

major benefit of Danazol is that it sustains partial remission and allows lower doses of steroids. *Cytotoxic immunosuppressants* (azathioprine, cyclophosphamide) have been used in refractory cytopenias⁴. The major indications being disease of months duration and contraindication for splenectomy in patients unresponsive to steroids. The disadvantage is that therapeutic response is slow to achieve (2-4 months), response rate is about 50% and associated side effects are well known. Vincristine has important role in refractory conditions as it achieves therapeutic response within several days. However, response lasts only a few days to weeks, as happened in our patients.

Various treatment modalities have been suggested for Evans' syndrome. In view of high relapse rate after splenectomy, medical treatment with multiagents i.e., IVIG, steroids, vincristine, Danazol and possibly cyclosporin has been advocated⁵. There have been reports in literature regarding the efficacy of cyclosporin in refractory Evans' syndrome. Cyclosporin appears as a salvage treatment in life threatening resistant autoimmune hematological diseases^{2,5}. Splenectomy was not considered in our patient because of lack of families consent and well known disadvantages like high relapse rate, procedure related morbidity and mortality and overwhelming

postsplenectomy infection (OPSI).

Hence Evans' syndrome unresponsive to steroids can be a challenging proposition. Situation becomes more complex, when IVIG fails to produce platelet rise. At this stage multiagent treatment modalities need to be used in such life threatening situations.

References

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Drug Profile

Alfuzosin

Alfuzosin is a selective alpha 1 adrenoreceptor antagonist. It distributes preferentially in the prostate compared to plasma and decreases the prostatic smooth muscle tone.

Mechanism of Action : The symptoms associated with benign prostatic hyperplasia (BPH) such as urinary frequency, nocturia, weak stream, hesitancy and incomplete emptying are related to two components, anatomical (static) and functional (dynamic). The smooth muscle tone is regulated by Alpha(x) - adrenergic receptors. Alfuzosin exhibits selectivity for alpha adrenergic receptors in the lower urinary tract. Blockade of these adrenoreceptors can cause smooth muscle in the bladder neck and prostate to relax, resulting in an improvement in urine flow and a reduction in symptoms of BPH. It is a selective antagonist of post-synaptic alpha adrenoreceptors, which are located in prostate, bladder neck, prostate capsule and prostate urethra.

Pharmacokinetics : Absolute bioavailability of Alfuzosin 10mg under basal conditions is 49%. Following multiple dosing of 10mg Alfuzosin lead to maximum concentration is 9 hours. It is moderately bound to human plasma proteins (82 to 90%). It undergoes extensive metabolism by the liver; it is metabolized by three metabolic pathways: oxidation, O-demethylation, and N-dealkylation CYP3A4 is the principal hepatic enzyme isoform involved in its metabolism. It is excreted 69% in feces and only 11% of the administered dose is excreted unchanged in urine. Half life is 10 hours. The extent of absorption is 50% under fasting conditions' therefore, alfuzosin should be taken immediately following a meal.

Indications : It is indicated for the treatment of the signs and

symptoms of benign prostatic hyperplasia.

Dosage and administration : Recommended dose is 10mg daily to be taken immediately after the same meal each day.

Precautions : (i) Carcinoma of the prostate and BPH cause many of the same symptoms. These two diseases frequently coexist. Therefore patients thought to have BPH should be examined prior to starting therapy with alfuzosin to rule out the presence of carcinoma of prostate. (ii) **Drug Interactions :** Pharmacokinetic and pharmacodynamic interactions between alfuzosin and other alpha blockers have not been determined. However' interactions may be expected and alfuzosin should not be used in combination with other alpha blockers. (iii) **Coronary insufficiency :** If symptoms of angina pectoris appear or worsen' alfuzosin should be discontinued. (iv) **Hepatic insufficiency :** It should not be given to patients with moderate or severe hepatic insufficiency. (v) **Renal insufficiency :** Systemic exposure increases by approximately 50% in patients with renal insufficiency. (vi) Patients with congenital or acquired Qt prolongation. Worsen with 40mg dose. (vii) Postural hypotension with or without symptoms (e.g. dizziness) may develop within a few hours following administration of extended-release alfuzosin.

Adverse Reactions : Dizziness-5.7% URT infection-3%, headache-3.0%, fatigue-2.7%, rarely abdominal pain, dyspepsia constipation nausea. impotence, bronchitis, sinusitis, pharyngitis rashes and tachycardia.

Compiled by Dr. P. Chattree

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