AMERICAN JOURNAL OF PHYSIOLOGY, BIOCHEMISTRY AND PHARMACOLOGY, 2021
VOL 11, NO. 6, PAGE 01-02

Short Commentary

Open Access

A commentary on "Emulated Clinical Trials from Longitudinal Real World Data Efficiently Identify Candidates for Neurological Disease Modification: Examples from Parkinson's disease" and its Relevance to COVID-19 challenges

Michal Rosen-Zvi*
Department of Medicine, The Hebrew University, Jerusalem, Israel

ABSTRACT

The paper "Emulated Clinical Trials from Longitudinal Real World Data Efficiently Identify Candidates for Neurological Disease Modification: Examples from Parkinson's Disease" to be published this month in Frontiers is timely given the rising interest in methods to consistently find new indications of existing drugs. Moreover, when a new disease strikes, drug repurposing becomes crucial [1]. In light of the current pandemic and the challenges of addressing COVID-19, finding new uses for existing drugs has become an even greater priority. We're constantly learning more about the long term effect of COVID-19 on a wide range of organs; neurological disorders are just one class of the recently found long term effects of the disease. Once a large enough cohorts of COVID-19 patients is assembled, the methods described in the paper including the procedures for assessing beneficial drugs for neurological conditions have the potential to find existing drugs that can help long term COVID-19 sufferers.

ARTICLE HISTORY
Received: April 14, 2021
Accepted: April 28, 2021
Published: May 05, 2021
KEYWORDS
Drug repurposing; Causal Inference; COVID-19

Commentary

The paper "Emulated Clinical Trials from Longitudinal Real World Data Efficiently Identify Candidates for Neurological Disease Modification: Examples from Parkinson's disease" demonstrates how advanced scalable causal inference technologies can accelerate discovery of new indications and successfully find new uses for existing drugs and therapeutics [1]. Two new potential treatments for the dementia that typically accompanies Parkinson's disease (known as Parkinson's disease Dementia, or PDD) are proposed in the paper. One treatment is rasagiline, an existing Parkinson's drug indicated for motor related problems, which has been found to be potentially protective against PDD. The second, perhaps more surprising finding, concerns a widely used insomnia medication called zolpidem that was not developed to treat Parkinson's disease. A single prior report published more than two decades ago speculated that zolpidem would not be effective against Parkinson's. That research was based on limited clinical experience with the drug and without specific consideration for cognition [2]. Since then, the potential beneficial value that zolpidem can bring to a variety of neurological conditions has been discussed in a number of papers; see the insightful literature review of Bomalaski et al. [3] for some examples. They conclude that since most of the papers are based on case reports and small interventional trials, further study is needed. Studies based on real world evidence (RWE) offer a consistent method for testing a large number of candidate drugs for repurposing.

A host of methods have been developed to consistently look for new indications of existing drugs, from performing pathway analysis based on human knowledge published in papers to studying the chemical structure and drug drug similarity, and more [4]. With the growing availability of extensively large datasets of patient records – Electronic Health Records (EHRs) and insurance claims data the AI-based technologies that employ scalable causal inference for retrospective emulation of clinical trials

Contact: Michal Rosen-Zvi ROSEN@il.ibm.com Department of Medicine, The Hebrew University, Jerusalem, Israel

are becoming ever more promising. In this paper [1], two inherently different causal inference methods are used for estimating the effect of hundreds of concomitant drugs on the emergence of PDD. One is based on inverse propensity weighting (IPT) and it includes training a prediction algorithm on the treatment assignment, the other is based on standardization [5,6]. These RWE based methods can be complemented with the other proposed methods to strengthen evidence from different sources regarding candidate drugs for repurposing. The details of how to integrate the different methods in the context of COVID-19 are reviewed in [7-10].

Conclusion

Indeed, the outbreak of a global pandemic that affects millions of lives requires an accelerated process to discover new drugs, including repositioning existing drugs. Recent reports provide accumulating evidence regarding neurological deficits in a substantial proportion of COVID-19 patients that seem to be caused by the SARS-CoV-2 infection. As discussed in, the status of neurological conditions such as dementia can be detected in EHRs through various proxy measures. Recently collected COVID-19 cohorts such as the international consortium for EHR data-driven studies of the COVID-19 pandemic called 4CE and the COVID-19 trends in clinical characteristics captured in Explorys dataset present an important opportunity to detect candidate drugs for effectively treating the long-term effects of COVID-19.

References

[1] Laifenfeld D, Yanover C, Ozery-Flato M, Shaham O, Rosen-Zvi M, Lev N, et al. Emulated Clinical trials from longitudinal real-world data efficiently identify candidates for neurological disease modification: Examples from parkinson's disease. medRxiv.2020.

[2] Daniele A, Albanese A. Zolpidem in parkinson's disease. The Lancet. 1997; 349(9060):1222-1223.

[3] Bomalaski MN, Claflin ES , Townsend W, Peterson MD. Zolpidem for the treatment of neurologic disorders: A systematic review. J American Med Asso. 2017; 74(9): 1130-1139.

[4] Pushpakom S , Iorio Fn, Eyers PA , Escott KJ, Hopper S, Wells A, et al. Drug repurposing: Progress, challenges and recommendations. Nat Rev Drug Discov. 2019;18(1): 41-58.

[5] Shimoni Y, Karavani E, Ravid S, Bak P, Ng TH , Alford SH, et al. An evaluation toolkit to guide model selection and cohort definition in causal inference. arXiv preprint.2019;1906.00442.

[6] Ozery-Flato M, Goldschmidt Y, Shaham O, Ravid S, Yanover C. Framework for identifying drug repurposing candidates from observational healthcare data. JAMIA Open. 2020; 3(4):536-544.

[7] Zhou Y, Wang F, Tang J, Nussinov R, Cheng F. Artificial intelligence in COVID-19 drug repurposing. The Lancet Digital Health. 2020.

[8] Heneka MT, Golenbock D, Latz E, Morgan D, Brown R. Immediate and long-term consequences of COVID-19 infections for the development of neurological disease. Alzheimer's research and therapy. 2020;12(1):1-3.

[9] Consortium for Clinical Characterization of COVID-19 by EHR

[10] El-Hay T, Karavani E, Perez A, Ninio M, Ravid S, Chorev M, et al. Trends in clinical characteristics and associations of severe non-respiratory events related to SARS-CoV-2. medRxiv. 2021.