Ocular Adverse Effects of Neuropsychiatric Agents
Incidence and Management

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Summary

Neuropsychiatric agents may adversely affect the eye in various ways. The more frequently encountered effects include corneal oedema and pigmentary changes in the lens and cornea which are induced by phenothiazine derivatives; thioridazine-induced retinopathy; tricyclic antidepressant–induced accommodation interference and glaucoma; and lithium carbonate–induced exophthalmos and papilloedema. Several adverse effects, such as corneal oedema, retinopathy and glaucoma, are vision-threatening, and patients often fail to describe their symptoms properly. A more precise understanding of these conditions is essential for prompt diagnosis and appropriate treatment.

Neuropsychiatric agents have a high therapeutic index and are generally considered to have a favourable risk-benefit ratio. However, ocular adverse effects, including pigmentary changes of the cornea and the crystalline lens, keratopathy, retinopathy, cycloplegia and glaucoma, are occasionally observed. Since psychiatric patients are frequently under prolonged treatment with neuropsychiatric agents, and often fail to describe their ocular symptoms adequately and promptly, a precise understanding of the possible adverse effects is a requisite for physicians practising in psychiatry, neurology and ophthalmology, to avoid unnecessary delays in treatment.

This article reviews several ocular adverse effects of neuropsychiatric agents and discusses their management. Basic structures of the eye are illustrated in figure 1.

1. Pigmentary Deposits in the Lens and Cornea

Pigmentary deposits in the lens and cornea are common among patients who have received prolonged
and intensive therapy with phenothiazine derivatives (chlorpromazine,[1-6] fluphenazine[7,8] and levomepromazine[9,10]). Thioridazine is not believed to produce these pigmentary changes.[11]

Pigmentary deposits in the lens can vary from fine, dot-like opacities on the anterior lens surface to a central, pearl-like, opaque mass surrounded by smaller clumps of pigment. Corneal pigmentary changes appear within the deepest stroma adjacent to Descemet’s membrane and endothelium, primarily in the palpebral fissure area. These changes occur almost invariably in patients who already have lenticular pigmentation. Pigmentary changes in the lens and the cornea are usually localised, and should be observable with a slit-lamp microscope. In some cases, the deposits eventually become heavy enough to be apparent on close inspection with a focused light without microscopy.[12]

These pigmentary deposits in the anterior segment of the eye rarely interfere with visual acuity,[13] but patients may occasionally report glare, halos around lights or hazy vision. There have been several reports of cases of reduced visual acuity in association with chlorpromazine pigmentation.[14-18] Active treatment of this condition (e.g. with pencycillamine) has not been helpful.

Clinical evidence has accumulated which suggests that pigmentary deposits in the lens do not lead to the formation of ordinary cataracts[6,13] (a cataract is defined as a cloudiness of the crystalline lens which prevents a clear image from forming on the retina). On the other hand, Isaac et al.[19] reported that patients who were exposed to phenothiazines for 2 to 5 years prior to cataract surgery were 3.5 times more likely to require cataract extraction than patients not exposed to these agents. The explanation for this difference remains unclear.

Granular deposits in the lens and cornea are thought to be similar to epidermal deposits which cause noticeable discoloration of the skin in some patients. The deposits tend to disappear spontaneously, although slowly, following discontinuation of the phenothiazine, but in many cases they appear to remain indefinitely.[12]

The exact mechanism of pigmentary deposit formation is unknown. The predominance of changes in the palpebral fissure and the association in some patients with photosensitisation of the skin by chlorpromazine suggest that exposure to light may be a factor in producing the deposits. In a patient who had drooping of 1 upper eyelid which shaded the eye, the deposits were less dense in that eye than in the other eye with a normal lid.[20] There have been several experimental studies which support the relationship between light and phenothiazine-induced anterior segment pigmentation,[21-24] but others have not.[25-27]

Critical dosages to provoke lens deposits have been reported to be not less than 300 mg/day for over 3 years[11] or a total of not less than 500g for chlorpromazine,[28] and over 200 mg/day for levomepromazine.[9]

No treatments have yet been established for pigmentary deposits in the lens and cornea. Suggested preventive measures include: (a) avoiding over-administration of antipsychotic agents; (b) administering drugs other than chlorpromazine; (c) wearing sunglasses and protecting the eyes from sunlight; and (d) installing ultraviolet-blocking window panes.[29]

2. Keratopathy

The term keratopathy refers to any pathological condition of the cornea. This section discusses abnormalities other than pigmentary deposits, described in section 1.