Microbial Contamination of In-Use Ocular Medications


Abstract

Two hundred twenty in-use medications from 101 patients with non-microbial ocular surface disease were studied by sterile culture of the bottle caps, a drop produced by simple inversion, and the interior contents. Conjunctival cultures were taken from these patients and 50 aged-matched controls. Pathogenic organisms were harvested from conjunctivae significantly more frequently (p < 0.01) from cases (34%) than from controls (10%). Twenty-nine percent of medications had microorganisms cultured from at least one medication site. Gram negative organisms were significantly more likely (p < 0.00001) to be isolated from all medication sites than gram positive organisms. Forty-nine percent of the gram negatives, but none of the pathogenic gram positives (p < 0.01), isolated from the conjunctivae were also found in the drops of their associated medications. We conclude that this cycle of contamination between in-use medications and conjunctivae may represent an important risk factor for microbial keratitis in patients with ocular surface disease.

Introduction

Microbial keratitis, except in the specific setting of soft contact lens wear, is predominantly associated with gram positive organisms, principally staphylococci and streptococci that are prevalent on the eyelids and conjunctiva and that opportunistically invade the corneal stroma through breaks in the epithelium [1]. Yet, in a recent extensive review of microbial keratitis at the Massachusetts Eye & Ear Infirmary, among the corneal ulcers not related to contact lens wear, gram negative organisms accounted for one-third of cases [2]. The origin of these gram negative organisms was not usually evident. Moreover, Schein and associates have recently collected 7 cases of severe gram negative keratitis where the same organism was cultured from both the cornea and the topical ocular medications concurrently in use by these patients [3]. In all instances, antibiograms by Kirby-Bauer disc sensitivities were identical for the corneal and topical medication isolates. Importantly, 6 positive cultures were from timolol maleate and one from prednisone acetate.
Examples from this case series include a 75 year-old woman with longstanding angle closure glaucoma and bullous keratopathy who developed *Pseudomonas* corneoscleritis eventually requiring enucleation, and a patient with aphakic bullous keratopathy who also developed *Pseudomonas* corneoscleritis resulting in light perception vision. Disasters such as these highlight *Pseudomonas aeruginosa* as a major contaminant of ocular medications.

Templeton reported 3 cases of *Serratia marcescens* keratitis in 1982, where the organism was recovered from either the inside of the eyedropper cap or from the grooves of the bottle top [4]. Solutions cultured directly from the medication bottles were sterile. Marion and Tapert uncovered significant growth of pathogens from the outside and inside of approximately one-third of timolol maleate bottles in a glaucoma clinic population [5].

The origin of these bacteria remains obscure. While it might be argued that it is actually the ocular surface which harbors the bacterial microorganisms and contaminates the eye drops, in fact pseudomonal colonization of the conjunctiva is infrequent (1% or less) and *Serratia* and *Proteus* are even more unusual in this setting [6, 7]. *Pseudomonas* and *Serratia* do not normally inhabit the skin. However both are commonly found in foodstuffs and in kitchens [8, 9]. *Pseudomonas* in particular has a predilection for moist environments like kitchens and bathrooms and has been cultured repeatedly from water supplies and faucets [10]. Hence it is perhaps not surprising that medications and contact lens solutions kept weeks at a time in a bathroom environment become contaminated with *Pseudomonas*.

The foregoing experiences heightened our concern about the source of these virulent gram negative organisms. Therefore we performed a prospective study to examine the bacteriology of the conjunctiva of patients using topical medications in comparison with controls using no medications in order: (1) to investigate the bacteriology and rate of contamination of in-use medications obtained from these patients, and (2) to determine the risk factors for contamination of topical medications.

**Materials and Methods**

The study involved 101 patients with noninfectious ocular surface diseases (49 unilateral, 52 bilateral) who had used topical medications for more than 2 months. Control subjects comprised 50 age-matched individuals not using medication. Conjunctival cultures were obtained from the retracted lower lid with a moistened cotton swab. The medications were cultured as follows: (1) a swab of the inside surface of the cap, (2) one drop from the bottle allowed to fall on the culture media, and (3) contents withdrawn steriley with a syringe. Multiple media were used for each culture and growth on one or more solid media (except for anaerobes) was required for a culture to be considered positive. Concordance was defined as the same organisms being isolated from the conjunctiva and from the medications applied to that conjunctiva.