11-27-2020

Comment on "High-dose, high-frequency infliximab: A novel treatment paradigm for hidradenitis suppurativa"

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Recommended Citation
Adelman M, Lyons AB, Hamzavi IH. Comment on "High-dose, high-frequency infliximab: A novel treatment paradigm for hidradenitis suppurativa". Journal of the American Academy of Dermatology 2020.

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To the Editor: Ghias et al[1] recently published the results of a study that evaluated the efficacy of high-dose, high-frequency infliximab therapy for patients with moderate to severe hidradenitis suppurativa (HS). In this trial, 42 patients received 7.5 mg and 16 patients received 10 mg of infliximab every 4 weeks for a total of 12 weeks.[1] By week 12, clinical response was achieved in 70.8% of patients receiving 7.5 mg and in 50% of patients receiving 10 mg.[1] They concluded that initiation of infliximab at 7.5 mg every 4 weeks, with possible dose escalation to 10 mg, provides optimal mitigation of HS-related disease activity.[1] Although their study provides valuable information regarding this therapeutic option, we were surprised to read that no infusion reactions were reported.

We performed a retrospective record review of all patients with HS who received infliximab infusions at a large academic HS referral center from 2008 to 2019. The Henry Ford Hospital Institutional Review Board approved the study.

We identified 51 patients (24 men, 27 women) with an average age of 45.5 years (range, 17-74 years) (Table I). Of these patients, 49% (25 of 51) remained on infliximab at the time of the medical record review. The main reasons for discontinuation of infliximab were an adverse infusion-related reaction (n = 10 [38.5%]), greater than 1 year of infliximab infusions with no improvement (n = 5 [19.2%]), lost to follow-up (n = 4 [15.4%]), development of a separate medical condition deterring treatment (n = 3 [11.5%]), insurance coverage (n = 3 [11.5%]), and development of infliximab-induced systemic lupus erythematosus (n = 1 [3.8%]) (Table II). Specifically, adverse infusion reactions included hives, palpitations, rigors, shortness of breath, and anaphylaxis, with the most common symptom being shortness of breath.

Infliximab works by neutralizing and blocking the biological activity of tumor necrosis factor-α, a proinflammatory cytokine.[2] The exact etiology of infusion-related reactions is unclear and made difficult by the overlapping clinical manifestations of allergic and immune responses. Analysis of symptoms helps elucidate possible mechanisms, including fever—supporting possible trigger of a cytokine storm, and wheezing and urticaria—suggestive of immunoglobulin E-mediated or mast cell histamine release.[3]

Table I. Demographic information

Variable*	No longer on infliximab	Still on infliximab	On infliximab >1 year
Patients	26 (51.0)	25 (49.1)	20 (39.2)
Sex			
Male	13 (50)	11 (44)	9 (45)
Female	13 (50)	14 (56)	11 (55)
Race			
Black	15 (58.7)	15 (60.0)	14 (70.0)
White	5 (31.8)	5 (20.0)	3 (15.0)
Asian	0 (0.0)	2 (8.0)	1 (5.0)
Unknown	3 (11.5)	3 (12.0)	2 (10.0)
Average age, (range), y	47.2 (21-74)	43 (16-64)	43.6 (24-59)
Average age at HS diagnosis, y	39.9	37.5	36.9
Tried adalimumab first	9 (34.6)	8 (32)	6 (30)

HS, Hidradenitis suppurativa.
*Data are presented as n (%) or as indicated otherwise.

Table II. Reasons for discontinuation of infliximab

Reason for discontinuation	No. (%) (n = 26)
Adverse infusion reaction	10 (38.5)
>1 year of treatment with no improvement	5 (19.2)
Lost to follow-up	4 (15.4)
Development of a separate medical condition	3 (11.5)
Insurance coverage	3 (11.5)
Infliximab-induced systemic lupus erythematosus	1 (3.8)

No., Number.

The overall reported incidence of infusion-related reactions to infliximab varies greatly. Two retrospective studies of infliximab in patients with Crohn's disease reported per-patient infusion reaction rates of 8.4% (479 infusions in 165 patients)[4] and 19.1% (6468 infusions in 447 patients).[5] In our patient population, adverse infusion reactions occurred in 19.6% (10 of 51) of patients.

We would like to acknowledge the authors for this contribution showing high-dose, high-frequency infliximab as an efficacious treatment for HS. We want to add findings from our patient population, where infusion reactions to infliximab were consistent with or even higher than previously reported infusion reaction rates, which should prompt physicians to be mindful of this possibility when prescribing infliximab.

Limitations of this study include its retrospective nature and small sample size. More studies with longer follow-up are needed to further elucidate risk factors, pathogenic mechanisms, and prophylactic management of infliximab infusion reactions.

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Funding sources: None.

IRB approval status: Reviewed and approved by the Henry Ford Hospital Institutional Review Board.

Reprints not available from the authors.

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Conflicts of interest

Dr Lyons is an investigator for Lenicura and General Electric. Dr Hamzavi has been an investigator for Lenicura and General Electric, is a consultant for Incyte, is on the AbbVie advisory board (noncompensated), and is the current president of the Hidradenitis Suppurativa Foundation (noncompensated). Author Adelman has no conflicts of interest to disclose.

REFERENCES

1. Ghias MH, Johnston AD, Kutner AJ, Micheletti RG, Hosgood HD, Cohen SR. High-dose, high-frequency infliximab: a novel treatment paradigm for hidradenitis suppurativa. *J Am Acad Dermatol*. 2020;82:1094-1101.
2. Lim SYD, Oon HH. Systematic review of immunomodulatory therapies for hidradenitis suppurativa. *Biologics*. 2019;13:53-78.
3. Lichtenstein L, Ron Y, Kivity S, et al. Infliximab-related infusion reactions: systematic review. *J Crohns Colitis*. 2015;9(9):806-815.
4. Cheifetz A, Smedley M, Martin S, et al. The incidence and management of infusion reactions to infliximab: a large center experience. *Am J Gastroenterol*. 2003;98:1315-1324.
5. Keshavarzian A, Mayer L, Salzberg B, et al. A multicenter retrospective experience of infliximab in Crohn's disease patients: infusion reaction rates and treatment persistency. *Gastroenterol Hepatol (NY)*. 2007;3:381-390.

https://doi.org/10.1016/j.jaad.2020.10.095