Ten months later the patient developed blepharoconjunctivitis and eczema of the right upper eyelid, which responded to 1% hydrocortisone cream. The ocular pressure of the right eye remained elevated at 26 mmHg and inferior angle laser trabeculoplasty was performed in December 1996. The IOPs were controlled until he presented with blurred vision and ocular discomfort in December 1997.

Visual acuities were 6/18 right eye and 6/6 left eye and IOPs measured 60 mmHg right eye and 26 mmHg left eye. The right cornea was mildly oedematous. Both eyes had a ciliary flush, anterior chamber cells and multiple medium-sized keratic precipitates. The anterior chamber angles were wide open. Metipranolol and dorzolamide were stopped and the patient was treated with intravenous acetazolamide, oral acetazolamide, apraclonidine 1% q.d.s., Minims prednisolone 0.5% 2-hourly and indomethacin 75 mg b.d. The uveitis and ocular pressures responded to treatment and 1 week later the IOPs were 18 mmHg right eye and 10 mmHg left eye. The ocular pressures are currently controlled with betaxolol HCl suspension 0.25% b.d. and latanoprost once daily.

Comment

The ocular findings in our patient were consistent with those of previously reported adverse drug reactions associated with metipranolol.[1–3] Dorzolamide drops were also being administered to both eyes at the time of presentation, but to our knowledge there have been no reported cases of granulomatous anterior uveitis associated with dorzolamide. Melles and Wong[2] described two patients, on metipranolol therapy who developed granulomatous anterior uveitis within a few months after argon laser trabeculoplasty. It was thought that the intraocular inflammation normally associated with laser trabeculoplasy sensitised these patients to the effects of metipranolol. This could explain why the uveitis was more severe in the right eye of our patient following argon laser trabeculoplasty to this eye.

Akingbehin and Villada[4] found that there was a significant elevation in IOP (>5 mmHg) in 45 of 78 (58%) different recorded episodes of metipranolol-induced adverse drug reactions. The marked elevation of IOP in the right eye of our patient was the most alarming sign in this case. Fortunately, there was rapid recovery of IOP control when metipranolol was discontinued and alternative antiglaucoma agents were used. In our patient the anterior uveitis in combination with an already compromised trabecular meshwork could have been responsible for the secondary elevation in IOP. Akingbehin and Villada[4] have suggested that the active drug, metipranolol, itself probably causes changes in the trabecular meshwork which can lead to elevation of IOP.

The adverse drug reactions reported thus far have been related to the use of multidose metipranolol.[1–5] O'Connor[5] has suggested that the gamma irradiation used to sterilise the multidose bottles may lead to free radical production with oxidative tissue damage and intraocular inflammation. The 0.3% and 0.1% Minims solutions of metipranolol are distributed in plastic containers not sterilised by gamma irradiation and are still approved for sale in the UK. To our knowledge there have been no reports of anterior uveitis associated with Minims metipranolol. This case suggests that the active drug is involved in the pathophysiology of the adverse drug reactions.

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Sir,

Adverse ocular effects following influenza vaccination

The influenza vaccination is one of the widely distributed vaccines in the population, particularly among the elderly and high-risk individuals. Its safety has been demonstrated in numerous studies. Adverse ocular effects following influenza vaccination are seldom reported. We hereby report on a series of three consecutive patients with severe ocular complications, manifesting in close association with the 1996–7 season influenza vaccination. All three had received the trivalent influenza vaccine prepared according to the recommendations of the CDC, including A/Texas/36/91-like (H1N1), A/Wuhan/359/95-like (H3N2) and B/Beijing/184/93-like haemagglutinin antigens.

Case reports

Case 1. In November 1996, a 41-year-old military officer was referred to the eye clinics at the Hadassah University Hospital because of a red and painful left eye. He was in good general health, and had received vaccination for influenza 2 weeks previously, as part of a vaccination programme in the military. On examination, his visual acuity was 20/20 in both eyes. In the left eye he had a follicular reaction in the lower fornix, keratic precipitates,

and in the anterior chamber there was flare (+1) and cells (+1). He was treated with topical 0.1% dexamethasone phosphate and 1% cyclopentolate three times daily, for a period of 12 days. During that period the anterior chamber reaction gradually subsided, and the treatment was tapered down. At his final examination he had few keratic precipitates, the eye was quiet, and the visual acuity remained 20/20.

Case 2. A 72-year-old woman received an influenza vaccination in October 1996. Seventy-two hours later she started complaining of a stinging sensation and redness in her right eye. After 4 days the patient was admitted to our department due to a decrease in the visual acuity in her right eye. The patient had a history of herpes stromal keratitis, inactive for more than 30 years. On examination, the right eye visual acuity was 20/300. There was ciliary injection, mild anterior chamber reaction, a central dendritic corneal ulcer, stromal oedema with keratic precipitates, and corneal scarring with vascularisation. Treatment with topical and systemic acyclovir was begun. The dendritic defect disappeared after 2 days, and topical 0.1% dexamethasone phosphate was started three times daily. A week later the anterior chamber reaction disappeared, and a central 1.5 × 1.0 mm corneal trophic ulcer was epithelialised within the next 4 days with the help of a soft contact lens. The oral acyclovir was stopped, and the local corticosteroids were gradually tapered down over the next few weeks. She recovered visual acuity of 20/100.

Case 3. A 74-year-old diabetic man had a history of perforating keratoplasty in his left eye due to pseudophakic bullous keratopathy in 1994. His best corrected visual acuity in the left eye was 20/45. The corneal graft was clear. In October 1996 he received an influenza vaccination. One month later he was referred to our eye clinic because of a red left eye with a decrease in visual acuity. His visual acuity was 20/80. Slit-lamp examination of the left eye revealed corneal stromal oedema with subepithelial infiltrates in the corneal graft, and keratic precipitates with inflammatory cells (+1) in the anterior chamber. A diagnosis of left eye corneal graft rejection was made. The patient received oral meticorten 60 mg daily, topical 0.1% dexamethasone phosphate hourly, and a periocular injection of 20 mg of methylprednisolone acetate. During the following 9 days the stromal oedema and keratic precipitates disappeared, and the intraocular inflammation subsided. The graft had cleared by the final examination.

Comment

Adverse ocular effects following influenza vaccination have been reported previously, including uveitis,[1] optic neuritis,[2] orbital myositis with posterior scleritis,[3] and corneal graft rejection occurring 3 to 8 weeks following influenza vaccination in four patients.[4]

We have treated four patients who had ocular manifestations following influenza vaccination. One case of bilateral corneal graft rejection was previously reported,[5] and three cases are reported in this paper. All had sight-threatening events in close association with the administration of influenza vaccination. The time intervals between the vaccination and the eye disease were 3 days to 6 weeks – similar to the previously reported cases. Two of these three patients probably had a reactivation of the immune system followed by anterior uveitis (case 1) and corneal graft rejection (case 3). The third patient presented epithelial and stromal herpetic keratouveitis (case 2).

To the best of our knowledge, this is the first report of vaccination-related herpetic recurrence. Definite laboratory evidence for the association between vaccination and the clinical manifestations is not available currently. However, the time interval between vaccination and the ocular adverse manifestations suggests a cause-and-effect relation.

We believe that adverse ocular effects of vaccines in general are far more prevalent than reported in the literature. Awareness of the possible eye responses following vaccinations, particularly during the season of influenza vaccination, is warranted. Caution is advised when administering the vaccine to patients who have had a corneal transplant.

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