The hypoalgesic effect of tramadol in relation to CYP2D6.

Poulsen L, Arendt-Nielsen L, Brøsen K, Sindrup S H in *Clinical pharmacology and therapeutics* (1996)
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Summary

Tramadol inhibits norepinephrine reuptake, stimulates serotonin release, and acts with mu-opioid receptors by way of its metabolite (+)-M1. Formation of M1 seems to depend on the genetic polymorphic CYP2D6. The analgesic effect of 2 mg/kg tramadol was evaluated in 15 extensive and 12 poor metabolizers of sparteine in two parallel, randomized, double-blind, placebo-controlled crossover studies that used experimental pain models. In extensive metabolizers, tramadol increased pressure pain detection (p = 0.03) and tolerance (p = 0.06) thresholds, as well as thresholds for eliciting nociceptive reflexes, after single (p = 0.0002) and repeated (p = 0.06) stimulation of the sural nerve. Peak pain and pain area in the cold pressor test were reduced (p = 0.0006 and 0.0009). In poor metabolizers, only thresholds to pressure pain tolerance (p = 0.02) and nociceptive reflexes after single stimulation (p = 0.04) were increased and the reflex threshold was less increased in poor metabolizers than in extensive metabolizers (p = 0.02). The serum concentration of (+)-M1 2 to 10 hours after tramadol ranged from 10 to 100 ng/L in extensive metabolizers, whereas in poor metabolizers serum concentrations of (+)-M1 were below or around the detection limit of 3 ng/ml. It is concluded that formation of (+)-M1 by way of CYP2D6 is important for the effect of tramadol on experimental pain.

Discussed In Paper

Molecules : tramadol

Genes : CYP2D6

Haplotypes : CYP2D6*1, CYP2D6*4

Related in Paper

- CYP2D6 is related to tramadol

Variant Annotations

Variant	Genes	Chemicals	Discusses	BioGeo Group
CYP2D6*1, CYP2D6*4	CYP2D6	tramadol	efficacy,metabolism/PK	

CYP2D6 poor metabolizer is associated with decreased metabolism of tramadol and decreased response to tramadol when treated with tramadol as compared to CYP2D6 normal metabolizer. more info

This study evaluated 15 extensive and 12 poor metabolizers of sparteine in randomized, double-blind, placebo-controlled crossover studies that used experimental pain models. A metabolizer ratio >=20 defined as poor metabolizer phenotype. A metabolizer ratio <20 defined as extensive metabolizer phenotype. no specific CYP2D6 allele was mentioned.

Please note that alleles in PharmGKB are mapped to the positive chromosomal strand. Therefore, variants in genes on the "minus" strand (eg. VKORC1) are complimented in PharmGKB annotations.

Prescribing Info

No dosing information related to this publication

Pathways

No related pathways