Drug-induced corneal disorders

Some disorders of the cornea can be caused by medication use, including not just topical agents (such as eye drops) but also systemic drugs.

Topical agents, such as eye drops containing antibiotics, corticosteroids and NSAIDs can cause keratitis, ulcers, corneal perforations, or corneal tissue degradation. These side-effects can cause painful, red or watery eyes, or visual problems (such as reduced visual acuity). It is important to note that the information about these side-effects derives from studies providing relatively low levels of research evidence, such as case series, cross-sectional studies or retrospective chart reviews, mostly conducted in secondary care settings among patients who had previously been treated by, or had been referred to, an ophthalmologist. These study types are subject to various kinds of bias. For instance, it is impossible to decide whether the ulcer or perforation was caused by the disease or infection or by the drug that was used to treat it. Glaucoma medications can also cause corneal disorders, such as keratitis punctata (beta-blockers), oedema (carbonic anhydrase inhibitors) or recurrent herpes simplex keratitis (prostaglandin analogues). Another potential source of side-effects is the preservative used in the eye drops, as preservatives often cause hypersensitivity reactions. In such cases, patients may be prescribed a preparation with a different preservative or without preservative.

A number of systemic agents can cause corneal depositions (cornea verticillata). Only a few of the drug information leaflets for these agents warn doctors and pharmacists about this risk. The agents for which the scientific literature provides the most convincing evidence that they may cause corneal depositions include amiodarone, chlorpromazine, chloroquine and tamoxifen. Corneal depositions do not always cause visual complaints, and treatment is only necessary when such complaints do occur. Hence, active detection is unnecessary. Although some case series did involve routine screening for depositions, there are also examples where the deposition was discovered by accident. This side-effect often depends on the dosage and the duration of use, and usually resolves after the patients stop using the drug. Other systemic drugs that may cause corneal disorders, including ulcers and perforations, are oncolytics (e.g. cytarabine and epidermal growth factor receptor (EGFR) inhibitors), isotretinoin, nicorandil, NSAIDs and rifabutin. Data on these systemic drugs are also often derived from studies providing lower-level evidence, often from case series, and sometimes even only from anecdotal reports. Evidence from cohort or case-control studies that is suitable for the monitoring of side-effects, especially rare ones, is largely lacking.

If a patient presents with symptoms that suggest corneal disorders, the doctor should take the possible role of medication into account. If it seems likely that it involves a side-effect, the doctor may consider reducing the dosage or terminating the use of the drug, in consultation with the prescribing doctor. Whether this is advisable depends on aspects like the severity and nature of the symptoms (a deposition that does not cause any symptoms does not require any measures) and on the indication for which the suspected medication is being used. Doctors and pharmacist should report such side-effects to the adverse effects reporting centres. It is as yet not well possible to check a particular side-effect on the website of the Netherlands Pharmacovigilance Foundation (Lareb) to see for which drugs that particular side-effect has been reported.

**References**

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*The literature refers to the Dutch text