Mashhad University of Medical Sciences (MUMS)

Reviews in Clinical Medicine

Clinical Research Development Center Ghaem Hospital

The effect of oral budesonide liquid therapy to alleviate clinical symptoms in patients with epidermolysis bullosa

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ARTICLE INFO

Article type
Original article

Article history
Received: 08 Nov 2022
Revised: 15 Nov 2022
Accepted: 01 Dec 2022

Keywords
Budesonide
Dysphagia
Epidermolysis bollusa
Liquid

ABSTRACT

Introduction: Epidermolysis bullosa is a genetic condition with skin fragility that leads to blister formation and erosion following minor trauma. This disease also involves the gastrointestinal tract by way of esophageal stricture and dysphasia. Some studies have recommended oral budesonide liquid therapy to decrease the need for balloon endoscopy and other aggressive treatments. The aim of the study was to evaluated clinical symptoms of patients who consumed oral budesonide in their daily routine therapies.

Methods: This cross-sectional study was conducted in Akbar Hospital of the Mashhad University of Medical Sciences. All enrolled patients were followed between July and October 2021. Ten milliliter oral budesonide (0.5 milligram) liquid was administrated one hour before eating. They were followed up to determine and document any side effects after treatment, and any improvement of clinical symptoms such as amelioration of dysphasia, volume of food intake, duration of food consumption, and kind of food consumed (solid versus liquid).

Results: About fifteen patients were studied. The mean duration + SD of using budesonide was 9.66±15.76 weeks. The mean percentage + SD was 41.33±34.61 for improvement in the volume of food intake, and the mean for improving dysphasia + SD was 42±33.63%. Three patients suffered from complications (i.e., mucositis and gastric fullness). Also, two patients did not want to continue treatment because they did not like the drug taste.

Conclusion: Oral budesonide liquid could be recommended for epidermolysis bollusa patients to improve clinical symptoms.

Please cite this paper as:
Kianifar H, Talebi S. The effect of oral budesonide liquid therapy to alleviate clinical symptoms in patients with epidermolysis bullosa. Rev Clin Med. 2022;9(4): 156-158.

Introduction

Inherited epidermolysis bullosa (EB) is a heterogeneous, skin fragility disorder that causes disruption at the dermoepidermal junction or in the basal layer of the epidermis leading to increases cutaneous vulnerability to mechanical stress (1). The clinical characteristics include blisters, erosions, nonhealing ulceration, and scars following minor trauma (2).

The incidence and prevalence rate varies by region and the time of data collection. For example, in the period of 1986 through 2002, the incidence of EB was estimated to be approximately 20 per million live births, and the prevalence was estimated to be approximately 11 per million. On the other hand, an incidence rate of 3.6 per million live births per year for EB over the period 2007 to 2011 has been reported (3). Patients with EB are classified based on the level of blister formation, which is diagnosis by immunofluorescence antigen mapping and/or transmission electron microscopy(DEB), and kindler epidermolysis bullosa (KEB) (4). Its dystrophic form (DEB) is caused by a defect in the alpha-1 chain of type VII collagen caused by mutations in the COL7A1

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gene on the chromosome 3p21.31 (5). In addition to skin and nail involvement, blistering occurs in the mucus membranes and upper third of the esophagus. Eating solid food increases blister formation, and repetitive blister formation with chronic inflammation and gastrointestinal reflex can causes esophageal stricture (6). Moreover, dystrophic teeth and mouth opening due to scaring, together with esophageal strictures, can lead to malnutrition (2). Several kinds of treatment exist for esophageal stricture. One approach is endoscopic balloon dilation (7). Data from patients with eosinophil esophagitis have revealed that topical corticosteroids in the form of oral viscous budesonide (OVB) could be used as an alternative treatment to corticosteroid use with remission rates between 55 to 87%. It can also help reduce esophageal fibrosis (8).

On the other hand, OVB has potential side effects such as increasing the risk of candida esophagitis (9). Little data exists regarding the actual effect of topical budesonide in patients with epidermolysis bullosa; hence, the present study aimed to evaluate the clinical features of topical corticosteroids in these patients.

Materials and Method

In this study, patients with EB who were evaluated at the special EB clinic of the tertiary center of the Akbar Children's Hospital in Mashhad, Iran, were followed between July and October 2021. Patients with symptoms of esophageal strictures were enrolled.

Any patient who was admitted to the hospital for endoscopic dilation or surgical removal within three months prior to the study was excluded. Patients were evaluating weekly for clinically improvement after consuming an acceptable dose of oral budesonide liquid.

Clinical improvement consists of measuring improvement in the volume of food intake, duration of food consumption, type of food (solid versus liquid) consumed, amelioration of dysphasia, and other gastrointestinal symptoms. Similarly, all sides effect related to treatment were considered. The oral budesonide liquid consisted of pulmicort 0.5mg/ml concentration (budesonide nebulizer), dexterous water 50%, and maltodextrin.The patients were recommended to consume about 10 milliliter (0.5 milligram of budesonide) an hour before eating food for about two to three times a day.

Results

The 15 patients were diagnosed as having dystrophic epidermolysis bullosa. Mean (SEM) and standard deviation (SD) age of patients was 16.066±4.99 years. The youngest was eight years old and the oldest was 25. The mean duration of using oral budesonide was 9.66±15.76 weeks. Mean improvement in the volume of food intake was 41.33±34.61%, and the mean of improvement of dysphasia was 42±33.63%. In ten patients, oral budesonide did not cause any side effects. Three patients suffered from complications such as mucositis and gastric fullness. Also, two patients did not want to continue the treatment because they did not like the drug taste. Other demographic and clinical features of the 15 cases are shown in Table 1.

Table 1: Demographic, clinical improvement and complications of epidermolysis bullosa patients after consuming oral budesonide liquid

Case	Type of disease	Age (year)	Duration (week)	Improvement in the volume of food intake (percentage)	Improvement of dysphasia (percentage)	Type of food consumed	Complication	Numbers of endoscopies before OVB
1	Dystrophic	16	48	50	70	Solid	None	2
2	Dystrophic	15	12	100	70	Solid	None	0
3	Dystrophic	10	4	60	70	Solid	None	0
4	Dystrophic	10	2	60	70	Solid	None	0
5	Dystrophic	20	4	0	0	Liquid	None	0
6	Dystrophic	17	3	0	0	Liquid	Mucositis	0
7	Dystrophic	24	4	40	40	Semi liquid	None	0
8	Dystrophic	16	4	50	50	Semi liquid	None	0
9	Dystrophic	22	1	0	0	Liquid	Mucositis	0
10	Dystrophic	13	4	50	50	Solid	None	0
11	Dystrophic	8	48	100	100	Solid	Unpalatable (bad taste)	0
12	Dystrophic	14	1	0	0	Semi liquid	Gastric fullness	6
13	Dystrophic	25	4	0	0	Semi liquid	Unpalatable (bad taste)	8
14	Dystrophic	15	2	50	50	Solid	None	12
15	Dystrophic	29	48	100	100	Solid	None	2

Discussion

The study was conducted to evaluate if oral budesonide liquid could improve oral intake in patients with dystrophic epidermolysis bullosa. We found that in about 45% of patients, improvement in the clinical symptoms was noticeable. Oral budesonide is a topical steroid that is effective in the treatment of eosinophilic esophagitis (EoE) as it controls inflammation and suppresses subepithelial fibrosis formation.

Although the main mechanism of strictures in the proximal esophageal in epidermolysis bullosa is not known, it seems that multiple erosion with repeated mechanical trauma by eating solid food following incomplete healing increases inflammation and stricture formation. In this situation, using topical corticosteroids could reduce chronic inflammation and stricture formation (10). There are limited studies that have evaluated OVB. Dohil et al. (2014) presented two cases of epidermolysis dystrophic (male: 16 years old, female: 9 years old).

The male patient could not swallow saliva and reported using OVB four to seven times per week. It was reported that after 18-months of therapy, his need for balloon dilation decreased from 17 times to only twice, and significant reduction in choking episodes was observed. The other case was a young girl who had experienced 11 episodes of choking and was treated with esophageal dilation, and her greatest complain was choking with meals. Significant decrease in the need for dilation was reported after treatment (10). Andrea et al. examined six pediatric patients with EB who had esophageal strictures.

After four months of using oral budesonide, stricture indices, which was defined as the ratio between the diameter of the esophagus above the stenosis and the diameter of the stricture, decreased significantly to about 0.178 (0.026-0.296). Also, duration of food intake decreased and the consistency of food increased as the patients were able to eat solid foods easily. The author concluded that their finding was limited to endoscopic dilation. The most common side effects of the drug was candidiasis that was treated with topical antimycotic (11).

There are some questions about the role of corticosteroids around the time of dilation, which leads to decreased risk of restenosis. Nevertheless, it should be mentioned that multiple factors play a role in increasing the need of recurrent esophageal strictures such as long segment involvement and multiple locations of strictures. In this situation, conclusions regarding the efficacy of oral budesonide are challenging and requires more randomized control studies. Our limitations in this study were related to the quantitative measurement of any changes of esophageal strictures as the patients were not content to swallow barium before and after the treatment; hence, clinically improvement was based on our evaluation method.

Conclusion

Oral budesonide liquid could be recommended to alleviate the symptoms of esophageal strictures and dysphagia in patients with epidermolysis bullosa.

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