The Epidemiology of Stevens - Johnson Syndrome and Toxic Epidermal Necrolysis in the United Kingdom:
A Comprehensive Observational Study

Author: Janine Jossi
Supervisors: Noel Frey, Dr. Julia Spoendlin
Prof. Dr. Christoph Meier

Hosting Institution: Basel Pharmacoepidemiology Unit, University of Basel, Department of Pharmaceutical Sciences
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Background Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but severe cutaneous adverse drug reactions. Evidence on SJS/TEN is sparse, and most previous studies were hospital-based case-control studies, which were not representative of the general population, and which were targeted to identify potential culprit drugs of SJS/TEN. We aimed to conduct a comprehensive epidemiological study using data that are representative of the UK population.
Methods We used a previously validated study population of 551 incident SJS/TEN patients, which was established based on data from the Clinical Practice Research Datalink. We conducted a cohort study to calculate population-based incidence rates of SJS/TEN in the United Kingdom between 1995 and 2013, stratified by age, sex, year, and season of diagnosis. We further quantified cumulative incidences of SJS/TEN within 4 months of new onset therapy with specific drugs of interest (e.g.. anticonvulsants, allopurinol, coxib analgesics, PPIs). For a case-control analysis we matched all incident SJS/TEN patients in a 1:4 ratio to SJS/TEN-free controls, and investigated the association between SJS/TEN and demographic characteristics, life-style factors, and immunogenic and non-immunogenic co-morbidities using conditional logistic regression analyses.
Results The overall incidence rate of SJS/TEN in the UK was 6.52 cases / million person-years, with the highest incidence rate of 9.72 cases per million person-years in children aged six to nine years. Incidence rates were similar in women and men (incidence rates were stratified by age, sex, year and season of diagnosis). We observed the highest cumulative incidences for new users of lamotrigine, phenytoin and carbamazepine (27.61, 27.52 and 21.83 cases / 100'000 new users respectively). Allopurinol revealed a cumulative incidence of 6.01 cases / 100'000 new users. While common co-morbidities such as asthma, hypertension, or hyperlipidemia as well as immunological co-morbidities (e.g.rheumatoid arthritis or hay fever) yielded odds ratios (OR) around unity, we observed an increased risk estimate among four patients with pre-existing lupus erythematosus (OR 16, 95% CI 1.79-143.15), of which all were female and were currently undergoing immunosuppression. 4
Conclusions This is the first study, which reports population-based incidence rates of SJS/TEN in the UK, as well as cumulative incidences in new drug users. Incidence rates were consistent in women and men, and did not change according to the year of diagnosis or season, although children may be at a slightly higher risk of SJS/TEN than adults. Our results confirm that anticonvulsants and allopurinol are associated with the highest risk of triggering SJS/TEN. Results from the case-control analysis showed that SJS/TEN is not associated with commonly occurring immunologic or non-immunologic diseases, but that patients with lupus erythematosus may be more susceptible for SJS/TEN.