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## Use of Systemic Steroids for Inflammatory Bowel Disease Can Increase Intraocular Pressure

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Corticosteroids are often utilized to induce clinical remission in inflammatory bowel disease (IBD).<sup>1</sup> Metabolic bone disease, increased blood pressure, and mood changes are well-established side effects of steroids. It remains unclear what impact corticosteroids have on intraocular pressure (IOP).<sup>2</sup> Steroid-induced ocular hypertension was first characterized in 1950, and a clear relationship between ophthalmic steroid medications and IOP elevation has been identified.<sup>3</sup> Periocular, intravitreal, and topical ophthalmic steroid medications have been identified as causes of ocular hypertension (IOP elevation) and increase the risk of glaucoma.<sup>3</sup> Additionally, steroid use is linked to the early cataract development. Currently, the link between systemic steroids and IOP in IBD patients has not been well studied. To bridge this knowledge gap, we examined the relationship between corticosteroids and IOP to identify the prevalence of elevated IOP and glaucoma in IBD patients undergoing corticosteroid treatment.

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Conflicts of Interest:

The authors disclose no conflicts.

Ethical Statement:

Approval for this project was granted on 6/14/2019 by the University of Maryland, Baltimore IRB, under protocol number HP-00084185.

Reporting Guidelines:

STROBE.

Supplementary Materials

Material associated with this article can be found in the online version at <https://doi.org/10.1016/j.gastha.2024.01.008>.

Fifty participants on chronic systemic steroids were grouped into normal or elevated IOP based on the highest IOP measurement of  $\geq 21$  mmHg. Those with a measurement in either eye of at least 21 were classified as elevated IOP (Table). Average left IOP in those with normal IOP was 14.7 mmHg (interquartile range [IQR] [11.0, 18.0]) vs 21.5 mmHg (IQR [20.3, 23.0]) in those with elevated IOP; average right IOP for the normal IOP group was 15.1 (IQR: [12.0, 18.4]) vs 22.9 (IQR: [19.6, 23.0]) in the elevated IOP group. Both left and right IOP were increased in the elevated IOP group ( $P$  value = .00434 and  $4.38 \times 10^{-7}$ , respectively), as were corresponding average and highest measured IOPs ( $P$  value = .001 and 0.001, respectively). The mean age was 43.5 years old, 42% of participants were male, 68% were White, and 16 were Black (32%). Fifty-eight percent of participants were never smokers, 22% were former smokers, and 12% were current smokers. The majority received prednisone (66%), while 34% received budesonide. Those exposed to prednisone and budesonide received an average maximum dose of 32.9 mg (IQR: [25.0, 40.0]) and 7.1 mg (IQR: [3.0, 9.0]), respectively. An additional course of 60 mg IV solumedrol was given to 12% of participants, while one participant received an additional course of budesonide after prednisone. There was no statistically significant difference in these demographics between those with vs without elevated IOP. Additionally, those with elevated IOP were likelier to have Crohn's disease (CD) (83.3% vs 47.4%), though this did not quite achieve statistical significance of  $< 0.05$  ( $P$  value = .067), likely due to sample size. No difference in age, sex, race, body mass index, or smoking behavior was observed in ulcerative colitis vs CD participants, nor was there a difference in primary steroid exposure, maximum steroid dosing, or need for additional solumedrol therapy (Table A1). Average and highest IOP trended higher in those with CD, though this was just short of statistical significance ( $P$  value = .061 and .076, respectively).

In this cohort, prednisone use resulted in no statistically significant difference in IOP compared to budesonide. Ocular hypertension is an IOP  $> 21$  mmHg<sup>3</sup>. The prevalence of ocular hypertension in the general population is between 2.7% and 3.8%, and it was previously estimated that 4% to 7% of the general population over the age of 40 meets criteria for ocular hypertension. In our cohort, 24% of participants had an IOP  $\geq 21$  mmHg. There is no consistent difference between males and females; we found this in our population as well.<sup>4</sup> While we found no difference based on race, elevated IOP has been shown to be increased in Black Americans,<sup>4</sup> and our population was too small to accurately assess this. Ophthalmic literature has noted oral prednisone use is associated with elevated IOP<sup>5</sup> but has not assessed oral budesonide, which exhibits high first-pass metabolism,<sup>6</sup> suggesting systemic effects should be limited. However, 4 participants (28.6%) on budesonide had elevated IOP. We also observed that participants with CD trended higher IOP than participants with ulcerative colitis. Though not statistically significant, given the increased rate of ocular extraintestinal manifestations in patients with CD<sup>7</sup>, the increased observance of elevated IOP in chronic uveitis and ocular inflammation,<sup>8</sup> and the high rate of asymptomatic ocular inflammation in IBD patients,<sup>7</sup> a larger sample size may identify disease as a predictor of elevated IOP. Steroids are also known to cause cataracts, and larger studies would also be needed to assess this outcome.

Currently, gastroenterology practice guidelines acknowledge the impact of chronic corticosteroids on metabolic bone health. IBD patients with corticosteroid exposure are

recommended to have vitamin D deficiency and metabolic bone disease screening. At this time, there are no guidelines for eye exam screenings for IBD patients on corticosteroid therapy. Therefore, a larger study would help fully understand the impact of corticosteroids on IOP and determine which subset of patients would benefit from additional screening.

Further analysis with a larger population can help improve steroid treatment dosage and duration guidelines, increase ophthalmic follow-up, and improve patient outcomes, in addition to identifying those who might be at a higher risk for steroid-induced IOP elevations.

Glaucoma is a chronic, progressive, “silent” disease, and the associated increase in IOP can cause irreversible optic nerve damage, resulting in irreversible blindness.<sup>9</sup> It is often asymptomatic until vision loss progresses to include central vision, impacting all activities of daily living. The only modifiable risk factor in the treatment of glaucoma is IOP reduction, which underscores the importance of early detection.<sup>9</sup> The ability to identify a patient with an elevated IOP early greatly improves the prognosis because it allows ophthalmologists the ability to intervene early and prevent any further loss of vision.

In conclusion, IBD patients undergoing corticosteroid therapy for 4 weeks may have an increased prevalence of ocular hypertension, even those on budesonide therapy. Patients taking either prednisone or budesonide are equally likely to have increased IOP. Although our pilot-study sample size is small, we hope to utilize this data and expand our findings in the future, exploring a potential dose-dependent relationship between corticosteroid exposure and IOP, including in comparison to a control group. IBD patients can benefit from yearly eye exams to assess for potential adverse effects from corticosteroid exposure including increased IOP, and to screen for extraintestinal manifestations of IBD.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations used in this paper:

<b>CD</b>	Crohn’s disease
<b>IBD</b>	inflammatory bowel disease
<b>IOP</b>	intraocular pressure
<b>IQR</b>	interquartile range

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**Data Transparency Statement:**

Data from this study are not publicly available but may be shared upon reasonable request by contacting the corresponding author.

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Demographic and Clinical Characteristics of Enrolled Individuals Without vs With Elevated IOP

Table.

	Cohort (n = 50)	Normal IOP (n = 38)	Elevated IOP (n = 12)	P value
IOP (mean, IQR) (range)				
Right IOP	17.0 (14.0, 19.8) (8.0, 46.0)	15.1 (12.0, 18.4) (8.0, 20.5)	22.9 (19.6, 23.0) (18.0, 46.0)	.004
Left IOP	16.4 (12.8, 19.0) (8.5, 26.0) 3 unknown	14.7 (11.0, 18.0) (8.5, 20.0) 3 unknown	21.5 (20.3, 23.0) (17.0, 26.0)	<.001
Average IOP	16.7 (13.1, 19.5) (8.5, 36.0)	14.9 (11.7, 17.7) (8.5, 20.0)	21.5 (20.3, 23.0) (17.0, 26.0)	<.001
Highest IOP	17.7 (14.0, 20.5) (9.0, 46.0)	15.6 (12.1, 18.9) (9.0, 20.5)	24.3 (21.0, 23.3) (21.0, 46.0)	.001
Age (mean, IQR) (range)	43.5 (33.0, 53.8) (19.0, 84.0)	44.6 (29.5, 59.3) (19.0, 84.0)	40.2 (33.0, 48.3) (26.0, 53.0)	.263
Sex				.999
Female	29 (58.0%)	22 (57.9%)	7 (58.3%)	
Male	21 (42.0%)	16 (42.1%)	5 (41.7%)	.292
Race				
Black	16 (32.0%)	14 (36.8%)	2 (16.7%)	
White	34 (68.0%)	24 (63.2%)	10 (83.3%)	.999
Smoking status				
Current	6 (12.0%)	5 (13.2%)	1 (8.3%)	
Former	11 (22.0%)	8 (21.1%)	3 (25.0%)	
Never	29 (58.0%)	22 (57.9%)	7 (58.3%)	
Unknown	4 (8.0%)	3 (7.9%)	1 (8.3%)	.999
Primary steroid exposure				
Prednisone	33 (66.0%)	25 (65.8%)	8 (66.7%)	
Budesonide	17 (34.0%)	13 (34.2%)	4 (33.3%)	
BMI (mean, IQR) (range)	28.0 (22.8, 31.5) (17.1, 59.2) 4 unknown	27.0 (22.8, 29.3) (17.1, 54.0) 3 unknown	31.2 (22.3, 36.4) (19.5, 59.2) 1 unknown	.294
Disease				.067
Ulcerative colitis	14 (28.0%)	13 (34.2%)	1 (8.3%)	
Crohn's disease	28 (56.0%)	18 (47.4%)	10 (83.3%)	

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	Cohort (n = 50)	Normal IOP (n = 38)	Elevated IOP (n = 12)	P value
Other	8 (16.0%)	7 (18.4%)	1 (8.3%)	
Highest dose				
Prednisone (mean, IQR) (range)	32.9 (25.0, 40.0) (3.0, 60.0) 6 unknown	35.2 (30.0, 40.0) (3.0, 60.0) 5 unknown	26.4 (15.0, 40.0) (5.0, 40.0) 1 unknown	.226
Budesonide (mean, IQR) (range)	7.1 (3.0, 9.0) (3.0, 9.0) 1 unknown	7.0 (3.0, 9.0) (3.0, 9.0) 1 unknown	7.5 (7.5, 9.0) (3.0, 9.0)	.783
Additional 60 mg IV solumedrol	6 (12.0%)	5 (13.2%)	1 (8.3%)	.999

BMI, body mass index.