Rasagiline Pharmacokinetics are affected by cytochrome P-450 1A2 genetic variants in different doses

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Rasagiline, a monoamine oxidase-B inhibitor is an alternative monotherapy or add-on therapy with Levodopa for managing Parkinson's disease. The pharmacokinetics of this drug are effected by various environmental factors resulting in therapeutic failure. To explore the effect of genetic variants of cytochrome P-450 1A2 which is the drug metabolizing enzyme, this study was carried out on total of 108 healthy volunteers. The study was conducted in three phases with 36 volunteers in each and with equal representation of AA, AC & CC variants of CYP1A2 enzyme. Rasagiline was given orally in different doses (1mg,2mg & 5mg) in each phase. Serial blood sampling was performed at 0, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8 & 12 hours. The plasma concentrations were determined using High performance liquid chromatography and pharmacokinetic variables were calculated using APO Pharmacologica software. Results were intriguing as the t1/2 and AUC were significantly lower in AA variants as compared to AC & CC variants and clearance (Cl) was highest in AA variants as compared to the other two in all three doses. However the drug showed dose-dependant pharmacokinetics as the t1/2 ranged from 0.3 to 1.5 hours in escalating doses. Similarly AUC was also highest at 5 mg in all three variants as compared to 1mg & 2mg doses. The study supports the idea of dose optimization in AA, AC and CC variants to avoid therapeutic failure of drug.