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Intermediate metabolizer:  
increased side effects in  
psychoactive drug therapy.  
The key to cost-  
effectiveness of  
pretreatment CYP2D6  
screening? CYP2D6 IMs  
and side effects

B Laika, S Leucht, S Heres and W  
Steimer

The cytochrome P450 2D6  
(CYP2D6) isoenzyme metabolizes  
about 25% of clinically used drugs.  
The impact of CYP2D6 metabolizer  
status on therapeutic outcome was  
assessed in 365 psychiatric in-  
patients treated with neuroleptics or  
antidepressants. Length of  
hospitalization and response onset  
were prolonged for patients  
receiving CYP2D6 drugs.  
Intermediate metabolizers (IMs)  
receiving CYP2D6 doses above the  
population median had more side  
effects after 4 weeks than extensive

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**metabolizers with above-median doses (9/13, 69% vs 4/23, 17%,  $P=0.003$ ), than IMs with below-median doses (5/22, 23%,  $P=0.012$ ) and IMs with other medication (24/84, 29%,  $P=0.009$ ). The Clinical Global Impression scale response was lower for IMs treated with CYP2D6 drugs (3/42, 7%) than for IMs with other medication (21/84, 25%,  $P=0.017$ ) probably due to increased side effects. Identification of IM status (38% of study population) may help to reduce side effects and length/cost of hospitalization. Thus, not only poor and ultrarapid metabolizer but also IMs may benefit from CYP2D6 genotyping. This is of paramount interest since it greatly improves cost/benefit estimations for pretreatment CYP2D6 screening.**

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