

plane it is interrupted and is present only at intervertebral levels. Posterior longitudinal ligament thickening of more than 2 mm was considered significant in our study.

Ossified spinal ligaments give signal similar to yellow marrow on T1 and T2 scans¹⁰. Thickening of posterior longitudinal and ligamentum flavum were first reported in 1836 and 1920 respectively and are seen in conditions like ankylosing spondylitis, secondary to trauma, diffuse idiopathic skeletal hyperostosis (DISH), calcium pyrophosphate deposition disease, hematochromatosis and hyperthyroidism¹¹ but still exact cause remains undetermined in many cases.

We found correlation between duration of illness & ossification of PLL and LF. In 7 cases where ossification of PLL was seen the mean duration of disease was 5.8 yrs as compared to 3.6 yrs. where PLL was only thickened & not ossified. Similarly mean duration of disease was 5.4 yrs in 11 cases of if ossification as against 3.5 yrs where LF was only thickened & not ossified. Thus, it takes on an average 5.5 yrs for PLL & LF to become ossified. It was seen that the neurological deficit was more in the patients having ossified ligaments.

Cord edema was seen in 92% cases and a good correlation was observed between extent of extradural compression on MRI and clinical severity. Nine patients had nerve root compression, in six of these it was due to herniated disc and in three patients extensive posterior longitudinal ligament extended far across midline to involve neural foramina. In two cases we noticed an interesting finding of alternating bands of low and high signals in intervertebral disc on T1 and T2W images giving target appearance. They represent dark nucleus pulposus in centre followed by bright inner annulus the dark outer annulus with bright signal of

syndesmophyte marrow at periphery. This appearance is considered characteristic of ankylosing spondylitis. However, this is a preliminary observation which requires further studies to confirm.

Till date only a small series of four cases has been reported by Gupta et al⁸ Our study has shown a direct correlation between duration of disease with neurological deficit and MRI changes, along with this we also observed target sign in 2 patients. These observations were not documented in the earlier study.

Aim of our study was to study the spectrum of MRI changes in fluoritic spine and their correlation with duration of disease and neurological deficit. However, further studies having large sample size are required for correlation of radiological changes on MRI with the prognostic outcome both by conservative and surgical methods.

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RANOLAZINE

DRUG PROFILE

Ranolazine is a compound that is approved by the US FDA for the treatment of chronic angina pectoris in combination with amlodipine, beta-adrenoceptor antagonists or nitrates, in patients who have not achieved an adequate response with other anti-anginals.

Mechanism of Action: The anti-anginal effect of ranolazine does not depend on changes in heart rate or blood pressure. The mechanism of action of ranolazine for anti-anginal effect has not been fully characterised. Ranolazine is an inhibitor of several ion channels, including the late inward sodium (I_{Na}) current which reduces calcium overload during ischaemic conditions. Reducing excess intracellular calcium can lead to improvement of left ventricular diastolic dysfunction by decreasing diastolic tension and thereby oxygen consumption. Ranolazine has been shown to improve left ventricular regional diastolic function in patients with ischaemic heart disease. Thus, inhibition of the late I_{Na} current by ranolazine is likely to contribute to the anti-anginal effect, but other mechanisms may also be involved.

Pharmacokinetics: Following administration of an oral solution or IR capsule, peak plasma concentrations (C_{max}) are observed within 1 hour. After administration of radiolabelled ranolazine, 73% of the dose was excreted in urine, and unchanged ranolazine accounted for <5% of radioactivity in both urine and faeces. The absolute bioavailability ranges from 35% to 50%. Food has no effect on rate or extent of absorption from the ER formulation. Ranolazine protein binding is about 61-64% over the therapeutic concentration range. Volume of distribution at steady state ranges from 85 to 180 L. Ranolazine is extensively metabolised by cytochrome P450 (CYP)

3A enzymes and, to a lesser extent, by CYP2D6, with approximately 5% excreted renally unchanged. Elimination half-life of ranolazine is 1.4-1.9 hours but is apparently prolonged, on average, to 7 hours for the ER formulation as a result of extended absorption (flip-flop kinetics). Elimination occurs through parallel linear and saturable elimination pathways, where the saturable pathway is related to CYP2D6, which is partly inhibited by ranolazine. Oral plasma clearance diminishes with dose from, on average, 45 L/h at 500 mg twice daily to 33 L/h at 1000 mg twice daily. The departure from dose proportionality for this dose range is modest, with increases in steady-state C_{max} and area under plasma concentration-time curve (AUC) from 0 to 12 hours of 2.5- and 2.7-fold, respectively. Ranolazine pharmacokinetics are unaffected by sex, congestive heart failure and diabetes mellitus. AUC increases up to 2-fold with advancing degree of renal impairment.

Dosages: Initial studies used an oral solution or an immediate-release (IR) capsule, but subsequently an extended-release (ER) formulation was developed to allow for twice-daily administration with maintained efficacy. Usual dose of extended release (ER) is 200mg twice daily.

Drug Interaction: Ranolazine is a weak inhibitor of CYP3A, and increases AUC and C_{max} for *simvastatin*, its metabolites and HMG-CoA reductase inhibitor activity <2-fold. *Digoxin* AUC is increased 40-60% by ranolazine through P-glycoprotein inhibition. Ranolazine AUC is increased by CYP3A inhibitors ranging from 1.5-fold for *diltiazem* 180 mg once daily to 3.9-fold for ketoconazole 200 mg twice daily. *Verapamil* increases ranolazine exposure approximately 2-fold. CYP2D6 inhibition has a negligible effect on ranolazine exposure.