

CORTICOSTEROID USE, INFECTION, AND ADVERSE EVENTS AMONG IMMUNOGLOBULIN A NEPHROPATHY (IgAN) PATIENTS IN A US REAL-WORLD SETTING

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Introduction

- Immunoglobulin A nephropathy (IgAN) is the most prevalent chronic glomerulonephritis¹. Approximately 15-40% of IgAN patients will progress to kidney failure within 10 to 20 years after diagnosis^{2,3}.
- Despite inconsistent data on effectiveness and well-known severe side-effects including infections, corticosteroids (CS) are often used to treat IgAN due to a lack of other alternative, especially non-steroidal options⁴.
- The aim of this study is to characterize rates of infection and other adverse events (AEs) among IgAN patients who received CS versus those who did not.

* These analyses were performed before a recent US approval of Tarpeyo (budesonide) for adult IgAN patients at risk of rapid disease progression.

Method

- This was a descriptive, non-interventional, retrospective cohort study. Adult (≥ 18 years) IgAN patients from Optum[®] de-identified Electronic Health Record dataset (EHRs) between January 2007 and December 2019 were included; this dataset contains clinical/medical administrative records from 96 million people in 50 US states.
- We selected patients from the natural-language pre-processed physician notes with at least two IgAN records without any secondary or negative notion (e.g. 'secondary', 'suspected', 'doubt', etc. - not IgAN linked); the first record was considered as the index date.
- In addition, we included only patients with a record of kidney biopsy captured via the International Classification of Diseases version 9 and 10 clinical modification (ICD-9-CM, ICD-10 CM) codes:
 - Patients without a record of kidney biopsy, valid eGFR and proteinuria levels, or with a history of kidney failure/kidney transplant were excluded.
- CS use up to 12 months after the index date (yes vs. no) was determined via the National Drug Codes (NDC), while infections (all types) and selected CS-related (as established by the existing literature) AEs such as osteoporosis, hypertension and diabetes were identified through the corresponding ICD-9-CM and ICD-10 CM codes.
- In this study we are reporting the AEs based on CS use (yes vs. no) and are not testing any correlation; in addition, these AEs might be a result of cumulative exposure to CS (use before the index date) and other unrelated factors.
- Since prescription information was incomplete in Optum EHRs, two sets of analyses were performed:
 - Set 1:** for all patients in our study with any treatment prescription information including CS (N=1,189).
 - Set 2:** on a subset of patients above with at least 1 prescription information on days of supply available (n= 324).

Results

Baseline characteristics:

- Overall, 1,189 patients with a record of kidney biopsy were included in set 1; their mean age was 48.3 years. The majority were male (60.2%) and White (74.9%), and 8.5% were Asian (Table 1).
- Patients in set 2 were slightly older (mean age = 50.4 years); 61.1% were male and 78.4% were White, while 9.6% were Asian (Table 2).
- The mean blood pressure was slightly lower in patients included in set 1 compared to set 2 (133.2/78.2 vs 134.6/79.0 mm of Hg) and the mean creatinine level was slightly higher in set 1 vs set 2 (3.1 vs 2.8 mg/dL).
- There was little difference in the mean estimated glomerular filtration rate (eGFR) among patients of the two sets (set 1: 43.9 and set 2: 43.7 ml/min/1.73m²). Similarly, more than half of the patients included in the two sets (set 1: 57.9% and set 2: 56.8%) were in chronic kidney disease (CKD) stage 3b or higher (i.e. eGFR <45 ml/min/1.73m²).
- The mean eGFR was lower in patients who were on corticosteroids vs. not in both sets (set 1: 38.3 vs 50.1 and set 2: 40.7 vs 48.1 ml/min/1.73m²) and the majority of the patients who were on corticosteroids in two sets were in CKD stage 3b or higher (set 1: 65.7% and set 2: 61.4%). However, there were less patients not on CS in stages 3b-5 (set 1: 49.3% and set 2: 50.0%).

Outcomes:

- The annualized AE rates were higher among patients who were on CS versus those who were not on CS, and this was true for patients in set 1 as well as those in set 2 (Figure 1 and Tables 1 and 2):
 - Infections:** 1.9 to 2.1 times higher [set 1: 0.41 vs. 0.22 and set 2: 0.39 vs. 0.18].
 - Osteoporosis:** 1.7 to 1.8 times higher [set 1: 0.05 vs. 0.03 and set 2: 0.05 vs 0.03].
 - Hypertension:** 1.1 to 1.2 times higher [set 1: 0.84 vs. 0.67 and set 2: 0.83 vs 0.78].
 - Diabetes:** 1.5 times higher [set 1: 0.29 vs. 0.19 and set 2: 0.34 vs 0.22].

References

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Conflict of Interest

Carolina Aldworth, Robert Perkins, Julia Katlun, Jim Doherty, Aneesh George, Jaydeep Das, Weijia Wang and Raymond Przybysz are all permanent employees of Novartis.

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Table 1. Annualized infection and other AE rates for patients with IgA Nephropathy, by corticosteroid treatment status, all patients (N=1,189) – Set 1

	All Patients	Patients on corticosteroids after index	Patients not on corticosteroids after index
Patients (n, %)	1189	593 (49.9)	596 (50.1)
Age (mean (SD), years)	48.3 (15.5)	49.7 (15.7)	46.8 (15.2)
Male (%)	60.2	60.2	60.2
White (%)	74.9	75.4	74.3
Asian (%)	8.5	9.1	7.9
Annualized rates per patient			
Infections	0.31	0.41	0.22
osteoporosis	0.04	0.05	0.03
hypertension	0.75	0.84	0.67
diabetes	0.24	0.29	0.19

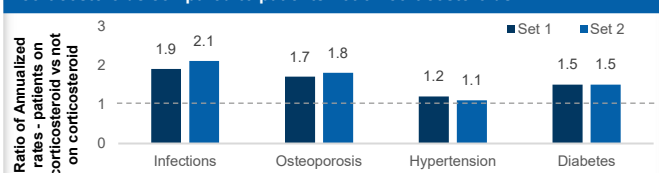
Note: Annualized rates were calculated as: the number of 1st events within follow-up (diagnosis on different dates) / total person-years in the follow-up, patients with different diagnostic codes for the same events were counted only once.

Table 2. Annualized infection and other AE rates for patients with IgA Nephropathy, by corticosteroid treatment status, patients with minimum prescription information (n=324) – Set 2

	All Patients	Patients on corticosteroids after index	Patients not on corticosteroids after index
Patients (n, %)	324 (27.2)	188 (15.8)	136 (11.4)
Age (mean (SD), years)	50.4 (14.9)	51.6 (15.2)	48.7 (14.4)
Male (%)	61.1	60.1	62.5
White (%)	78.4	78.7	77.9
Asian (%)	9.6	10.6	8.1
Annualized rates per patient			
infections	0.30	0.39	0.18
osteoporosis	0.04	0.05	0.03
hypertension	0.81	0.83	0.78
diabetes	0.29	0.34	0.22

Note: Annualized rates were calculated as: the number of 1st events within follow-up (diagnosis on different dates) / total person-years in the follow-up, patients with different diagnostic codes for the same events were counted only once.

Figure 1: Ratio of annualized rates of infections and other AEs in patients on corticosteroids compared to rates not on corticosteroids



Limitations

We identified IgAN patients through the physician notes and not the diagnostic coding and as such, our patient selection might not be fully accurate. In addition, we could only use a record of biopsy not necessarily linked to IgAN, and only biopsies recorded in Optum EHRs and not elsewhere. We also encountered some data limitations for treatment and thus, some patients recorded as not on CS in our study might have been on this therapy in real world. This might have also affected our outcomes. In addition, this analysis does not reflect the likely future increased use of lower dosing strategies with CS after recent results of low dose TESTING⁴ trial were reported.

Conclusion

In this analysis, IgAN patients with a record of CS usage (these patients also seemed to be in more advanced CKD stages based on their eGFR levels) experienced a higher rate of infections, osteoporosis and diabetes versus those who were not on CS, and this was true for both sets of patients. These findings highlight a need for targeted non-steroidal interventions that can reduce treatment burden and delay the progression of this disease at the same time.