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Title: PHARMACOKINETICS OF OXYBUTYNIN AND N-DESETHYL OXYBUTYNIN FOLLOWING ORAL AND INTRAVESICAL OXYBUTYNIN

Aims Of Study:

To evaluate the urodynamic effects, and the pharmacokinetics/dynamics of oxybutynin (OXY) and N-desethyl oxybutynin (DEOB) following oral and intravesical (IVe) administration of OXY.

Methods:

Twelve patients with detrusor hyperreflexia unresponsive to standard anticholinergic regimens were administered oxybutynin 5 mg orally, 15 mg IVe with passive diffusion and 15 mg IVe with 15 mA electric current. Urodynamic monitoring, plasma profiles of OXY and DEOB over 8 hours, and IVe uptake of OXY were assessed following each administration mode.

Results:

Oral OXY induced no urodynamic improvement, resulted in conventional plasma profiles of OXY and DEOB with an area under curve (AUC) ratio DEOB/OXY = 11/1 and combined AUC DEOB + OXY = 16297 ng/8h; anticholinergic side effects occurred in 8/12 patients. Passive diffusion OXY resulted in ~ 12 mg IVe uptake, improvement in 3/8 urodynamic measurements, an AUC ratio DEOB/OXY = 1.2/1 and combined AUC = 2123 ng/8h. Electromotive OXY resulted in almost complete IVe uptake (15 mg), caused significant improvement in 8/8 urodynamic measurements, demonstrated a DEOB/OXY ratio = 1/1.4 and a combined AUC = 4574 ng/8h. All comparable differences are highly significant. Both IVe techniques resulted in unique biphasic plasma OXY profiles; neither IVe administration caused side effects.

Conclusions:

A large proportion of intravesical oxybutynin is sequestered, probably in the urothelium, and intravesical oxybutynin administration confers therapeutic benefits via a localized direct action on detrusor receptors.

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