Comparison of Intravitreal Corticosteroids for Management of Diabetic Macular Edema: A Scoping Review of Long-Term Randomized Trials

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Introduction: A significant proportion of patients with diabetic macular edema (DME) require second-line corticosteroid therapy after insufficient response to anti-vascular endothelial growth factor (anti-VEGF) treatment. Currently, dexamethasone implant, fluocinolone acetonide inserts, and intravitreal triamcinolone acetonide are approved for second-line intravitreal corticosteroid therapy. However, there are scarce evidence-based guidelines advising the delivery of these corticosteroids for DME. Current guidelines recommend subjective clinical judgement to guide management. It also remains unclear whether there is sufficient evidence in the literature to support the creation of such guidelines. This study aimed to summarize the published repertoire of long-term randomized controlled trials (RCTs) that evaluate current corticosteroid treatments for DME patients.

Methods: Scoping review of RCTs following PRISMA guidelines. Using a validated search strategy, MEDLINE, EMBASE, and Cochrane CENTRAL were searched to April 2022 for RCTs evaluating monotherapy or combination steroid (with laser or anti-VEGF) treatments against control (placebo, sham, or observation), laser (grid or panretinal photocoagulation), or anti-VEGF agents (bevacizumab, ranibizumab, or aflibercept). Exclusion criteria included studies with patients undergoing concomitant ocular surgery at baseline (as a co-intervention), prophylaxis studies, follow-up fewer than 6 months, and duplicate publications. Paired independent reviewers conducted title and abstract screening, full-text selection, and data extraction. Information related to patient enrollment, study interventions, and study durations were abstracted for each trial included in the final summary.

Results: From 2906 records, we identified 55 RCTs across 7014 patients (7294 eyes) comparing corticosteroid treatments against other treatment modalities (median follow up: 6 months). Of most concern, there were zero published trials directly comparing corticosteroid monotherapies (dexamethasone implant, fluocinolone acetonide insert, or intravitreal triamcinolone acetonide) against one another. As well, we identified zero studies directly comparing different corticosteroids through combination regiments. This result precluded summary of the comparative efficacy between corticosteroids. However, between studies, RCTs overwhelmingly compared all corticosteroid agents against common comparator mono-interventions (control: n=9 studies; anti-VEGF agents: n=27 studies; laser therapy: n=18 studies).

Conclusions: RCTs predominantly compare corticosteroid treatments against other treatment modalities. However, to-date, there is insufficient evidence directly comparing available corticosteroids to identify an agent that optimizes patient outcomes and safety. Corticosteroid therapy remains a viable option for patients who cannot adhere to monthly anti-VEGF treatment. Our results indicate need for head-to-head corticosteroid trials to further substantiate evidence-based DME treatment guidelines. Although such trials require prolonged longitudinal follow-up, we report sufficient evidence for network meta-analyses to derive preliminary evidence comparing corticosteroid monotherapy and combination regiments.