

to enhance meniscal healing.⁴³

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DRUG PROFILE

Naftopidil

Background: In the past Alpha- AR blockers were mainly used as anti hypertensive agents. Around 1980, prazosin was introduced in quinazoline group which are selective α_1 receptor blocker. During various scientific studies the effectiveness of α_1 - AR blocker on BPH was discovered but major limitation of their applications are prominent first dose hypotension. Tamsulosin was introduced which is uro selective α_1A - receptors blocker. There are less episodes of postural hypotension with tamsulosin as compared to old α_1 -AR blockers. Around 1990, Naftopidil was developed as a novel anti hypertensive agents but failed to show satisfactory effects on blood pressure. Later on various molecular studies proved that Naftopidil is a $\alpha_1D/1A$ receptors blocker useful in patients of BPH. **Pharmacodynamics: Uroselectivity:** Naftopidil was found to be more potent for the $V1D$ - adrenoreceptor (AR) than for other $V1$ -AR subtypes. It has approximately 17 fold higher selectivity for the $V1D$ -AR than for the $V1b$ subtypes so it has fewer effects on peripheral blood vessels and less chance of postural hypotension and dizziness. Alpha 1- adrenoreceptors in the urethral smooth muscle are mainly the α_1A subtype. Naftopidil has a high affinity for α_1D -AR, which is used for the treatment of LUTS associated with BPH; Naftopidil is assumed to improve urinary flow by relieving urethral pressure, which is elevated by the sympathetic nervous system, because it antagonistically suppresses the noradrenaline- induced contraction of human prostatic urethral smooth muscle. **Pharmacokinetics:** After oral administration 80%-90% dose is rapidly absorbed. The absolute bioavailability is approximately 17-20% after oral administration of 50 mg Naftopidil. The time to peak plasma concentration is approximately 0.5-1 hour post dose. If Naftopidil is given on full stomach time to peak plasma concentration is delayed but no effect on absorption and bioavailability. The steady state volume distribution (VD) of Naftopidil is 2-3.3 l/kg; plasma protein binding ranges from 70-90%. After hydroxylation in liver which yields two active metabolites 1) (phenyl) hydroxyl- naftopidil (PHN), 2) (naphthyl 1) hydroxynaftopidil (NHN). The metabolic conversion of Naftopidil is primarily consists of conjugation with glucuronidate and sulphate, whereas hydroxylation, demethylation and ether cleavage are less prominent. The pharmacological inactive metabolites of Naftopidil are mainly eliminated in urine. While pharmacologically active metabolites (PHN, NHN) are excreted in faeces. The renal clearance rate of Naftopidil is 9-11 ml/min/kg. **Indication:** Naftopidil is indicated in the treatment of BPH associated with lower urinary tract symptoms. **Dose and Administration:** The recommended dose of Naftopidil is 50mg once in a day. The dose adjustment is necessary in patients with liver impairment; no dose adjustments is needed in patients receiving hemodialysis. Adverse Effects include dizziness, abnormal ejaculation and, less frequently headache, asthenia, postural hypotension, palpitations and rhinitis. Nausea, vomiting diarrhoea, and constipation can occasionally occur. Hypersensitivity reactions syncope has been reported rarely. **Drug Interactions:** Antihypertensive medication and nitrates: Co administration causes increased risk of hypotension/postural syncope.