

exercise⁶. Sensory function is normal. In majority of the patients, deep tendon reflexes are markedly diminished or absent, although some may show evidence of brisk or normal jerks even during paralysis³. In TPP, hypokalemia is the underlying biochemical disturbance which provokes paralysis². Hypokalemia occurs due to a massive shift of potassium into the cells rather than a net loss from the body. In addition to hypokalemia, hypophosphatemia and hypomagnesemia have been reported. Rebound hyperkalemia after therapy may occur in about 40% of patients⁷. Electromyography during a paralytic attack, reveals myopathic changes in the form of decrease in the duration of compound muscle action potential, increase in polyphasic potentials, and reduced amplitude of evoked muscle action potential on nerve stimulation. Peripheral nerve function is normal⁸. The pathophysiology of TPP remains unclear. Hypokalemia occurs due to rapid and massive shift of potassium from the extracellular into the intracellular compartment mainly into the muscles. This is probably due to increased Na/K-ATPase pump activity in patients of TPP⁹. Development of paralysis is partly influenced by the hyperadrenergic state characteristic of thyrotoxicosis thereby, further increasing Na/K-ATPase activity. Exercise releases potassium from the skeletal muscles whereas rest promotes influx of potassium. This explains why paralytic attacks occur only during recovery from exercise and resumption of exercise can abort an attack⁴. Regarding role of genetics in the development of TPP there is association with HLA-DRW8 gene as revealed in Japanese men¹⁰. Treatment consists of emergent correction with I.V KCl and management of thyrotoxic state alongwith ECG monitoring. Oral propranolol in doses of 3 mg/Kg is given to reverse paralysis, hypokalemia and hypophosphatemia¹¹. Genetic counselling and

prenatal testing may be helpful in few patients of TPP because it may be inherited in autosomal dominant manner.

CONCLUSION

Early diagnosis and prompt treatment are important. Clinically TPP mimics many common diseases which must be excluded. It is a curable disorder that resolves when an euthyroid state is achieved.

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DRUG PROFILE

Aliskiren

Pharmacology: Aliskiren 2(S),4(S),5(S),7(S)-N (2-carbamoyl-2- methylpropyl)-5-amino-hydroxy- 2-7-diisopropyl-8(4-methoxy-3-13-methoxypropyl) octanamide, is the first in a new class of orally active non peptide, , molecular weight (551.8 g/mol) rennin inhibitor. The active with four chiral carbons, but exists as a single diastereoisomer. It is a highly affinity and specificity for human renin. It binds to the S1/S3 conversion of angiotensinogen to Ang I. Aliskiren, is first DRI with bioavailability of 2.5% and has shown to be generally well tolerated when given as single or multiple dose. **Pharmacokinetics:** The plasma concentration of aliskiren increased in a dose dependent manner, following oral administration in healthy volunteers, with peak concentration reached after 3-6 hours. Oral bioavailability of aliskiren was about 5% (for 95% it is excreted unchanged in faeces) and plasma steady state level were reached after 5-8 days of treatment. An average plasma half- life of 23.7 hours (range 20-45 hours) makes drugs suitable for once daily administration. Aliskiren is not metabolized by cytochrome P450 system and interact with warfarin, and a number of other compound. Drug showed no clinically, valsartan. HCTZ and ramipril, in healthy volunteers. **Mechanism of Action:** Elevated PRA has been identified independent predictor of morbidity and mortality (p=0.0025) in a large scale trial of 4300 patients with congestive heart failure. Aliskiren inhibits the rennin by directly targeting the renin enzyme, at the point of activation and blocking the conversion of angiotensinogen to Ang I and decreasing levels of Ang I and II. Aliskiren decreases PRA by approximately 50-08% and provides similar reduction when administered in combination with drugs know to increase PRA such as the ACE inhibitor ramipril, the ARB valsartan or the diuretic HCTZ. **Efficiency & indication:** Aliskiren decrease PRA, Ang I and Ang II levels in normotensive volunteers in a dose dependent manner, decrease in plasma and urine aldosterone levels were also noted with daily aliskiren doses of 80 mg and above. Aliskiren 160 mg and enalapril 20 mg doses were comparable in terms of their inhibitory effects on Ang II levels BP nor heart rate was affected by aliskiren and enalapril in these normotensive subjects, In a within -study, 12 sodium-depleted normotensive subjects were randomly given placebo, aliskiren 300 mg/day, valsartan (150 mg/day, +80 mg/day, As expected, aliskiren along decrease PRA while valsartan along increased PRA, Ang I and Ang II. The combination of aliskiren and valsartan completely eliminated the rise in PRA elicited by valsartan.