

INPLASY PROTOCOL

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Conflicts of interest:
No conflicts of interest.

Comparison Between Ozurdex and TA as An Adjunct Drug Combined with Intravitreal anti-VEGF Treatment for Diabetic Macular Edema: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: The aim of this meta-analysis of randomized controlled trials is to evaluate the efficacy and safety of comparison between ozurdex and triamcinolone acetonide as an adjunct drug combined with intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema.

Condition being studied: This study mainly evaluate the efficacy and safety of comparison between ozurdex and TA as an adjunct drug combined with intravitreal anti-VEGF treatment for diabetic macular edema. Intravitreal injection of anti-VEGF drugs combined with glucocorticoid is widely used in clinical treatment of this disease. The main limitations are that frequent injection therapy is required to ensure the efficacy, and the commonly used TA has obvious side effects and cannot be used for a long time. Ozurdex has only been introduced into China in recent years. This paper conducted a meta-analysis on the effects of the above two glucocorticoids as adjuvant drugs in the treatment of this disease, hoping to provide a more comprehensive reference for clinical treatment in the future.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 June 2020 and was last updated on 08 June 2020 (registration number INPLASY202060027).

INTRODUCTION

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and safety of comparison between ozurdex and triamcinolone acetonide as an adjunct drug combined with intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema.

Condition being studied: This study mainly evaluate the efficacy and safety of comparison between ozurdex and TA as an adjunct drug combined with intravitreal anti-VEGF treatment for diabetic macular edema. Intravitreal injection of anti-VEGF drugs combined with glucocorticoid is widely used in clinical treatment of this disease. The main limitations are that frequent injection therapy is required to ensure the efficacy, and the commonly used TA has obvious side effects and cannot be used for a long time. Ozurdex has only been introduced into China in recent years. This paper conducted a meta-analysis on the effects of the above two glucocorticoids as adjuvant drugs in the treatment of this disease, hoping to provide a more comprehensive reference for clinical treatment in the future.

METHODS

Participant or population: Adults with T2DM (as diagnose by a clinician, after endocrinology treatment, insulin was used to control blood glucose and keep it stable) will be included.

Intervention: Ozurdex as an adjunct drug combined with intravitreal anti-VEGF treatment was the main intervention.

Comparator: TA as an adjunct drug combined with intravitreal anti-VEGF treatment was the main intervention.

Study designs to be included: Randomized clinical trials (RCTs) will be included irrespective of blinding , publication status or language.

Eligibility criteria: (1)Adults with T2DM (as diagnose by a clinician, after endocrinology treatment, insulin was used to control blood glucose and keep it stable) will be included.(2) Blood pressure is controlled within the normal range.(3) Blood lipid level was controlled within the normal range.(4) 5-15 years of diabetes history.(5) Regardless of gender, age 30 ~ 80 years old.(6) Patients diagnosed as mild or moderate NPDR according to FFA

examination.(7) Intraocular pressure is in the normal range.(8) Agree and willing to cooperate with the treatment, and sign the informed consent for the treatment.

Information sources: (1)Adults with T2DM (as diagnose by a clinician, after endocrinology treatment, insulin was used to control blood glucose and keep it stable) will be included.(2) Blood pressure is controlled within the normal range.(3) Blood lipid level was controlled within the normal range.(4) 5-15 years of diabetes history.(5) Regardless of gender, age 30 ~ 80 years old.(6) Patients diagnosed as mild or moderate NPDR according to FFA examination.(7) Intraocular pressure is in the normal range.(8) Agree and willing to cooperate with the treatment, and sign the informed consent for the treatment. 17. Information sources We will search articles in three electronic database including PubMed, EMBASE and Cochrane Library. All the English publications until 5 June 2020 will be searched without any restriction of countries or article type.Reference list of all selected articles will independently screened to identify additional studies left out in the initial search.

Main outcome(s): Main outcomes of this study are to compare to between ozurdex and triamcinolone acetonide as an adjunct drug combined with intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema.Observing the disease progression, changes in patients' visual acuity, changes in macular center thickness, changes in VEGF and inflammatory factors in the eye, and changes in the number of intravitreal injections in the two groups.

Quality assessment / Risk of bias analysis: Main outcomes of this study are to compare to between ozurdex and triamcinolone acetonide as an adjunct drug combined with intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema.Observing the disease progression, changes in patients' visual acuity, changes in macular center thickness, changes in VEGF and

inflammatory factors in the eye, and changes in the number of intravitreal injections in the two groups. 21. Quality assessment /Risk of bias analysis Two reviewers will independently assesses the quality of the selected studies according to the Cochrane Collaboration's tool for randomized controlled trials. Items will be evaluated in three categories: Low risk of bias, unclear bias and high risk of bias. The following characteristics will be evaluated: Random sequence generation (selection bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other biases Results from these questions will be graphed and assessed using Review Manager 5.3.

Strategy of data synthesis: Risk ratio (rr) for both fixed and random effects models (weighting by inverse of variance) will be used. A continuity correction will also be used for cells with zero values. Between-study heterogeneity will be assessed using the t^2 , x^2 (Cochran Q) and I² statistics. According to the Cochrane handbook, the will be considered non-important (< 30%), moderate (30%-60%) and substantial (>60%). Results will be assessed using forest plots and presented as RRs for the main outcome and secondary outcomes. An influence analysis will be performed to ascertain the results of the meta-analysis by excluding each of the individual studies. Publication bias will be assessed by a funnel plot for meta-analysis and quantified by the Egger method. Statistical analysis will be conducted using STATA software for Mac V15.0 (Stata Corp., College Station, Texas) [module "meta"] and R studio v1.0.136 (The Foundation for Statistical Computing) [package "meta v4.2"] .

Subgroup analysis: We will consider subgroups such as jurisdiction, clinic type, and location(rural /urban).

Sensibility analysis: Two authors will independently extract data. Any disagreement will be resolved by discussion until consensus is reached or by consulting a third author.

Keywords: triamcinolone acetonide; anti-VEGF; ozurdex; DME.

Contributions of each author:

Author 1 - Tianhua Piao.

Author 2 - Hongyang Ma.

Author 3 - Rui Wang.