**DRUGS - INDUCED DISSEMINATED INTRAVASCULAR COAGULATION: A PHARMACOEPIDEMIOLOGICAL STUDY BASED ON WHO DATABASE OF ADVERSE DRUG REACTIONS**

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**Introduction**: Disseminated intravascular coagulation (DIC) is a rare and serious syndrome characterized by the wide activation of coagulation process resulting in fibrin formation and consequent thrombosis of small to medium vessels (H. Wada et al., 2014). At the same time, depletion of coagulation proteins and platelets brings to severe bleeding. Few studies clarified the pathogenetic pathway of the syndrome (M. Levi et al., 1999) that could also be considered as an adverse drug reaction (ADR) induced by drug intake. We aimed to investigate the association between several drug classes use and the onset of DIC using the reports of suspected adverse drug reactions (ADRs) collected in the WHO database.

**Material and methods**: Data were obtained from VigiBase, the WHO Global Individual Case Safety Report (ICSR) database, at the Uppsala Monitoring Centre. We collected all suspected reports of drug-related DIC between 1968 to September 2015 and classified in VigiBase according to MedDRA (Medical Dictionary for Regulatory Activities) term “disseminated intravascular coagulation” and “disseminated intravascular coagulation in new born”. A disproportionality analysis using Reporting Odds Ratio (ROR) with 95% confidence interval and p value ≤ 0.05 was performed.

**Results**: After exclusion of duplicates, 4653 reports of drug-associated DIC collected in the VigiBase, corresponding to 1111 drug-reaction pairs, were selected. Among these, DIC was significantly (ROR > 1, 95% confidence interval and p value ≤ 0.05) associated with 88 drugs. According to ATC classification system, drugs more frequently related to DIC were antineoplastic agents, antithrombotic agents and antibacterials for systemic use. Furthermore, drugs that were most frequently reported and, at the same time, were statistically significant were paracetamol (n = 117) ROR = 1.21 (CI95% 1.00 – 1.48), dabigatran (94) ROR = 1.34 (1.08 – 1.67), oxaliplatin and bevacizumab both with 75 reports and ROR = 1.77 (1.38 – 2.27) and 2.02 (1.57 – 2.61), respectively. For all these drugs, DIC was an unknown ADR. Only 10 drugs out of 88 have DIC listed in their SPCs: sunitinib, tegafur/gimeracil/oteracil, heribulin, eptacog alfa, hetastarch, edaravone, rifampicin, quinine, acetylsalicylic acid and dinoprostone.

**Conclusions:** The high number of drugs involved and the great number of fatal outcomes (more than 50%) underline the importance to evaluate this condition such as an ADR that might occur during therapy. Clinicians should be aware of the importance to report every case of suspected drug-related DIC and regulatory authorities should update the SPCs (summary of product characteristics) of several drugs accordingly.

**References**

H. Wada et al. (2014), Journal of Intensive Care, 2: 15.

M. Levi et al. (1999), New England Journal of Medicine, 341:586-592