Study reports validation of the first point-of-care genetic test in medicine, regarding use of antiplatelet therapy

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A study published Online First by the *Lancet* reports the successful validation and clinical application of the first point-of-care genetic test in medicine. The test successfully identifies the CYP2C19*2 allele: a common genetic variant associated with increased rates of major adverse events in individuals given clopidogrel after percutaneous coronary intervention (PCI), thus avoiding complications in those patients. The Article is by Dr Derek Y F So, University of Ottawa Heart Institute, Ottawa, Canada, and colleagues.

Treatment with aspirin and clopidogrel is standard care for patients after PCI, in order to reduce the risk of blot clots. However, many patients given this dual antiplatelet regimen remain vulnerable to major adverse cardiovascular events. This persistent vulnerability is associated with high on-treatment platelet reactivity (that can lead to sudden blockage within stents causing heart attacks or death), which is characterised by inadequate inhibition of the platelet P2Y12 receptor after treatment with clopidogrel. Although several clinical variables have been implicated, the strongest predictor is the loss-of-function CYP2C19*2 allele (rs4244285). This common genetic variant is carried by nearly 30% of individuals of western European ancestry and as many as 50% of those of Asian descent.

Prasugrel and ticagrelor are novel P2Y12 inhibitors that provide more potent platelet inhibition than does clopidogrel. Both agents reduce major adverse cardiovascular events after acute coronary syndrome; however, they are also associated with increased bleeding complications.

Notably, retrospective genetic studies showed that prasugrel and ticagrelor were unaffected by the CYP2C19*2 allele. Prospective identification of CYP2C19*2 carrier status might allow personalisation of dual antiplatelet treatment after PCI that successfully minimises major adverse cardiovascular events and adverse bleeding events.

A point-of-care genetic test for the CYP2C19*2 allele with a buccal swab has been developed (Spartan RX CYP2C19, Spartan Biosciences, Ottawa, ON, Canada). This bedside technology enables health-care personnel with no previous training in genetic laboratory techniques to undertake genotyping. Thus the authors aimed to assess the clinical feasibility and pharmacodynamic efficacy of personalised dual antiplatelet treatment in patients receiving PCI for treatment of acute coronary syndrome and stable coronary artery disease. Usual care generally consists of treating all patients with the same medical regimen (most often aspirin and clopidogrel) whereas this new genetic test enables physicians to personalise therapy and selectively administer a more potent anti-platelet agent (such as prasugrel) to those at high risk of treatment failure with clopidogrel.

200 patients were enrolled into our prospective, randomised, proof-of-concept study. Patients undergoing PCI for acute coronary syndrome or stable angina were randomly assigned to rapid point-of-care genotyping or to standard treatment. Individuals in the rapid genotyping group were screened for the CYP2C19*2 allele. Carriers were given 10 mg prasugrel daily, and non-carriers and patients in the standard treatment group were given 75 mg clopidogrel daily. The primary endpoint was the proportion of CYP2C19*2 carriers with high on-treatment platelet reactivity (P2Y12 reactivity unit [PRU] value of more than 234) after 1 week of dual antiplatelet treatment, which is a marker associated with increased adverse cardiovascular events.

After randomisation, 187 patients completed follow-

up (91 rapid genotyping group, 96 standard treatment). 23 individuals in each group carried at least one CYP2C19*2 allele. None of the 23 carriers in the rapid genotyping group had a PRU value of more than 234 at day 7, compared with seven (30%) given standard treatment. The point-of-care genetic test had a sensitivity of 100% and a specificity of 99%.

The authors conclude: "As far as we are aware, our study is the first to validate and to show clinical use of point-of-care genetic testing. It is the first randomised investigation of selective use of prasugrel in CYP2C19*2 carriers after PCI. Our findings suggest that personalisation of antiplatelet therapy might reduce adverse ischaemic outcomes; use of prasugrel only in high-risk individuals might also minimise adverse bleeding events. The development of practical point-of-care genetic testing in our study will help to integrate genetics into the clinical setting and will allow large-scale investigations to definitively assess the value of pharmacogenetic strategies."

Dr So adds*: "For the first time in clinical medicine, we have proven that a simple bedside test can enable rapid genetic testing and subsequent personalised therapy. This is an important step towards integrating pharmacogenomic strategies into clinical care."

In a linked Comment, Dr Amber L Beitelshees, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA, says: "The RAPID GENE study provides much-needed impetus by showing that genotyping can be done in a timely manner and incorporated into the clinical workflow as we wait for the results of large outcome-driven randomised trials."

More information: Study online: www.thelancet.com/journals/lan … (12)60161-5/abstract

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