Unexpected Opioid Metabolite Patterns Suggestive of CYP2D6 Variability in Chronic Pain Patients

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BACKGROUND

- CYP2D6 contributes to the metabolism of oxycodone and hydrocodone.
- CYP2D6 variability may alter metabolite profiles, analgesic response, and dosing requirements.
- Unexpected UDT patterns can complicate interpretation.

OBJECTIVE

Characterize opioid metabolite patterns in chronic pain patients with inadequate analgesic response and possible CYP2D6 variability.

METHODS

- Retrospective case series of 7 chronic pain patients with inadequate pain control
- Confirmatory LC-MS/MS UDT while prescribed opioids
- Parent-drug and metabolite concentrations compared with expected opioid metabolic profiles

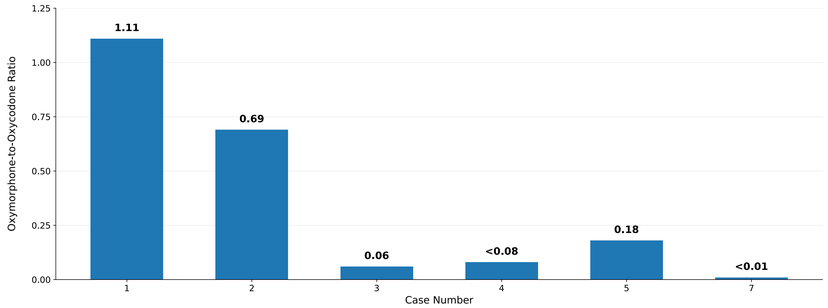
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5 of 7 **patients with inadequate opioid response demonstrated UDT patterns suggestive of reduced CYP2D6-mediated metabolism**

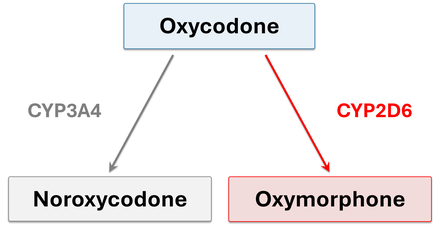
Unexpected metabolite patterns may suggest metabolic variability when UDT findings and clinical response do not align.

OXYMORPHONE-TO-OXYCODONE RATIOS



Cases 3–5 demonstrated low ratios. Case 7 had no detectable oxymorphone.

OXYCODONE METABOLISM



SUMMARY OF CASES

Case	Prescribed Opioid	Ratio*	Interpretation
1	Oxycodone IR 30 mg TID	1.11	Higher oxymorphone conversion
2	Oxycodone IR 30 mg QID	0.69	Oxymorphone formation within expected variability
3	Oxycodone IR 30 mg QID + ER 27 mg BID	**0.06**	Reduced oxymorphone formation
4	Oxycodone IR 30 mg QID	**<0.08**	Reduced oxymorphone formation
5	Oxycodone IR 30 mg TID + ER 54 mg BID	**0.18**	Reduced oxymorphone formation
6	Hydrocodone 10 mg TID	**0.36†**	Detectable but reduced hydromorphone formation
7	Oxycodone IR 30 mg QID	**<0.01**	Oxymorphone not detected

* Oxymorphone-to-oxycodone ratio for oxycodone-treated patients. † Hydromorphone-to-hydrocodone ratio for Case 6.

KEY FINDINGS

- **Cases 3–5**: Reduced oxymorphone formation
- **Case 6**: Reduced hydromorphone formation
- **Case 7**: Oxymorphone not detected

These patterns suggest a spectrum of reduced CYP2D6-mediated metabolism.

CLINICAL IMPLICATIONS

Atypical UDT ≠ Medication Misuse

- Reduced CYP2D6-mediated metabolism may contribute to poor opioid response and increased dosing requirements.
- Recognition of metabolic variability may improve UDT interpretation and reduce misclassification as medication misuse.

TAKE-HOME

When UDT findings and clinical response do not align, consider metabolic variability before concluding medication misuse.

NEXT STEP

Prospective pharmacogenomic testing may clarify CYP2D6 phenotype variation and help individualize opioid therapy.