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Systemic effects of topical ophthalmic preparations

Ophthalmic medications are used for a number of conditions such as glaucoma, infection, allergy and inflammation, often on a chronic basis. Generally the drugs used in this manner have good safety profiles, but they do have the potential to cause significant adverse drug events, and can interact with other systemic medications.

The pharmacokinetic profile associated with ocular drug delivery resembles that of intravenous administration more closely than that of oral administration. Ophthalmic medications pass through the lacrimal sac and have access to the highly vascular nasal mucosa. Drugs are variably absorbed from this site, but importantly they avoid first-pass hepatic metabolism. This can be important for drugs that undergo a high degree first-pass metabolism, such as timolol. One drop of a 0.5% solution of timolol in each eye is approximately equivalent to a 10mg oral dose of the drug.

Beta-blockers administered as eye drops may aggravate a number of co-morbidities. Examples include bronchospasm in asthma/COPD patients, aggravation of heart failure or bradyarrhythmias, and even depression. In glaucoma patients, the use of beta-blocker eye drops has been rated as the most significant cause of falls.

Parasympathomimetics such as pilocarpine may cause hypotension, bradycardia, bronchospasm, GI symptoms and urinary frequency. Topical carbonic anhydrase inhibitors are not associated with any systemic adverse affects, apart from idiosyncratic bone marrow suppression and sulphonamide allergy. While topical prostaglandin analogues have not been associated with cardiovascular or respiratory side effects, they have been associated with headache, flu-like symptoms and myalgia in about 10% of patients.

The possibility of drug interactions should also be considered. Concurrent use of topical and systemic beta-blockers has been known to reduce heart rate in patients, while the concurrent use of oral verapamil has caused severe bradycardia. In Australia about 20,000 patients a year are exposed to co-supply of topical and systemic beta-blockers. Optometrists in a number of countries have prescribing rights for these medications independent of medical supervision, making a thorough assessment of the above issues more difficult. Further to this some, clinicians may not consider that topical therapy can have systemic implications, and patients may fail to mention eye drops when asked about their medications.

The systemic absorption of ophthalmic medication can be minimised using the “double DOT” technique (Don’t Open Eyes Technique and Digital Occlusion of the Tear duct). This involves closing the eyes and applying pressure with the finger over the lacrimal sac (outside corner of the eye) for 1-2 minutes. This can reduce systemic absorption by up to 70%, thus decreasing the likelihood of significant systemic absorption. Topical ophthalmic preparations should always be considered as a possible cause of systemic side effects or drug interactions.

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