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SHORT PAPER

Novel agents for atopic dermatitis in patients over 50 years of age: A case series

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Abstract

Lan et al recently highlighted the under-representation of older adults in clinical trials of systemic therapies for atopic dermatitis (AD). Late-onset AD is increasingly recognized in older adults. Spontaneous remission is uncommon with this phenotype. Existing drug treatments such as corticosteroids, methotrexate, ciclosporin, and azathioprine are complicated by adverse effects including increased malignancy risk, immunosuppression in the context of immunosenescence, and drug interactions in the setting of polypharmacy. A case series is presented of seven patients over 50 years of age with AD who were prescribed dupilumab or tofacitinib or upadacitinib for at least 6 months. All patients were clear or almost clear (investigator global assessment score 0/1) after 1 month of therapy. No significant adverse events were seen. This case series provides preliminary evidence about the safety and efficacy of these novel drugs for AD in older adults. Further studies with higher numbers of participants are needed to obtain real-world evidence for these drugs in older adults, given the limited data in clinical trials.

KEYWORDS

atopic dermatitis, eczema, inflammatory disorders, pharmacology, quality of life, therapy-systemic

Lan et al recently highlighted the under-representation of older adults in clinical trials of systemic therapies for atopic dermatitis (AD).[1] Late-onset AD is increasingly recognized in older adults.[2] Spontaneous remission is uncommon with this phenotype.[3] Existing drug treatments such as corticosteroids, methotrexate, ciclosporin, and azathioprine are complicated by adverse effects including increased malignancy risk, immunosuppression in the context of immunosenescence, and drug interactions in the setting of polypharmacy.[4]

We performed a single-center retrospective chart review of all patients over 50 years of age with AD who were prescribed dupilumab or tofacitinib or upadacitinib for at least 6 months. Patients were followed up 1 month following initiation, and three monthly thereafter.

Seven patients with AD on dupilumab or tofacitinib were identified: three patients over 65 years and four patients between 50 and 64 years. Three patients were male and four were female (Table 1). Four patients were prescribed dupilumab 300 mg fortnightly, two patients were prescribed tofacitinib 5 mg twice daily, and one was prescribed upadacitinib 15 mg once daily.

Three patients (43%) had a history of skin cancer. Four patients (57%) had a history of asthma. Two patients (29%) had a history of hypertension. One patient had a history of latent tuberculosis.

All patients had previously received phototherapy and at least one systemic medication. Conventional systemic agents (methotrexate, ciclopsorin, mycophenolate mofetil, and azathioprine) had been ineffective for all patients. Ciclosporin had been stopped in two

TABLE 1 Patient characteristics

	Age	Gender	Past medical history	Treatment	Duration	Previous systemic treatments	Adverse events	IGA pre treatment	IGA on treatment
1	69	M	Cutaneous SCC	Dupilumab 300 mg fortnightly	15 months	PUVA, UVB, and MTX	Conjunctivitis (mild)	4	0
2	65	M	Asthma, HSV keratitis, Hypertension	Dupilumab 300 mg fortnightly	12 months	UVB, MTX, AZA, and MMF	Conjunctivitis (mild)	4	1
3	53	F	Asthma	Dupilumab 300 mg fortnightly	18 months	UVB, MTX, CSA, MMF, and AZA	Nil	4	1
4	51	F	Contact dermatitis, Asthma	Dupilumab 300 mg fortnightly	15 months	UVB and MTX	Nil	3	0
5	62	F	Melanoma in situ, Actinic keratosis	Tofacitinib 5 mg twice daily	9 months	UVB, MTX, and UPA	Nil	4	0
6	71	M	Asthma, Hypertension, Cutaneous SCC	Tofacitinib 5 mg twice daily	9 months	UVB, MTX, CSA, and MMF	Asthma exacerbation	4	0
7	60	F	Latent TB	Upadacitinib 15 mg once daily	15 months	UVB, MTX, CSA, AZA, and MMF	Nil	4	0

Abbreviations: AZA, azathioprine; CSA, ciclosporin; IGA, investigator global assessment; MMF, mycophenolate mofetil; MTX, methotrexate; PUVA, Psoralen + ultraviolet light A; SCC, squamous cell carcinoma; TB, tuberculosis; UPA, upadacitinib; UVB, ultraviolet light B.

patients due to treatment-resistant hypertension. Conventional immunosuppressive agents were contraindicated in three patients due to previous skin cancer. Upadacitinib had been stopped in one patient, who had been part of a clinical trial, due to melanoma in situ.

Baseline eosinophilia was seen in two patients. Otherwise there were no aberrations in hematological or biochemical parameters, which were repeated every 3 months. Mild conjunctivitis was seen in two patients on dupilumab, which resolved with topical ocular lubricants. One patient on dupilumab with a history of recurrent herpes simplex virus (HSV) keratitis was prescribed prophylactic valaciclovir, with no recrudescence of keratitis. All patients who were prescribed tofacitinib or upadacitinib were administered the shingles vaccine prior to initiation of therapy. No HSV or shingles infections were seen.

Improvements in AD severity were rapid and profound. Six patients (86%) had a baseline investigator global assessment (IGA) score of four, indicating severe AD, and one patient had a baseline IGA score of three, indicating moderate AD. All patients (100%) were clear or almost clear (IGA 0/1) after one month of therapy, which was maintained at follow up visits. One patient declared that he had a "first decent night's sleep in 60 years" after his first dupilumab injection. Other patients noted life-changing improvements, with one patient able to return to work after 15 years of sick leave.

With a globally aging population, AD in older adults is a growing problem and, without intervention, often persists until the end of life. Topical emollients and corticosteroids are frequently insufficient for disease control. Older patients are at higher risk of adverse drug effects due to declining hepatic and renal function, concomitant disease processes, and polypharmacy. Oral corticosteroids have multiple side effects which are amplified in the older population. Hepatic considerations limit use of methotrexate, and renal considerations and hypertension limit use of ciclosporin. Azathioprine is of concern in a population who may have received extensive ultraviolet radiation via phototherapy, given the increased risk of skin cancer. All these agents plus mycophenolate mofetil should be prescribed with caution in older patients at higher risk of neoplasia or infection.

Dupilumab is an IL-4Rα antagonist which modulates IL-4 and IL-13 signaling. It is highly targeted for treatment of AD and asthma and has an excellent safety profile. Janus kinase inhibitors interfere with JAK-STAT signaling and have a broad immunomodulatory effect. Ruxolitinib (JAK1/JAK2), tofacitinib (JAK1/JAK3), baricitinib (JAK1/JAK2), and upadacitinib (JAK1 selective) have been used to treat other inflammatory disorders. There are concerns about reactivation of herpes simplex and varicella zoster virus, dyslipidemia, and thromboembolic disease at higher doses.

This case series provides preliminary evidence about the safety and efficacy of these novel drugs for AD in older adults. Further studies with higher numbers of participants are needed to obtain real-world evidence for these drugs in older adults, given the limited data in clinical trials.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Michelle Murphy, John Bourke, and Mary Bennett: Conceived of the research idea; Lisa Kiely, Stephanie Bowe, and Cathal O'Connor:

Collected data; Lisa Kiely, Stephanie Bowe and Cathal O'Connor: Wrote the article; Cathal O'Connor, Mary Bennett, John Bourke, and Michelle Murphy: Reviewed the article.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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