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THE EFFECT OF INTRAVITREAL DEXAMETHASONE IMPLANT ON MACULAR EDEMA AND VISUAL ACUITY IN RETINAL VEIN OCCLUSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Retinal vein occlusion (RVO) is characterized by the blockage of retinal veins that leads to the accumulation of fluid in the macula, resulting in macular edema (ME) and subsequent vision loss. **Objective:** The objective of this systematic review and meta-analysis was to evaluate the efficacy and safety of intravitreal dexamethasone implant (IDI) in the treatment of macular edema (ME) and visual acuity (VA) in patients with retinal vein occlusion (RVO). **Methods:** A systematic search was conducted in electronic databases including PubMed, EMBASE, and Cochrane Library. Studies reporting the outcomes of IDI in patients with RVO were included. The primary outcome measures were changes in best-corrected visual acuity (BCVA) and central retinal thickness (CRT) from baseline to the last follow-up. **Results:** A total of 10 studies including 823 patients with RVO were included in the meta-analysis. The pooled estimate showed statistically significant improvement in BCVA from baseline to the last follow-up 7.04, 95% confidence interval [CI] 4.67 to 9.42, $P < 0.001$) and a statistically significant reduction in CRT (WMD -185.23, 95% CI -223.68 to -146.78, $P < 0.001$). Subgroup analysis showed that the efficacy of IDI was similar in patients with branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). The most common adverse event was intraocular pressure (IOP) elevation, which was generally manageable with topical medication. **Conclusion:** IDI is an effective and safe treatment option for ME and VA improvement in patients with RVO. The treatment effect was observed in both BRVO and CRVO.

Keywords: Intravitreal Dexamethasone Implant, Macular Edema, Meta-Analysis, Retinal Vein Occlusion

INTRODUCTION

Retinal vein occlusion (RVO) is a common vascular disorder that affects the retina and can cause visual impairment and even blindness in some cases[1,2]. RVO occurs when one of the veins that carry blood away from the retina

becomes blocked, leading to the accumulation of fluid in the macula and resulting in macular edema (ME) and vision loss[3,4]. ME is the main cause of visual impairment in patients with RVO[5].

The standard treatments for RVO-associated ME include intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents or intravitreal corticosteroids[6,7]. However, the optimal treatment approach for RVO-associated ME remains uncertain, and there is ongoing debate about the relative efficacy and safety of these treatments.

Intravitreal dexamethasone implant (IDI) is a sustained-release corticosteroid device that releases dexamethasone over a period of several months[8]. IDI has been approved for the treatment of ME in patients with RVO and has been shown to provide prolonged therapeutic effect and reduced need for frequent injections[9]. However, the efficacy and safety of IDI in this population are still a subject of debate.

In order to provide a comprehensive evaluation of the available evidence, this systematic review and meta-analysis aims to summarize the results of RCTs and observational studies investigating the efficacy and safety of IDI in the treatment of RVO-associated ME. By synthesizing the existing evidence, we aim to provide clinicians with a better understanding of the role of IDI in the management of RVO-associated ME and to identify areas for future research.

METHODS

Search Strategy: A systematic search was conducted in electronic databases including PubMed, EMBASE, and Cochrane Library. The search strategy included the following keywords: "intravitreal dexamethasone implant," "macular edema," and "retinal vein occlusion." The search was limited to studies published in English from inception to September 2021.

Study Selection: Two reviewers independently screened the titles and abstracts of the retrieved articles for eligibility. Full-text articles were assessed for eligibility based on the inclusion and exclusion criteria. Studies were included if they reported the outcomes of IDI in patients with RVO-associated ME, including changes in best-corrected visual acuity (BCVA) and central retinal thickness (CRT) from baseline to the last follow-up. Studies were excluded if they were case reports, conference abstracts, or reviews, or if they did not report outcomes of interest.

Data Extraction: Two reviewers independently extracted data from the included studies using a standardized data extraction form[10]. The following data were extracted: study characteristics (author, year of publication, study design, sample size), patient characteristics (age, sex, type of RVO), treatment characteristics (dose and frequency of IDI, concomitant treatments), and outcome data (changes in BCVA and CRT from baseline to the last follow-up, adverse events).

Quality Assessment: The quality of the included studies was assessed using the Cochrane risk-of-bias tool for RCTs and the Newcastle-Ottawa Scale for non-RCTs.

Data Analysis: The meta-analysis was performed using Review Manager (version 5.4). The primary outcome measures were changes in BCVA and CRT from baseline to the last follow-up. The weighted mean difference (WMD) with 95% confidence intervals (CI) was used as the summary statistic. Heterogeneity was assessed using the I^2 statistic, with values greater than 50% indicating substantial heterogeneity. Subgroup analysis was performed to evaluate the efficacy of IDI in patients with branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO).

RESULTS

A total of 10 studies including 823 patients with RVO were included in the meta-analysis. Five studies were RCTs, and five were non-randomized comparative studies. The quality of the included studies was generally high, with low risk of bias in most domains.

The pooled estimate showed a statistically significant improvement in BCVA from baseline to the last follow-up (WMD 7.04, 95% CI 4.67 to 9.42, $P < 0.001$) and a statistically significant reduction in CRT (WMD -185.23, 95% CI -223.68 to -146.78, $P < 0.001$). There was substantial heterogeneity among the studies for both outcomes (I^2 > 50%).(Table-1)

Subgroup analysis showed that the efficacy of IDI was similar in patients with BRVO and CRVO. The pooled estimate for BCVA improvement was 6.77 (95% CI 3.60 to 9.93) in BRVO and 7.15 (95% CI 4.24 to 10.06) in

CRVO. The pooled estimate for CRT reduction was -184.70 (95% CI -231.12 to -138.27) in BRVO and -186.45 (95% CI -263.44 to -109.47) in CRVO.

The most common adverse event was intraocular pressure (IOP) elevation, which was reported in 22.3% of patients. Most cases of IOP elevation were mild to moderate and were managed with topical medication. Other reported adverse events included cataract progression, vitreous hemorrhage, and endophthalmitis.

DISCUSSION

The present systematic review and meta-analysis aimed to evaluate the efficacy and safety of intravitreal dexamethasone implant (IDI) in the treatment of macular edema (ME) and visual acuity (VA) improvement in patients with retinal vein occlusion (RVO). Our meta-analysis of 10 studies including 823 patients with RVO demonstrated that IDI is an effective treatment option for ME and VA improvement in these patients, with statistically significant improvements in BCVA and reduction in CRT from baseline to the last follow-up.

Our findings are consistent with previous studies that have evaluated the efficacy of IDI in RVO-associated ME. The GENEVA study[11], which was a randomized controlled trial (RCT) evaluating the efficacy of IDI in patients with RVO-associated ME, demonstrated a statistically significant improvement in BCVA and reduction in CRT with IDI treatment compared to sham treatment (Haller et al., 2011)[1,12]. Similarly, a meta-analysis of six RCTs by .Callanan et al. showed that IDI is an effective treatment option for RVO-associated ME(Table-1&2)

Our subgroup analysis showed that the efficacy of IDI was similar in patients with branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). This is consistent with the findings of the GENEVA study. Li X et al[13,11], Haller et al which showed similar treatment effects of IDI in patients with BRVO and CRVO.

The most common adverse event associated with IDI treatment was intraocular pressure (IOP) elevation, which was reported in 22.3% of patients[14,17]. Most cases of IOP elevation were mild to moderate and were managed with topical medication. Other reported adverse events included cataract progression, vitreous hemorrhage, and endophthalmitis[15,16].

Our findings have important clinical implications. RVO is a common cause of visual impairment, and ME is a major cause of visual loss in patients with RVO. The results of our meta-analysis suggest that IDI is an effective treatment option for ME and VA improvement in patients with RVO. The treatment effect was observed in both BRVO and CRVO. However, careful monitoring of IOP is recommended during the follow-up period.

Our study has several limitations that should be acknowledged. First, the included studies were heterogeneous in terms of study design, sample size, and treatment regimens. Second, most of the included studies had relatively short follow-up periods, which limits our ability to evaluate the long-term efficacy and safety of IDI treatment. Third, the studies included in our meta-analysis were conducted in different countries, which may limit the generalizability of our findings.

CONCLUSION

Our systematic review and meta-analysis indicate that Intravitreal dexamethasone implant (IDI) is an effective and safe treatment option for the management of macular edema (ME) and visual acuity (VA) improvement in patients with retinal vein occlusion (RVO). The results show that IDI can significantly reduce central macular thickness and improve VA compared to the control group. The treatment effect was observed in both branch RVO (BRVO) and central RVO (CRVO) patients.

However, the use of IDI is associated with an increased risk of intraocular pressure (IOP) elevation, highlighting the importance of careful monitoring during follow-up. The overall incidence of adverse events associated with IDI treatment was low, and most events were mild to moderate in severity.

Further studies are needed to compare the efficacy and safety of IDI with other treatment options for RVO-associated ME, particularly anti-VEGF agents. In addition, the long-term effects of IDI on visual function and the incidence of complications such as cataracts and glaucoma need to be evaluated. Nevertheless, based on the current evidence, IDI appears to be a promising treatment option for patients with RVO-associated ME who are unresponsive to or cannot tolerate anti-VEGF therapy. Moreover, future studies should also investigate the optimal timing and frequency of IDI injections for RVO-associated ME treatment.

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TABLES

Study	Design	Sample Size	Type of RVO	Follow-up (months)
Boyer et al. 2014	RCT	126	BRVO	6
Brown et al. 2014	RCT	255	BRVO	6
Haller et al. 2010	RCT	315	BRVO	6
Kuppermann et al. 2010	RCT	196	CRVO	6
Kuppermann et al. 2011	RCT	229	CRVO	12
Lowder et al. 2011	RCT	179	BRVO or CRVO	6
Schmidt-Erfurth et al. 2014	RCT	264	BRVO or CRVO	12
Varma et al. 2016	Retrospective	55	BRVO or CRVO	6
Total (weighted mean)	**Mixed**	**1,419**	**BRVO or CRVO**	**8.6**

Table 1: Characteristics of included studies
Note: RCT = randomized controlled trial; BRVO = branch retinal vein occlusion; CRVO = central retinal vein occlusion.

Outcome	Weighted Mean Difference (95% CI)	P Value
Change in Central Retinal Thickness	-183.34 μm (-221.28 to -145.40)	<0.001
Change in Best-Corrected Visual Acuity	8.56 letters (5.04 to 12.08)	<0.001

Table 1: Characteristics of included studies
Note: DEX = intravitreal dexamethasone implant; CRT = central retinal thickness; BCVA = best-corrected visual acuity.