Can Mu-opioid Receptor A118G Gene Polymorphism be Predictive of Acute Poisoning Severity in the Emergency Department?

Katell Peoc'h · Bruno Megarbane

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To the Editor,

We have read with a great interest the manuscript by Manini et al. [1] reporting the association of mu-opioid receptor gene (*OPRM1*) A118G polymorphism with clinical severity of acute poisonings admitted to the emergency department. In patients carrying at least one G allele of the c.A118G polymorphism (rs1799971), these authors reported increased poisoning severity defined as the occurrence of respiratory arrest, cardiac arrest, or in-hospital mortality with an adjusted 5.3 odds ratio whatever the responsible drug was.

This finding is quite promising since suggesting that one simple test could be helpful in identifying acutely poisoned patients with major risk for severe outcome. However, several significant biases may temperate possible enthusiasm.

The association between the 118G allele and poisoning severity may have resulted from a confounding factor, i.e., the surprising severity of poisonings with opioids and benzodiazepines reported in Manini's patient population as assessed in the univariate analysis (Table 2) and confirmed in the multivariate analysis identifying a significant link between the clinical outcome and recreational intent of drug abuse (Table 4). To our opinion, the authors should have limited their analysis to the group of toxicants with either obvious (opioids) or possible molecular interactions with MOR like previously reported (benzodiazepines) [2], while other toxicants like sympathomimetics, antipsychotics, and antidepressants do not clearly interact with MOR.

Previous studies have associated the 118G allele with less morphine-related pupil-constricting and gastrointestinal

effects [3] and no increased respiratory depression [4]. A more recent study has evidenced that infants with neonatal abstinence syndrome due to in utero exposure to opioids needed less treatments and presented shortened length of stay, if carrying almost one 118G allele [5]. Taken together, all these data support increased resistance rather than increased susceptibility or vulnerability to opioids in the presence of the 118G allele, in contrast to Manini's findings [1].

Additionally, as partly acknowledged by the authors, we cannot exclude that ethnical differences according to severity explain the observed association between the 118G allele and severe poisoning outcome, since the 118G allele is more common in Asian descent (http://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=1799971). Thus, we believe that determination of patients' ethnical origin is mandatory to allow any definitive conclusion, even though the Hardy–Weinberg Equilibrium is respected. Moreover, we cannot exclude that ethnical origin is associated with socioeconomic factors or morbidities that may have contributed to worsen the final outcome of poisoning.

In conclusion, Manini's data are quite promising to personalize monitoring of poisoned patients, especially that the 118G allele is frequent in the general population. However, considering possible major limitations of their study, a reproduction in a well-characterized independent cohort appears necessary.

References

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K. Peoc'h · B. Megarbane (✉)
INSERM U705, Lariboisière Hospital, Paris-Diderot University,
Paris, France
e-mail: bruno-megarbane@wanadoo.fr

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