Identification of putative drugs against viral respiratory infections by the pharmacovigilance analysis tool OpenVigil 2

Ruwen Böhm[1], Claudia Bulin[1], Vicki Wätzig[1], Ingolf Cascorbi[2], Hans-Joachim Klein[3], and Thomas Herdegen[1]

[1]University Medicine Schleswig-Holstein
[2]University Hospital Schleswig-Holstein
[3]Kiel University

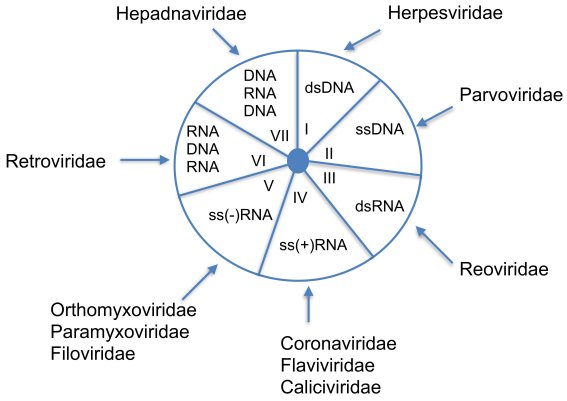
June 16, 2020

Abstract

Aim: Pharmacovigilance data are primarily used to identify adverse drug reactions. However, scanning for associations of drugs and adverse events that occur less frequently than expected provides hypotheses for drug repurposing, i.e. a known drug could be therapeutically beneficial for a new indication like the coronavirus disease (COVID-19). Methods: Drugs associated with viral respiratory tract infections and/or influenza were extracted from the U.S. FAERS pharmacovigilance data using OpenVigil2.1-MedDRA17, filtered for significant inverse associations (punadj<0.05), checked for plausibility, and categorised by their WHO Anatomical Therapeutic Chemical (ATC) classification code. Results: ATC clustering of 82 candidate drugs revealed anti-diabetics, neuropharmacologic sigma-receptor agonists, peptidase inhibitors, kinase inhibitors and anti-androgens. Chloroquine appears as a statistically significant risk factor for viral diseases supporting actual knowledge. Conclusion: OpenVigil 2 delivers new hypotheses for drug repurposing, theoretically for all indications. There is affirmative data for some of our results; the remaining proposed candidate drugs without already known antiviral mechanism of action should stimulate further exploration.

Hosted file

`manuscript.pdf` available at https://authorea.com/users/333943/articles/460037-identification-of-putative-drugs-against-viral-respiratory-infections-by-the-pharmacovigilance-analysis-tool-openvigil-2



A

	+ Drug	- drug	Sums
+ Adverse Event	DE	dE	E
- adverse event	De	de	e
Sums	D	d	N

B

	Drug(s) of interest	All other drugs	∑
Adverse event(s) of interest	6	614	620
All other adverse events	25986	6692804	6718790
∑	25992	6693418	6719410

Rate (DE/D): 0.023084%

Chi-Squared with Yates' correction: 4.027426
Interpretation: Do the observed frequencies differ from expected frequencies? The greater the chi-squared value, the greater the differences. Chi square values greater than 4 are considered statistically significant.

Measurements of disproportionality (observed-expected ratios like RRR, PRR, ROR)
Interpretation: Generally, the higher the value, the more likely an association between drug(s) and adverse event(s) has been found. Lower bounds of confidence intervals can be used instead of the chi-squared value above to assecure statistical significance.

Relative Reporting Ratio (RRR) and 95% confidence interval (lower bound; upper bound): 2.501791 (1.11971 ; 5.589801)

Proportional Reporting Ratio (PRR) and 95% confidence interval (lower bound; upper bound): 2.516466 (1.126236 ; 5.622802)

Reporting Odds Ratio (ROR) and 95% confidence interval (lower bound; upper bound): 2.516816 (1.126185 ; 5.624623)

According to the criteria of Evans 2001 (n > 3, chisq > 4, PRR > 2) this combination of drug(s) and adverse event(s) is considered: **likely an adverse reaction**