Artículo de investigación

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Dupilumab in children and adolescents with atopic dermatitis, a 52-week real-life experience: First report in Colombia

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SUMMARY

Atopic dermatitis (AD) is a chronic inflammatory disease characterized by relapsing eczema and pruritus. Dupilumab has demonstrated safety and efficacy in improving symptoms of moderate to severe AD, however, very few Latin American patients are included in studies, so comprehensive real-world data is needed. To our knowledge, there are no real-world studies published in Colombia, nor regarding this ethnicity on long-term treatment with dupilumab for AD in adolescents. We present a case series of adolescents with moderate to severe AD treated with dupilumab with a similar response in the measured scores compared to pivotal studies.

Key Words: Atopic dermatitis; Biologic; Dupilumab; Eczema; Real-world evidence.

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DUPILUMAB EN NIÑOS Y ADOLESCENTES CON DERMATITIS ATÓPICA, UNA EXPERIENCIA EN LA VIDA REAL DE 52 SEMANAS: PRIMER INFORME EN COLOMBIA

RESUMEN

La dermatitis atópica (DA) es una enfermedad inflamatoria crónica recidivante caracterizada por prurito. El dupilumab es un fármaco biológico que ha demostrado eficacia y seguridad en los ensayos clínicos y de extensión a largo plazo para el manejo de la DA moderada a severa en adolescentes; sin embargo, estos incluyen pocos o ningún paciente en Latinoamérica, por lo que son importantes los estudios de vida real en nuestra población. Luego de una revisión de la literatura indexada, no encontramos estudios publicados en Colombia respecto al tratamiento de la DA con dupilumab en pacientes adolescentes, ni tampoco en Latinoamérica a largo plazo. Presentamos una serie de casos de pacientes adolescentes con DA moderada tratados con dupilumab con respuesta similar y mejor en comparación con los ensayos clínicos.

Palabras Clave: Biológico; Dermatitis atópica; Dupilumab; Eczema.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory disease characterized by relapsing eczema and pruritus[1]. Recently, dupilumab has been shown to be safe and effective in improving symptoms of moderate to severe AD in adolescents for up to 52 weeks [2, 3]; however, very few Latin American patients were included, so comprehensive real-world data is needed. To our knowledge, there are no real-world studies published on this ethnicity regarding long-term treatment with dupilumab for AD in adolescents.

METHODS

We conducted an observational, monocentric, retrospective analysis. Patients had informed consent and institutional ethical committee approval. Medical records were reviewed for patients starting dupilumab at <18 years of age, with moderate to severe AD at the Central Military Hospital in Bogota, Colombia, from January 2020 to May 2022.

All patients received a loading dose of 400 mg followed by 200 mg every 2 weeks subcutaneously. Demographics, AD Scores (Scoring Atopic Dermatitis score [SCORAD], Peak Pruritus Numerical Rating Scale [ppNRS], Children's Dermatology Life Quality Index [cDLQI], Patient-Oriented Eczema Measure [POEM]) and safety data were collected from visits at week 0, 16 and 52.

RESULTS

Five patients were included (three males and two females), whose average onset of AD was 4.6 months old. The median age of dupilumab initiation was 13.2 years (range 12-15). All patients had allergic rhinitis; three had a history of recurrent herpes, of which two had at least one episode of eczema herpeticum, and two had chronic erythroderma. Patients' characteristics are summarized in **Table 1**.

All patients were classified as difficult-to-treat due to extensive treatment without disease control (all had been treated with at least with three systemic medications combined with topical corticosteroids and calcineurin inhibitors).

Patients completed at least 52 weeks of therapy with dupilumab. At week 16, the mean percentage of improvement (range) in SCORAD and cDLQI were 62.9% (12.5%-94.9%) and 68.4% (45.5%-91.7%), respectively; and the mean total points improvement (range) in ppNRS and POEM were 3.4 (3.2-6.6) and 11.8 (6.6-18.4), respectively. Subsequently, at week 52, the mean percentage of improvement (range) in SCORAD and cDLQI were 70% (26.6%-91.2%) and 66.7% (50%-80%), respectively; and the mean total points improvement (range) in ppNRS and POEM were 3.2 (1-6) and 13.4 (5-18.4), respectively. Patients' scores are detailed in **Figure 1**.

Patient	Sex	Age	BMI	Months at ad on set	Clinical course	Atopic comorbidities	Prior topical medications	Prior systemic medications	Blood eosinophil (count/m)	IgE level (IU/mL)	SCORAD	POEM	DLQI	NRS itch score
1	M	15	18	5	R	Rh, C	TC, CNI	AH, Az, CyC, PT, SC, MM, MTX	1065	9674	79.6	25	12	9
2	F	12	19,1	8	P	Rh	TC, CNI	AH, SC, CyC, MTX	300	12468	55.2	10	12	5
3	F	12	15,8	3	P	Rh, CE, FA	TC, CNI	AH, Az, CyC, MM, SC	250	2500	80	9	10	10
4	M	12	22,2	5	P	Rh, FA	TC, CNI	AH, Az, CyC, SC, MTX, MM, PT	240	2000	41,9	16	11	4
5	M	15	17,2	2	P	Rh, CE	TC, CNI	AH, Az, PT, CyC, SC	680	2500	63,7	15	5	6

Table 1. Baseline demographics and clinical characteristics of five adolescents with moderate to severe atopic dermatitis treated with dupilumab
A: Asthma; AH: Antihistamines; Az: Azathioprine; C: Conjunctivitis; CNI: Calcineurin inhibitors; CE: Chronic erythroderma; CyC: Ciclosporin; F: Female; FA: Food allergy; MM: Mycophenolate; MTX: Methotrexate; P: Persistent; PT: Phototherapy; R: Relapsing; Rh: Rhinitis; SC: Systemic corticosteroids; TC: Topical corticosteroids.

The adverse events identified were conjunctivitis (n=2), facial redness (n=1), eye pruritus (n=2), injection-site pruritus (n=1) and alopecia areata (n=1). Neither oral herpes, serum sickness, anaphylactic reaction, arthralgia nor eczema herpeticum were reported.

DISCUSSION

At week 16, the improvement of our patients in the POEM score was larger than in the LIBERTY-AD ADOL study (10% vs 11.8%) [4], but the ppNRS score did not improve as much as in the Italian real-life study [5] at this week (51.5% vs 64.6%).

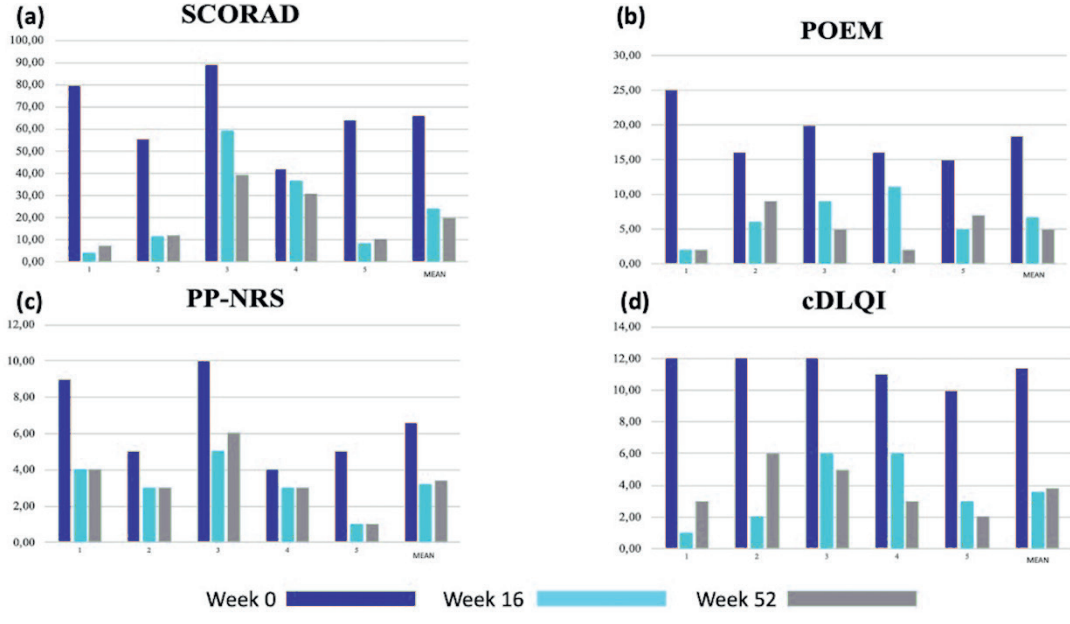

Figure 1. Atopic dermatitis scores in adolescents treated with dupilumab at baseline, week 16 and week 52. SCORAD (A), POEM (B), PP-NRS (C), and cDLQI (D) in five patients with severe atopic dermatitis. Data are shown as the total score of each patient at three visits: baseline, week 16 and week 52.

We documented a better response in our patients by week 52, in the cDLQI (≥6-point improvement) and the SCORAD, than in the LIBERTY AD PED-OLE (86.4% vs 100% and 65% vs 70%) [2, 3].

Adverse effects were identified in 80% of the patients, a greater percentage compared to the LIBERTY AD PED-OLE [2, 3] and the Italian study [5] (73.9% and 20.1%, respectively). However, all resolved spontaneously or were treatment without dupilumab discontinuation.

CONCLUSION

In conclusion, the results from our case series showed overall long-term efficacy and safety of dupilumab treatment in a real-life setting in Latin American adolescents with moderate-to-severe difficult-to-treat AD, as expressed by a significant mean improvement of AD signs and symptoms, measured by objective and subjective scores. Two patients had persistent moderate to severe AD, and we were unable to identify possible characteristics that may explain this outcome.

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key points

- Dupilumab is a biological agent that inhibits IL-4 and IL-13 signaling through IL-4R.
- In adolescents, dupilumab seems to be safe for moderate to severe atopic dermatitis, but larger prospective studies are needed [6].
- The response of all patients was similar or better in the measured scores compared with pivotal studies. The adverse events were also similar.