Routine childhood vaccines and Stevens Johnson Syndrome

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Introduction

During a screening of pediatric individual case safety reports (ICSRs) in VigiBase© we identified Stevens Johnson Syndrome (SJS) as an ADR reported for several vaccines routinely administered in childhood immunization programmes.
VigiBase™

Database of the WHO Programme for International Drug Monitoring

Over 14 mio spontaneous reports from 124 countries, covering 95% of the world population (September 2016)

VigiBase is maintained and developed on behalf of WHO by the Uppsala Monitoring Centre (UMC), situated in Uppsala, Sweden
VigiBase: geographical distribution
Age distribution in VigiBase

VigiBase age distribution 2016

- 0 - 17 yrs: 10%
- 18 - 64 yrs: 51%
- > 65 yrs: 29%
- Unknown: 10%
Pediatric reports: 1 243 709

VigiBase children age

- 0 - 27 d: 2%
- 28 d - 23 mths: 30%
- 2 - 11 yrs: 41%
- 12 - 17 yrs: 27%
Vaccine related reports in VigiBase

VigiBase vaccine reports

- 93% vaccines
- 7% non-vaccines
Steven Johnson Syndrome/TEN

- Immune-complex-mediated hypersensitivity reaction involving skin and mucous membranes
- Rare (1-3 cases/mio SJS, 04-1.2/mio TEN)
- All ages
- Strong genetic predisposition (HLA)
- Aetiology:
  - Infection
  - Drugs (very rarely vaccines)
  - Malignancy
  - Idiopathic
Drugs most commonly involved

**Antibiotics:** sulphonamides, penicillins, cephalosporins

**Anti-convulsants:** lamotrigine, carbamazepine, phenytoin, phenobarbitone

**Allopurinol**

**Paracetamol/acetominophen**

**Nevirapine** (non-nucleoside reverse-transcriptase inhibitor)

**Nonsteroidal anti-inflammatory drugs (NSAIDs)** (oxicam type mainly)

46,228 reports on TEN/SJS (MedDRA PT)

All ages represented but mainly 18-64 yrs

362 reports (1.9%) on (mainly viral) vaccines
Childhood vaccines: case series in VigiBase

As per 1 November 2015

- 40 ICSRs with ADR SJS reported
- Vaccines included:
  - Diphteria
  - Tetanus
  - Pertussis
  - Polio
  - Pneumococcal
  - Hepatitis B
  - HiB
- Vaccines excluded:
  - Meningococcal
  - Live attenuated
Exclusion:

• Cases reported as non-serious
• Cases associated with meningococcal/live attenuated vaccines or with comedication known to be associated with SJS

14 reports with no reported confounders
7 girls, 6 boys, 1 unknown

6 months to 2 years (median 12 mths)

Australia, USA, Venezuela, Vietnam, and UK

TTO: 4 hrs to 9 days, unknown in 3 reports

All children were hospitalized

Outcome: 3 not recovered, 11 not stated
33 reports on SJS/TEN after immunization identified

28 selected for follow up (reporter/records)

6 reports with no confounders and reasonable time to onset

Age reported 6m, 15m, 2.3y, 3.7y, 24.1 y

Hep B, HiB/MMR, DTP/HiB/MMR/OPV and influenza
If vaccines causes SJS/TEN, then very rarely

Vaccine induced immune responses include the same cytokines as implicated in the pathophysiology of SJS/TEN (IL-1, IL-6, and TNF-alpha)
Further evidence from literature


Conclusions

- SJS has been very rarely reported with vaccines
- Important to recognize and treat promptly
- Benefit-risk balance of childhood vaccines remains positive
- Further research into identification of individual risk factors would benefit both patients and immunization programmes