27.5%)
Disease's severity according to Mayo score n (%)	
1	9 (17.6%)
2	26 (45.1%)
3	19 (37.3%)
Clinical severity (PUCAI score) n (%)	50.00 (0–75.0)
Mild	8 (14.0%)
Moderate	35 (49.1%)
Severe	17 (29.8%)
Biological treatment n (%)	
Before CSA initiation	11 (18.6%)
After CSA initiation	25 (42.4%)
Before and after CSA therapy	2
Medication at the time of CSA's initiation n (%)	
Steroids	46 (79.3%)
Azathioprine	48 (82.8%)
5-Aminosalicylic acid	49 (84.5%)

Discussion

The most children treated with CsA had moderate/severe diseases activity. The most common endoscopic findings were left sided colitis and pancolitis. The majority of children had been treated with other agents. CsA is more frequently administered than biological agents in our department in case of steroid-dependency/relapses. When biological agents were applied, in majority cases INF a was Q5 administered. The main limitation of the study is its retrospective character. On the other hand we believe it is so far the biggest described group of patients treated with CsA in the course of UC. CsA has a high short-term efficacy in children (87%). Colectomy was avoided in 72% of the

Please cite this article in press as: Osiecki M, et al. A clinical characteristic of paediatric ulcerative colitis patients qualified for a Cyclosporin A therapy. Pediatr Pol. (2017), http://dx.doi.org/10.1016/j.pepo.2017.04.005