Comparative safety of antiplatelet agents: a study of 'real-world' data from the Italian National Pharmacovigilance Network

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According to the Italian National report on drug use, thienopyridines and ticagrelor represent the most prescribed antiplatelet agents for primary and secondary prevention of serious vascular events, besides aspirin (OSMED 2013).
A need for more extensive information remains about the comparative safety profile of these drugs. Aim of this study was to analyse data from the Italian National Pharmacovigilance Network between January 2009 and May 2014, in order to evaluate the 'real-world' safety profile of ticlopidine, clopidogrel, prasugrel and ticagrelor, even if it shows several limitations mainly related to under/over-reporting (Palleria C et al. 2013).
All suspected adverse drug reactions (ADRs) were classified by frequency, severity, outcome, age and system organ class (SOC) according to the Medical Dictionary for Regulatory Activities (MedDRA).
Clopidogrel showed the higher absolute number of suspected ADRs, followed by ticlopidine, ticagrelor and prasugrel (figure 1). Prescription rates were significantly higher for ticlopidine and clopidogrel, and this may provide a reason for the relatively higher number of ADRs with these drugs. Non-serious ADRs were the most represented type of reactions, except for ticlopidine (figure 2). The most frequent serious conditions were those that resulted in 'hospitalization/extended hospitalization', followed by 'other clinically relevant condition' (Figure 3). 'Complete recovery' or 'improvement' account for more than a half of the overall outcomes (Figure 4), probably due to the higher percentage of non-serious ADRs. Most of suspected ADRs were in patients > 65 years old, except for prasugrel (Figure 5). On a total of 1212 clinical conditions associated with ticlopidine, the most frequently reported events were gastrointestinal conditions, haematologic diseases, respiratory, thoracic and mediastinic diseases and cutaneous and subcutaneous reactions (Table 1). On a total of 2391 clinical conditions associated with clopidogrel, the most frequent events were gastrointestinal diseases, cutaneous and subcutaneous reactions, respiratory, thoracic and mediastinic diseases and haematologic diseases (Table 2). On a total 99 clinical conditions associated with prasugrel, the most frequent events were cutaneous and subcutaneous reactions, respiratory, thoracic and mediastinic diseases, haematologic diseases, gastrointestinal conditions (Table 3). On a total of 192 clinical conditions associated with ticagrelor, the most frequent events were respiratory, thoracic and mediastinic diseases, cutaneous and subcutaneous reactions, gastrointestinal conditions, and neurological diseases (Table 4). Taken all together, the most frequent events were represented by bleedings. Aspirin represented the first associated suspected drug, in particular in case of bleeding.
Our results suggest that the higher number of ADRs associated with clopidogrel and ticlopidine could be related to the wider prescription rate of these drugs compared to that of ticagrelor and prasugrel. Most of suspected ADRs were reported in the elderly, in particular in the case of ticlopidine. This could be partly explained by ticlopidine indications, supporting a possible larger use in this age group. However, the inclusion of ticlopidine among the list of medicines to avoid in the elderly (American Geriatrics Society 2012) suggests that use of ticlopidine in this population could be inappropriate, and a reconsideration of its place in therapy could be useful for clinical practice.
Further studies are necessary in order to better define the overall risk-benefit ratio of these drugs in 'real-world', and to ensure both prescription appropriateness and safety for patients.

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