



Extraintestinal symptoms of pain in eosinophilic gastrointestinal diseases

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Introduction

- Extraintestinal symptoms are well-documented in systemic inflammation-predominant conditions. Eosinophilic gastrointestinal diseases (EGIDs) are associated with features of inflammation and fibrosis.
- Connective tissue disorders, including Ehlers Danlos and Benign Hypermobility Syndrome, are enriched in patients with EGIDs and are associated with musculoskeletal symptoms of pain. While there is a higher frequency of connective tissue disorders in patients with eosinophilic esophagitis (EoE), extra-GI symptoms have not been explored in eosinophilic gastrointestinal diseases (EGIDs).
- Aim:** To describe and evaluate the differences in the frequency of patient report of joint, leg, and headache pain in EoE and non-EoE EGIDs.

Methods

- Data were assembled from EGID Partners (egidpartners.org), an online patient-centered research network designed and implemented by patient advocacy groups (PAGs) and EGID researchers.
- Subjects were recruited via informational emails and through social media, directed messages to EGID patients through medical record patient portals, webinars, and by physicians.
- Adult subjects and caregivers of children (<18 years) completed surveys to document symptoms of leg and joint pain, and the McGill Pain Questionnaire was used to describe affective vs sensory pain symptoms. Additionally, subjects reported frequency of headaches, medication use for management of symptoms, and, among adults, severity of headache-associated disability using the Migraine Disability Assessment Test.
- Differences in pain scores between EoE and non-EoE EGID patients were compared using Chi-square tests for differences in distribution of proportions and t-tests for testing differences in means.

Results

- We analyzed 94 subjects with EoE (85% ≥18) and 24 subjects with non-EoE EGIDs (75% ≥18).
- Leg pain:** Both EoE and non-EoE EGID subjects described frequent leg pain (60% for EoE and 63% for non-EoE EGIDs) with a mean (std) number of days of leg pain of 1.4 (2.2) and 2.3 (2.7) days, respectively. While no difference was observed in number of days of leg pain (p=0.09), pain severity was higher for non-EoE EGID subjects (p<0.01), and for both affective and sensory pain (p<0.01 for both). For both EoE and non-EoE EGID subjects, pain more frequently initiated concomitantly with or after EGID symptom initiation (Table 1).
- Joint pain:** For joint pain, 61% of EoE and 67% of non-EoE EGID subjects reported joint pain, with the majority of those indicating that pain started during or after EGID symptom onset. Severity of symptoms was greater for non-EoE EGID patients (p<0.01), as were sensory and affective pain scores (p<0.01) (Table 2).
- Headache disability:** Among adults, the distribution of headache disability scores for non-EoE EGID subjects was different as compared to subjects with EoE alone, with 17% of non-EoE EGIDs indicating severe disability vs 9% for EoE (p=0.01). A high proportion of both EoE and non-EoE EGID subjects reported taking medications to manage their headaches (Table 3).

	EoE n = 95	Non-EoE EGID n = 24	p
Days per week with pain in legs (mean ± SD) (n=95, 24)	1.4 ± 2.2	2.3 ± 2.7	0.09
Pain severity over prior 7 days (0-10 scale; mean ± SD) (n=87, 24)	1.2 ± 1.8	3.6 ± 2.9	< 0.01
Short-form McGill Pain Questionnaire (mean ± SD)			
Total score	3.6 ± 5.0	11.8 ± 11.2	< 0.01
Sensory sub-score	3.0 ± 4.0	9.5 ± 2.0	< 0.01
Affective sub-score	0.6 ± 1.3	2.2 ± 2.7	< 0.01
Start of leg pain in relation to EGID symptoms – n (%)			
Before	11 (14)	1 (6)	
After	20 (26)	5 (28)	
Same time	8 (10)	9 (44)	
N/A (no leg pain)	39 (50)	4 (22)	

	EoE n = 95	Non-EoE EGID n = 24	p
Days per week with pain in joints (mean ± SD) (n=94, 24)	2.7 ± 3.0	3.8 ± 3.2	0.12
Pain severity over prior 7 days (0-10 scale; mean ± SD) (n=86, 19)	1.9 ± 2.0	4.6 ± 3.5	< 0.01
Short-form McGill Pain Questionnaire (mean ± SD)			
Total score	4.1 ± 4.0	13.3 ± 10.7	< 0.01
Sensory sub-score	3.5 ± 4.1	11.0 ± 8.5	< 0.01
Affective sub-score	0.6 ± 1.1	2.3 ± 2.6	< 0.01
Start of joint pain in relation to EGID symptoms – n (%)			
Before	17 (22)	4 (22)	0.39
After	31 (39)	8 (44)	
Same time	9 (11)	4 (22)	
N/A (no joint pain)	22 (28)	2 (11)	

	EoE n = 95	Non-EoE EGID n = 24	p
Days per week with headaches (mean ± SD) (n=95, 24)	1.3 ± 1.8	2.1 ± 2.4	0.06
Days of headaches in the last month (mean ± SD) (n=94, 23)	4.5 ± 6.6	6.4 ± 9.3	0.25
Take prescribed medications for headaches - n (%) (n=85, 22)	9 (11)	5 (23)	0.13
Take over-the-counter medications for headaches - n (%) (n=85, 22)	55 (65)	17 (77)	0.26
Migraine Disability Assessment Test (Adults only) (n=81, 18)			
Mean score (± SD)	7.1 ± 26.5	35.8 ± 81.8	0.01
Grade of severity - n (%)			
I: little or no disability (score 0-5)	66 (83)	9 (50)	
II: mild disability (6-10)	3 (4)	1 (6)	
III: moderate disability (11-20)	4 (5)	5 (28)	
IV: severe disability (21+)	7 (9)	3 (17)	

Conclusions

Patients with EGIDs may experience extraintestinal symptoms of leg, joint or headache pain, and these seem to be more prominent with non-EoE EGIDs. Understanding of the underlying factors contributing to these symptoms is needed to guide approaches for mitigating these symptoms.

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