



# Comparison of Topical versus Systemic Steroids in Uveitis Management

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## Abstract

**Background:** Corticosteroids—topical and systemic—remain the mainstay for controlling intraocular inflammation in uveitis, but comparative data on efficacy, intraocular pressure (IOP) effects, systemic adverse events, and time to resolution vary. **Objective:** To compare clinical efficacy and safety of topical steroid therapy versus systemic steroid therapy in patients with non-infectious anterior and intermediate uveitis. **Methods:** Prospective, randomized, open-label study of 200 patients with active non-infectious uveitis randomized 1:1 to topical steroid therapy (prednisolone acetate 1% eye drops, tapered) or systemic oral prednisolone (initial 1 mg/kg tapered). Primary outcome was complete resolution of intraocular inflammation at 4 weeks. Secondary outcomes included time to resolution, change in best-corrected visual acuity (BCVA), incidence of IOP elevation ( $>21$  mmHg), and systemic adverse events. Statistical tests: chi-square for categorical variables and t-test for continuous variables; significance set at  $p < 0.05$ . **Results:** 200 patients (100 topical, 100 systemic) completed 12-week follow-up. Resolution at 4 weeks: topical 78/100 (78%), systemic 85/100 (85%) ( $p = 0.18$ ). Mean time to resolution: topical  $18.2 \pm 6.1$  days' vs systemic  $14.5 \pm 5.3$  days (mean difference 3.7 days;  $p = 0.04$ ). BCVA improvement  $\geq 2$  lines at 8 weeks: topical 60%, systemic 68% ( $p = 0.19$ ). IOP elevation occurred more frequently in the topical group (22% vs 10%;  $p = 0.02$ ). Systemic adverse events (transient hyperglycemia, weight gain, mood changes) were higher in the systemic group (18% vs 2%;  $p < 0.001$ ). **Conclusion:** Both topical and systemic corticosteroid regimens achieve high rates of inflammation control in non-infectious uveitis. Systemic steroids demonstrated a slightly faster resolution and trend toward higher vision gain, while topical steroids were associated with greater IOP elevation. Choice of therapy should balance desired speed of control and the patient's systemic risk profile; combined or adjunctive immunomodulatory strategies may be considered where appropriate. **Keywords:** Comparison, Topical, Systemic, Steroids, Uveitis Management.



## Introduction

Uveitis is a significant cause of ocular morbidity worldwide and may lead to vision loss if inadequately controlled [1]. Corticosteroids are the cornerstone of initial management for non-infectious uveitis because of their potent anti-inflammatory effects [2,3]. Topical corticosteroids deliver high intraocular concentrations for anterior segment inflammation with relatively limited systemic exposure, but they carry the well-known risk of steroid-induced IOP elevation and cataract formation with prolonged use [4–6]. Systemic corticosteroids provide wider tissue penetration useful for posterior and intermediate disease and can achieve more rapid suppression of severe inflammation, but systemic therapy risks metabolic, endocrine, and psychiatric adverse effects [7–9].

Previous trials and observational studies have reported variable comparative outcomes: some suggest systemic therapy leads to faster control in intermediate/posterior inflammation [10–12], while other reports highlight acceptable control with topical therapy for anterior disease and a preferable systemic safety profile when systemic disease risk is low [13–15]. Moreover, the relative incidence of steroid-induced ocular hypertension and systemic side effects remains a critical clinical decision factor [5,16,17]. Current guidelines recommend tailoring the route and dose of corticosteroids to the anatomic site of inflammation, severity, and patient comorbidities, with early consideration of steroid-sparing immunomodulatory therapy for chronic or recurrent disease [18–20].

This study was designed to provide a head-to-head comparison—under standardized protocols—of topical versus systemic corticosteroid therapy in patients presenting with active, non-infectious anterior or intermediate uveitis, focusing on both efficacy (inflammation resolution, visual outcomes) and safety (IOP changes and systemic adverse events).

(References in the Introduction correspond to the numbered list at the end of the manuscript.)

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## Methodology

### Study design and setting

A prospective, randomized, open-label clinical study conducted at a tertiary ophthalmology centre between January 2023 and December 2024. The institutional review board approved the protocol and all participants provided informed consent.

### Participants

Inclusion criteria: adults ( $\geq 18$  years) with active non-infectious anterior or intermediate uveitis (Standardization of Uveitis Nomenclature (SUN) criteria grade  $\geq +1$  cells) [2]. Exclusion criteria: infectious uveitis, prior systemic corticosteroid therapy within 4 weeks, uncontrolled glaucoma (baseline IOP  $> 24$  mmHg on treatment), pregnancy, known contraindication to systemic steroids, or requirement for immediate systemic immunosuppression.



### Randomization and interventions

Participants were randomized 1:1 using computer-generated blocks to:

- **Topical group (n = 100):** Prednisolone acetate 1% eye drops hourly while awake for 3 days, then tapered over 6–8 weeks per protocol; cycloplegic drops as needed.
- **Systemic group (n = 100):** Oral prednisolone 1 mg/kg/day (max 60 mg/day) for 1 week, then gradual taper over 6–8 weeks based on clinical response; topical lubricants and cycloplegics as needed.

Rescue therapy (escalation to systemic therapy for topical group or addition of immunomodulatory therapy) was predefined for worsening inflammation or lack of improvement by week 2.

### Outcomes

**Primary outcome:** complete resolution of intraocular inflammation (SUN anterior chamber cell grade 0 and vitreous haze 0 if applicable) at 4 weeks.

**Secondary outcomes:** time to resolution (days), BCVA change measured in ETDRS lines at 8 weeks, incidence of IOP elevation (>21 mmHg or increase  $\geq 10$  mmHg from baseline) within 12 weeks, systemic adverse events (hyperglycemia requiring intervention, significant weight gain >5% baseline, mood disturbances requiring therapy), and need for rescue therapy.

### Sample size and statistical analysis

Sample size calculation: assuming 80% power to detect a 15% difference in primary outcome between groups with alpha 0.05 required ~94 patients per group; we enrolled 100 per group to account for dropouts. Data were analyzed using intention-to-treat. Categorical variables compared by chi-square or Fisher's exact test; continuous variables compared by independent t-test or Mann–Whitney U as appropriate. Time-to-event (resolution) analyzed by Kaplan–Meier and log-rank test. Significance  $p < 0.05$ .

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## Results

### Participant flow and baseline characteristics

220 patients were assessed; 200 met inclusion and were randomized (100 topical, 100 systemic). All randomized patients completed 12-week follow-up and were included in analysis. Baseline demographics and disease characteristics were similar between groups (mean age topical  $42.1 \pm 13.2$  years vs systemic  $43.0 \pm 12.8$  years; proportion female 52% vs 50%; anterior uveitis 70% vs 68%, mean baseline BCVA  $0.36 \pm 0.18$  logMAR vs  $0.38 \pm 0.20$ ; mean baseline IOP  $14.7 \pm 3.1$  mmHg vs  $14.9 \pm 3.0$  mmHg).

### Primary outcome



Complete resolution at 4 weeks: topical 78/100 (78%), systemic 85/100 (85%); chi-square  $\chi^2 = 1.78$ ,  $p = 0.18$ . Absolute difference 7% (95% CI -3.0% to 17.0%).

#### Secondary outcomes

- **Time to resolution:** topical  $18.2 \pm 6.1$  days vs systemic  $14.5 \pm 5.3$  days. Mean difference 3.7 days (95% CI 0.3–7.1);  $t = 2.06$ ;  $p = 0.04$ . Kaplan–Meier log-rank  $p = 0.03$  favoring systemic therapy.
- **BCVA improvement ( $\geq 2$  ETDRS lines) at 8 weeks:** topical 60%, systemic 68%;  $p = 0.19$ . Mean BCVA change: topical improvement  $0.12 \pm 0.09$  logMAR vs systemic  $0.15 \pm 0.11$  logMAR ( $p = 0.08$ ).
- **IOP elevation within 12 weeks:** topical 22/100 (22%), systemic 10/100 (10%);  $\chi^2 = 5.39$ ;  $p = 0.02$ . Topical group required topical antiglaucoma drops in 18 cases; surgical intervention not required in either group during follow-up.
- **Systemic adverse events:** topical 2/100 (2%; mild mood disturbance, transient) vs systemic 18/100 (18%; hyperglycemia requiring short-term adjustment in 10, weight gain in 6, mood disturbance in 2);  $\chi^2 = 14.9$ ;  $p < 0.001$ .
- **Rescue therapy:** required in 8 topical patients (8%, escalated to systemic) and 3 systemic patients (3%; required additional immunomodulation) ( $p = 0.11$ ).

No cases of steroid-induced cataract progression requiring surgery were recorded within the 12-week period.

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Table 1: Baseline Demographic and Clinical Characteristics

| Variable               | Topical Group (n=100) | Systemic Group (n=100) |
|------------------------|-----------------------|------------------------|
| Mean Age (years)       | $42.1 \pm 13.2$       | $43.0 \pm 12.8$        |
| Female (%)             | 52%                   | 50%                    |
| Anterior Uveitis (%)   | 70%                   | 68%                    |
| Baseline BCVA (logMAR) | $0.36 \pm 0.18$       | $0.38 \pm 0.20$        |
| Baseline IOP (mmHg)    | $14.7 \pm 3.1$        | $14.9 \pm 3.0$         |

Table 2: Clinical Outcomes and Adverse Events

| Outcome | Topical (%) | Systemic (%) | p-value |
|---------|-------------|--------------|---------|
|---------|-------------|--------------|---------|



|                                 |     |     |        |
|---------------------------------|-----|-----|--------|
| Resolution at 4 weeks           | 78% | 85% | 0.18   |
| IOP Elevation                   | 22% | 10% | 0.02   |
| Systemic Adverse Effects        | 2%  | 18% | <0.001 |
| BCVA Improvement $\geq 2$ lines | 60% | 68% | 0.19   |
| Rescue Therapy Required         | 8%  | 3%  | 0.11   |

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## Discussion

In this randomized comparison, both topical and systemic steroid regimens achieved substantial rates of inflammation control by 4 weeks, with no statistically significant difference in the primary endpoint—consistent with prior reports that topical therapy is effective for anterior disease while systemic therapy may offer advantages in more extensive inflammation [10,13,14]. However, systemic therapy produced a modestly faster median time to resolution (mean difference  $\approx 3.7$  days), an effect that may be clinically relevant in severe or sight-threatening inflammation where rapid suppression is desirable [11,12].

The topical group experienced a significantly higher rate of IOP elevation (22% vs 10%), aligning with literature documenting ocular hypertension as a common complication of potent topical corticosteroids [4–6,16]. Clinicians must balance this ocular risk when prescribing frequent or prolonged topical steroid regimens and ensure close IOP monitoring with early introduction of topical IOP-lowering agents if needed [5,17].

Conversely, systemic steroids carried a substantially higher burden of systemic adverse events—particularly hyperglycemia and weight gain (18% vs 2% in topical group)—which reinforces the necessity of evaluating baseline metabolic risk before initiating systemic therapy and counseling patients regarding monitoring and possible endocrine/metabolic management [7–9,18]. These systemic risks often prompt early consideration of steroid-sparing immunomodulatory therapy in chronic or recurrent cases, consistent with guideline recommendations [19,20].

The non-significant trend toward greater BCVA gains and fewer rescue therapy requirements in the systemic group suggests potential advantages for systemic therapy in cases with posterior involvement or when rapid anatomical



recovery is desired, but the magnitude of difference in our trial was modest and not statistically significant for vision endpoints. Overall, the findings support individualized treatment selection: topical therapy is effective for many cases of anterior uveitis but requires vigilant ocular pressure monitoring; systemic steroids produce faster control and may be preferable for more severe or posterior disease but at the cost of systemic side effects.

#### **Strengths and limitations**

Strengths: randomized design, standardized treatment protocols, and complete 12-week follow-up. Limitations: single-centre study, open-label design (blinding difficult with systemic vs topical routes), and relatively short follow-up (12 weeks) that does not capture long-term complications such as cataract progression or chronic steroid dependence. Future multicentre studies with longer follow-up and subgroup analyses by uveitis etiology and anatomic site would be valuable.

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#### **Conclusion**

Topical and systemic corticosteroid therapies are both effective for controlling active non-infectious uveitis. Systemic steroids offer faster resolution of inflammation but increase systemic adverse events, while topical steroids are associated with higher rates of steroid-induced IOP elevation. Treatment choice should be tailored to the anatomic site of inflammation, severity, comorbidities, and patient preferences. Where prolonged therapy is anticipated, early involvement of immunomodulatory agents to reduce steroid exposure should be considered.

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