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The association between diabetes, level of glycaemic control and eye infection: Cohort database study

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ABSTRACT

Aim: To examine whether diabetes and the degree of glycaemic control is associated with an increased risk of acute eye infection, and prescribing of ocular antimicrobial agents.

Design and setting: A retrospective cohort study was carried out using the Royal College of General Practitioners Research and Surveillance Centre database (RCGP RSC), a large primary care database in the United Kingdom. We compared ocular infection rates in people aged ≥15 years without diabetes to those with diabetes, both type 1 and type 2. We developed logistic regression models to assess the excess risk in diabetes of: conjunctivitis, blepharitis, stye/chalzion, periorbital cellulitis, keratitis/keratoconjunctivitis, lacrimal gland infection, endopthalmitis, and ocular antimicrobial prescriptions over a six-year period (2010–2015). We also analysed the impact of glycaemic control on infection rates in those with diabetes. All models were adjusted for potential confounders.

Results: We analysed infection risk in 889,856 people without diabetes and 48,584 people with diabetes (3273 type 1, and 45,311 type 2). After adjustment for confounders both type 1 and type 2 were associated with increased incidence of conjunctivitis (OR 1.61; 95% CI 1.38–1.88; $p < 0.0001$ and OR 1.11; 95% CI 1.06–1.16; $p < 0.0001$ respectively). No association was found with blepharitis, stye/chalzion, periorbital cellulitis, keratitis/keratoconjunctivitis, lacrimal gland infection, and endopthalmitis in the whole population. In subgroup analyses blepharitis was more common in those with type 1 diabetes under 50 years old and endopthalmitis in those under 50 with type 2 diabetes. Glycaemic control was not found to be associated with any infection. Diabetes was also associated with an increased incidence of antimicrobial prescriptions (Type 1 OR 1.69; 95% CI 1.51–1.88; $p < 0.0001$ and type 2 OR 1.17; 95% CI 1.13–1.20; $p < 0.0001$).

Conclusions: Conjunctivitis is recorded more frequently in people with diabetes. However, no substantial increase in recording of other ocular infections was noted. Infection risk was not found to be associated with the degree of glycaemic control.

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1. Introduction

Research into the ocular manifestations of diabetes has focused on management of diabetic retinopathy and maculopathy due to the risk of proliferative retinal disease leading to blindness [1]. Ocular infections however also pose a significant challenge for this population, affecting quality of life and contributing to a significant number of healthcare visits in both primary and secondary care [1].

Bacterial, fungal, and viral infections can affect a number of structures of the eyes. Infections of the eyelids, nasolacrimal duct, conjunctiva, corneal surface, and infectious keratitis have all been suggested to occur more frequently in people with diabetes [2–7]. However, there is a paucity of systematically collected data to support these assertions. There is even more uncertainty about the role of glycaemic control in ocular infection risk. A recent review of observational studies and clinical trials demonstrated a correlation between poor glycaemic control and increased risk of a wide variety of infections in people with diabetes [8]. This review identified only one small scale study ($n = 328$) carried out to determine the association between glycaemic control and superficial eye infections [9]. The authors found no significant relationship. Other studies have discussed poor glycaemic control as a possible risk factor for infectious conjunctivitis: conclusions have been limited by small sample size and limited measurements of glycaemic control [9,10].

Managing eye infections represents a significant health service workload despite the low morbidity of the conditions. Almost 1% of all primary care consultations are due to conjunctivitis [11,12], with more than five million episodes annually in the United States and 1 million in the United Kingdom [12]. Identification of modifiable risk factors for eye infections could therefore provide targets for reduction of this disease burden.

We explored whether infectious disease affecting the external eye and surrounding structures is associated with diabetes, and if poor glycaemic control increases risk of ocular infection in the population with diabetes. We hypothesised the following:

- People with diabetes have a higher frequency of ocular infections than those without diabetes.
- People with diabetes and poor glycaemic control have a higher number of ocular infections than those with diabetes and good glycaemic control.

2. Methods

We performed a two stranded study using data from the Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) database; a large UK based primary care cohort. The two study strands comprised; (1) a whole population cohort study to investigate the frequency of eye infections in people with diabetes compared to those without diabetes, and (2) a diabetes only population cohort study to investigate the impact of glycaemic control on eye infection rates in people with diabetes. We explored a wide range of infections of the eye and surrounding structures; conjunctivitis, blepharitis, stye/chalzion, periorbital cellulitis, keratitis/keratoconjunctivitis, lacrimal gland infection, endopthalmitis, ocular infection prescriptions, and all eye infections combined.

2.1. Data source

The RCGP RSC database comprises electronic patient records collated from a network of over 100 GP practices distributed across England containing over 1 million patient records. The characteristics of the RCGP-RSC population and participating practices have been recently described elsewhere [13]. Coded information for diagnostic, prescription, demographic and biochemical data is recorded in the database.

2.2. Study population and definition of variables

The study period for analysis of infection events was defined as the 5-year period between 1st January 2010 and 31st December 2015. All individuals aged ≥15 years who were registered with an RCGP RSC practice on 31st December 2015 were included for analysis. Patients in which the type of diabetes could not be determined were excluded from the analysis.

Clinical codes (Read version 2) and codes for medication use (EMIS codes in the RCGP RSC database) were used to determine patient characteristics and conditions, as these were the code types used by the participating practices. Diabetes was identified using recorded diabetes diagnosis codes, codes for diabetes clinical review, diabetes medication codes (oral hypoglycaemic agents, excluding metformin, and injectable agents), and laboratory results (two or more HbA1c values consistent with diabetes, or two or more blood glucose measurements consistent with diabetes, and depending on test provenance; fasting, random, glucose tolerance test, etc.) [14]. Other potential predictor variables for risk of eye infections were also extracted from coded data and included; age, gender, ethnicity, smoking status, body mass index (BMI), deprivation quintile, and the presence of connective tissue disorders. Age was defined as that at beginning of study period. Smoking status was categorised as current smoker, ex-smoker or never smoked and BMI as <18.5, 18.5–25, 25–30, and >30 kgm^{-2}. Ethnicity was categorised as Asian, Black, Mixed, White and other ethnic group, as per Office for National Statistics and Public Health England classification [15,16]. Where multiple values for the variable of interest were recorded the value nearest to the start of the follow up (1st January 2010) was used. Where information on the variable of interest was missing, people were categorised as 'not recorded' rather than excluded from the analysis. We have previously demonstrated that missing data can be correlated with outcomes in people with diabetes [17], and therefore this was our preferred approach to missing data.

Ocular infections investigated comprised conjunctivitis, blepharitis, stye/chalzion, periorbital cellulitis, keratitis/keratoconjunctivitis, lacrimal gland infection, and endopthalmitis. We also investigated the outcome measure of prescriptions for acute infectious ocular disease, all eye infections combined, and all eye infections excluding conjunctivitis (a post hoc group added during peer review). A final group

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