RESEARCH LETTER

Safety of Intramuscular Triamcinolone Injections for Hidradenitis Suppurativa Flares: Findings from a Retrospective Cohort Study

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ABSTRACT

Introduction Hidradenitis Suppurativa (HS) is an inflammatory skin condition that is typically controlled with systemic antibiotics, anti-androgen agents, and biologic therapies. HS flares can also be managed with short courses of oral prednisone (OP) or Intramuscular triamcinolone injection (ITI) therapy, however, the safety profile of multiple ITIs in HS is unknown. We assess the short-term (one-month) and long-term (one-year) risk of adverse effects after multiple ITIs in HS patients.
Methods Using the TriNetX Research Network, we identified 892 HS patients who received one ITI and 892 matched HS patients who received three or more ITIs within one year. A second analysis of patients compared the risk profile of multiple ITIs to multiple courses of OP in HS patients. We matched 650 HS patients who received three or more ITIs to 650 HS patients who received three or more regimens of 20mg OP within one year.
Results Compared to single ITI, in patients with multiple ITIs, no significantly increased one-month or one-year risk of metabolic conditions, infections, psychiatric syndromes, or peptic ulcers was observed. There was no observed increased one-year risk of metabolic conditions, adrenocortical insufficiency, osteoporosis, cataracts, or glaucoma. Compared to OP, patients with multiple ITIs did not have an observed significant difference in the one-year risk of metabolic conditions, osteoporosis, cataracts, glaucoma, psychiatric syndromes, peptic ulcers, or infections. Patients with OP had a significantly higher risk of hypertension.
Discussion We demonstrate that multiple ITIs do not increase the short- or long-term risk of adverse corticosteroid effects compared to multiple regimens of OP or singular ITI.

INTRODUCTION

Hidradenitis Suppurativa (HS) is a chronic and recurrent inflammatory skin disease that is commonly managed with systemic antibiotics, anti-androgen therapies, and biologic agents.[1-4] HS flares remain difficult to manage, and may also be treated with short courses of oral prednisone (OP).[4] Intramuscular triamcinolone injections (ITI) have been reported for use of severe HS flares, in addition to intralesional triamcinolone.[2-5] However, the safety of administering multiple ITIs in HS remains unclear. Concern for systemic absorption of intramuscular triamcinolone causing disruption of the hypothalamic-pituitary-adrenal axis limit their usage, although evidence has suggested that appropriate dosing and frequency may mitigate clinically significant HPA axis disruption.[5] To better

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inform clinical decision-making regarding this efficacious therapy, we evaluated the short-term (one-month) and long-term (one-year) risk of adverse effects following multiple ITIs in HS patients.

METHODS

Using the TriNetX Research Network between January 1, 2018, and December 31, 2019, four cohorts were determined, and two analyses were conducted. We identified 892 HS patients who received only one ITI within a one-year duration. These patients were matched to 892 HS patients who received three or more ITIs in one year. The second analysis compared the risk profile of multiple ITIs to multiple courses of OP in HS patients. In this analysis, 650 HS patients who received at least three ITIs in one year were matched to 650 HS patients who received three or more regimens of 20mg OP within one year. The prescription dosage of 20mg OP represents the total dose taken over an unknown time duration. Due to limitations of the TriNetX platform, we could not identify dosage of ITIs administered, however, most ITIs are weight-based injections of 40mg or 80mg. The index date was defined as the date of the first ITI or OP. Patients were classified into treatment groups based on the number of treatments received during the subsequent one-year period. To avoid immortal time bias, adverse outcomes were assessed only after treatment group classification was completed. Patients with any outcome of interest occurring before or during the treatment classification period were excluded. Short- and long-term adverse outcomes were assessed only after this classification period.

We used propensity scores and 1:1 greedy nearest neighbor matching to limit the effect of confounding variables. We excluded individuals younger than 18 years of age. Cohorts were matched by demographics and outcome of interest risk factors including diabetes mellitus, chronic ischemic heart disease, chronic kidney disease, heart failure, and acute myocardial infarction. Patients with these chronic conditions have an elevated risk for one or more of the adverse effects evaluated in this study and therefore must be accounted for to more accurately assess the risk profile of ITIs.[6] ICD and CPT codes utilized are listed in **Supplemental Table 1**. A standardized mean difference of less than 0.1 indicated that the cohorts were well balanced. Risk ratios and 95% confidence intervals were utilized to identify associations between cohorts.

RESULTS

After propensity score matching, mean age was similar between groups, and the majority of patients were female (**Supplemental Table 2 and 3**). Key comorbidities were comparable between cohorts with all standardized mean differences <0.1 (**Supplemental Tables 2 and 3**). Compared with patients who received a single ITI, those who received three or more ITIs did not demonstrate a statistically significant increase in one-month risk of metabolic conditions, infections, psychiatric syndromes, or peptic ulcers (**Table 1**). Among patients who received multiple ITIs, no statistically significant increase in one-year risk of infections, metabolic conditions, adrenocortical insufficiency, osteoporosis, cataracts, glaucoma, psychiatric syndromes, or peptic ulcers were observed (**Table 1**). When compared with OP, patients receiving multiple ITIs had no significant difference in one-year risk of metabolic conditions, infections, osteoporosis, cataracts, glaucoma, psychiatric syndromes, or peptic

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ulcers (**Table 2**). In contrast, patients treated with oral prednisone had a significantly higher observed risk of hypertension (**Table 2**).

Table 1. Short-term and long-term risk of glucocorticoid adverse effects of ITI in HS patients

One-month glucocorticoid adverse effects			
	Multiple ITI (*n* = 892)	**Single ITI (*n* = 892)**	
Outcomes	Number of eligible individuals[a] (# of outcomes)	Number of eligible individuals[a] (# of outcomes)	Risk ratio (95% CI)
Infections of the skin and subcutaneous tissue	349 (10)	441 (10)	1.26 (0.53, 3.00)
Abnormal weight gain	788 (10)	806 (10)	1.02 (0.43, 2.44)
Hyperglycemia	798 (10)	846 (10)	1.06 (0.44, 2.53)
Hypertension	455 (0)	472 (10)	N/A[b]
Depressive episode	536 (10)	540 (10)	1.01 (0.42, 2.40)
Behavioral syndromes associated with disturbances and physical factors (ex: eating, sleeping, or sexual dysfunction disorders)	766 (10)	783 (10)	1.02 (0.43, 2.44)
Bacterial and viral infections	645 (10)	660 (10)	1.02 (0.43, 2.44)
Peptic ulcers	879 (0)	884 (0)	N/A[b]
One-year glucocorticoid adverse effects			
	Multiple ITI (*n* = 892)	Single ITI (*n* = 892)	
	Number of eligible individuals[A] (# of outcomes, 1-y)	Number of eligible individuals[A] (# of outcomes, 1-y)	Risk ratio (95% CI)
Infections of the skin and subcutaneous tissue	349 (35)	441 (38)	1.16 (0.75, 1.80)

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Abnormal weight gain	788 (10)	806 (12)	0.85 (0.37, 1.96)
Hyperglycemia	798 (18)	846 (13)	1.49 (0.72, 2.98)
Hypertension	455 (18)	472 (22)	0.85 (0.46, 1.56)
Depressive episode	536 (31)	540 (27)	1.16 (0.70, 1.91)
Behavioral syndromes associated with disturbances and physical factors (ex: eating, sleeping, or sexual dysfunction disorders)	766 (21)	783 (16)	1.34 (0.71, 2.55)
Bacterial and viral infections	645 (34)	660 (38)	0.92 (0.58, 1.44)
Peptic ulcers	879 (10)	884 (10)	1.0 (0.42, 2.40)
Hyperlipidemia	568 (26)	613 (25)	1.12 (0.66, 1.92)
Metabolic syndrome	885 (0)	886 (10)	N/A[b]
Adrenocortical insufficiency	882 (10)	887 (10)	1.0 (0.42, 2.40)
Osteoporosis	843 (10)	850 (10)	1.01 (0.42, 2.41)
Cataract	837 (10)	842 (10)	1.01 (0.42, 2.40)
Glaucoma	814 (10)	834 (10)	1.03 (0.43, 2.45)
Myopathy	889 (0)	890 (0)	N/A[b]
Drug-induced Cushing's syndrome	888 (10)	891 (10)	1.0 (0.42, 2.40)

[a]All patients with the clinical outcome of interest prior to the index event were excluded.
[b]Analysis could not be performed due to lack of patients with this outcome.

Table 2. Risk of one-year glucocorticoid adverse effects in HS patients with ITI and OP

	ITI (*n* = 650)	**OP (*n* = 650)**	
Long-term outcomes	Number of eligible individuals[a] (# of outcomes)	Number of eligible individuals[a] (# of outcomes)	Risk ratio (95% CI)

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Infections of the skin and subcutaneous tissue	251 (27)	250 (34)	0.79 (0.49, 1.27)
Abnormal weight gain	573 (10)	603 (10)	1.05 (0.44, 2.51)
Hyperglycemia	572 (15)	564 (24)	0.62 (0.33, 1.16)
Hypertension	325 (10)	285 (29)	0.30 (0.15, 0.61)
Hyperlipidemia	398 (18)	403 (23)	0.79 (0.43, 1.45)
Metabolic syndrome	646 (0)	647 (10)	N/A[b]
Adrenocortical insufficiency	643 (10)	641 (10)	1.0 (0.42, 2.38)
Osteoporosis	614 (10)	596 (10)	0.97 (0.41, 2.32)
Cataract	605 (10)	610 (10)	1.01 (0.42, 2.41)
Glaucoma	592 (10)	607 (10)	1.03 (0.43, 2.45)
Depressive episode	372 (21)	346 (21)	0.93 (0.52, 1.67)
Behavioral syndromes associated with disturbances and physical factors (ex: eating, sleeping, or sexual dysfunction disorders)	554 (17)	569 (10)	1.75 (0.80, 3.78)
Bacterial and viral infectious agents	470 (26)	408 (34)	0.66 (0.40, 1.09)
Peptic ulcers	639 (10)	637 (10)	0.99 (0.42, 2.38)
Drug-induced Cushing's syndrome	647 (0)	646 (10)	N/A[b]
Myopathy	647 (0)	644 (10)	N/A[b]

[a]All patients with the clinical outcome of interest prior to the index event were excluded.
[b]Analysis could not be performed due to lack of patients with this outcome.

DISCUSSION

We did not observe an increased short- or long-term risk of adverse corticosteroid effects with multiple ITIs compared to multiple regimens of OP or singular ITI. Our findings are consistent with previous studies that have reported a comparable safety profile of ITIs in other dermatologic conditions.[5] While all formulations of steroids have a risk of the adverse effects analyzed in this study, the side effects are related to total steroid dose.[4,5] The total steroid dose in ITI is lower than OP, likely accounting for the lower incidence of side effects.[5]

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This study has limitations. TriNetX policies conceal the exact number of outcomes if fewer than ten events, limiting our study's power and statistical precision. Patients could have developed outcomes of interest after the one-year study time frame. The possibility of inaccurate coding is always a limitation with research based on ICD codes. Additionally, without an ICD code for HS improvement, we cannot compare which treatment provided greater symptom resolution. Further studies are needed to support our findings; however, this study provides valuable insight into the safety profile of ITIs and HS treatment.

Conflict of Interest Disclosures: None

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SUPPLEMENTAL FILES

Supplemental Table 1. Medication, Covariate, and Outcome ICD codes

Diagnosis	Codes
Hidradenitis Suppurativa	L73.2
Medications	
Triamcinolone	10759, J3301
Prednisone	8640
Covariates	
Diabetes Mellitus	E08-E13
Chronic Ischemic Heart Disease	I25
Chronic Kidney Disease	N18
Heart Failure	I50
Acute Myocardial Infarction	I21
Outcomes	
Infections of the skin and subcutaneous tissue	L00-L08
Abnormal Weight gain	R63.5
Hyperglycemia	R73.9
Primary Hypertension	I10
Hyperlipidemia	E78.5
Metabolic Syndrome	E88.810
Adrenocortical Insufficiency	E27.40
Osteoporosis	M81
Cataract	H26.2, H26.3, H26.4, H26.49, H26.8, H26.9, 366
Glaucoma	H40-H42
Depressive Episode	F32
Behavioral Syndromes	F50-F59
Bacterial and Viral Infectious Agents	B95-B97
Peptic Ulcer	K27
Cushing's Syndrome	E24
Myopathy	G72.0, G72.9

Supplemental Table 2. Baseline Characteristic Data After Propensity Score Matching Between Multiple and Single ITIs

Demographics	Multiple ITIs	% of Cohort	One ITI	% of Cohort	P-Value	Standardized Mean Difference
Age at Index	892	100%	892	100%	0.8355	0.0098
Male	199	22.309%	193	21.637%	0.7315	0.0162
Female	667	74.776%	679	76.121%	0.5092	0.0313
White	422	47.309%	417	46.749%	0.8125	0.0112

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African American	307	34.417%	307	34.417%	1	< 0.0001
Not Hispanic or Latino	704	78.924%	718	80.493%	0.4098	0.039
Hispanic or Latino	76	8.52%	69	7.735%	0.5442	0.0287
Asian	12	1.345%	17	1.906%	0.3492	0.0443
Diagnoses						
Diabetes mellitus	250	28.027%	244	27.354%	0.7509	0.015
Chronic ischemic heart disease	94	10.538%	89	9.978%	0.6964	0.0185
Chronic kidney disease (CKD)	78	8.744%	77	8.632%	0.933	0.004
Heart failure	73	8.184%	73	8.184%	1	< 0.0001
Acute myocardial infarction	29	3.251%	23	2.578%	0.3984	0.04

Supplemental Table 3. Baseline Characteristic Data After Propensity Score Matching Between Multiple ITIs and OPs

Demographics	Multiple ITIs	% of Cohort	One ITI	% of Cohort	P-Value	Standardized Mean Difference
Age at Index	650	100%	650	100%	0.8952	0.0073
Male	141	21.692%	140	21.538%	0.9463	0.0037
Female	509	78.308%	510	78.462%	0.9463	0.0037
White	390	60%	386	59.385%	0.8211	0.0125
African American	218	33.538%	219	33.692%	0.9532	0.0033
Not Hispanic or Latino	557	85.692%	548	84.308%	0.4845	0.0388
Hispanic or Latino	51	7.846%	53	8.154%	0.838	0.0113
Asian	10	1.538%	10	1.538%	1	< 0.0001
Diagnoses						
Diabetes mellitus	197	30.308%	201	30.923%	0.8098	0.0134
Chronic ischemic heart disease	82	12.615%	89	13.692%	0.5657	0.0319
Chronic kidney disease (CKD)	68	10.462%	74	11.385%	0.5937	0.0296
Heart failure	68	10.462%	67	10.308%	0.9276	0.005
Acute myocardial infarction	27	4.154%	30	4.615%	0.6845	0.0225

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