Public Awareness of a Vision-Threatening Toxicity: Infodemiology in Pentosan Polysulfate Maculopathy

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Table of Contents

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Abstract

Background: In this age of information (and misinformation), the ophthalmology community faces an ongoing challenge in shaping the distribution of information regarding ophthalmic health to the lay public. Our infodemiology study yields unique insights into factors associated with public awareness of PPS maculopathy and provides valuable insights for public health efforts.

Objective: To explore factors associated with increased public awareness of pentosan polysulfate (PPS) maculopathy

Methods: This cross-sectional study assessed global trends in internet search queries regarding PPS maculopathy using Google Trends from September 2017 to August 2022, with results reported in terms of relative search volume (RSV). Trends in search volumes were assessed following notable events related to the discovery of PPS maculopathy, using the mean RSV prior to the initial e-publication on PPS maculopathy as the comparator.

Results: The mean (SD) global RSV for “pentosan polysulfate sodium,” “Elmiron,” “Elmiron side effects,” and “Elmiron lawsuit” over the study period were 5.03 (5.72), 47.45 (16.5), 2.23 (2.16), and 2.06 (2.16), respectively. Qualitatively, there was an approximate 22-month latency period between the initial e-publication regarding PPS maculopathy and a sustained rise in RSV for the search term “Elmiron.” Compared to baseline mean (SD) global RSV of 35.08 (5.03) for “Elmiron,” the mean (SD) RSV was statistically significantly higher in the month following the initial lawsuit filing regarding PPS maculopathy [50.5 (2.38); $P < .001$] and the drug label change [80.25 (6.55); $P < .01$)], and not significantly higher following other events such as the original publication regarding PPS maculopathy.

Conclusions: Publication in traditional scientific media did not appreciably impact internet search volumes, while other ancillary news events were associated with significant rises. These findings may inform future efforts to educate the public regarding time-sensitive public health concerns.

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Running Title: Infodemiology in Pentosan Polysulfate Maculopathy

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Conclusions: Publication in traditional scientific media did not appreciably impact internet search volumes, while other ancillary news events were associated with significant rises. These findings may inform future efforts to educate the public regarding time-sensitive public health concerns.
Keywords: Elmiron lawsuit, Elmiron, Elmiron toxicity, Google Trends

Introduction

Pentosan polysulfate sodium (PPS) (trade name: Elmiron, Janssen Pharmaceuticals, Inc) is used to treat interstitial cystitis (IC), also known as bladder pain syndrome. PPS was approved by the Food and Drug Administration (FDA) in 1996, and remains the only FDA approved oral agent for treating IC. In 2018, Pearce et al. reported a distinctive vision-threatening maculopathy associated with long-term PPS use.[1–3] This condition appears to progress even after drug cessation, and in severe cases may be associated with legal blindness.[4–7] Given that this drug has been widely used for nearly three decades, and that some regions globally are continuing to see increases in PPS use, [8,9] this public safety concern warrants broad dissemination.

Google Trends (Google, Mountain View, CA), a tool first launched in 2006, allows users to evaluate trends in search queries in Google, and has previously been leveraged in infodemiology approaches to understand public awareness of health-related issues.[11,12] This study evaluates trends in internet search queries following the discovery of PPS maculopathy. The objective is to better understand how information regarding this discovery has been disseminated to the lay public. We hypothesize that there is a latency period between the discovery of PPS maculopathy and increased internet search volumes, and that news events regarding the topic may variably impact search volumes.

Materials and Methods

This cross-sectional study evaluated internet search queries regarding PPS maculopathy using Google Trends. This tool outputs relative search volumes (RSV) in the Google search engine, with each data point normalized to the total number of searches for the specified time and region it represents, and then indexed on a 0 to 100 scale, with 100 representing the maximum normalized search volume for that query.[13]

We evaluated trends in searches related to PPS maculopathy between September 4, 2017 and August 28, 2022. Data were collected on September 4, 2022. Google Trends permits analysis of up to five search terms at a time for comparison of search volumes. Search terms were selected after discussion among the authors to include queries that would best inform our understanding of public interest in the topic of PPS maculopathy. To enable comparison of RSV across search terms, we used a single Google Trends input with the following terms: “pentosan polysulfate sodium,” “Elmiron,” “Elmiron side effects,” and “Elmiron lawsuit.” Given the higher RSV for “Elmiron” relative to other search terms, this term was used for secondary analyses. Unless otherwise indicated, results are reported for worldwide Google search data. To assess regional variation in use of the search terms “pentosan polysulfate sodium” versus “Elmiron,” we performed separate queries by selected regions using these two terms. The study is not considered human subjects research and was exempt from review by the Emory University Institutional Review Board.

Weekly RSV data was downloaded into a comma-separated values (CSV) file and analyzed in Excel (Microsoft, Redmond, WA). Descriptive statistics included mean and standard deviation (SD) RSV over the entire study duration for each search term. To assess the impact of notable events on search volumes, the mean RSV values for the search “Elmiron” were evaluated during the month following pre-specified events and were compared to the mean baseline RSV using an unpaired t-test. The baseline comparator represented the mean RSV from the study start date (September 9, 2017) through the day before the initial e-publication on PPS maculopathy (May 21, 2018). We evaluated the impact of the following events:

1. 22nd May 2018: E-publication of the initial paper describing PPS maculopathy[1]
2. 13th September 2018: Initial messaging regarding PPS maculopathy on an internet forum for interstitial cystitis[14]
3. 1st November 2018: Print publication of the original paper on PPS maculopathy
4. 25th October 2019: Health Canada drug label change[15]
5. 26th March 2020: Filing of the first lawsuit against the manufacturer of PPS in the U.S.[16]

6. 16th June 2020: U.S. FDA drug label change[17]

Results

The mean (SD) global RSV for “pentosan polysulfate sodium,” “Elmiron,” “Elmiron side effects,” and “Elmiron lawsuit” over the study period were 5.03 (5.72), 47.45 (16.5), 2.23 (2.16), and 2.06 (2.16), respectively. “Elmiron” had a higher mean (SD) RSV relative to “pentosan polysulfate sodium” in the U.S. [37.97 (17.43) vs 1.82 (2.28), respectively] and Canada [9.75 (11.18) vs 1.78 (4.13)], but not India [9.31 (15.31) vs 9.67 (16.1)] and Australia [1.5 (2.83) vs 2.03 (2.03)].

Qualitatively, there was an approximate 22-month latency period for the search term “Elmiron” between the initial e-publication regarding PPS maculopathy and a sustained rise in RSV. (Figure 1) Compared to baseline mean (SD) global RSV of 35.08 (5.03), the mean (SD) RSV was statistically significantly higher in the month following the initial lawsuit filing regarding PPS maculopathy [50.5 (2.38); $P < .001$] and the FDA label change [80.25 (6.55); $P < .01$]. (Figure 1) Mean (SD) global RSV was not significantly higher following other events, including the first e-publication regarding PPS maculopathy [35.75 (3.09); $P = 0.45$], the initial messaging on an online IC forum [33.0 (4.16); $P = 0.31$], the first print publication regarding PPS maculopathy [35.0 (3.46); $P = 0.67$], and the Health Canada label change [36.6 (2.38); $P = 0.33$].

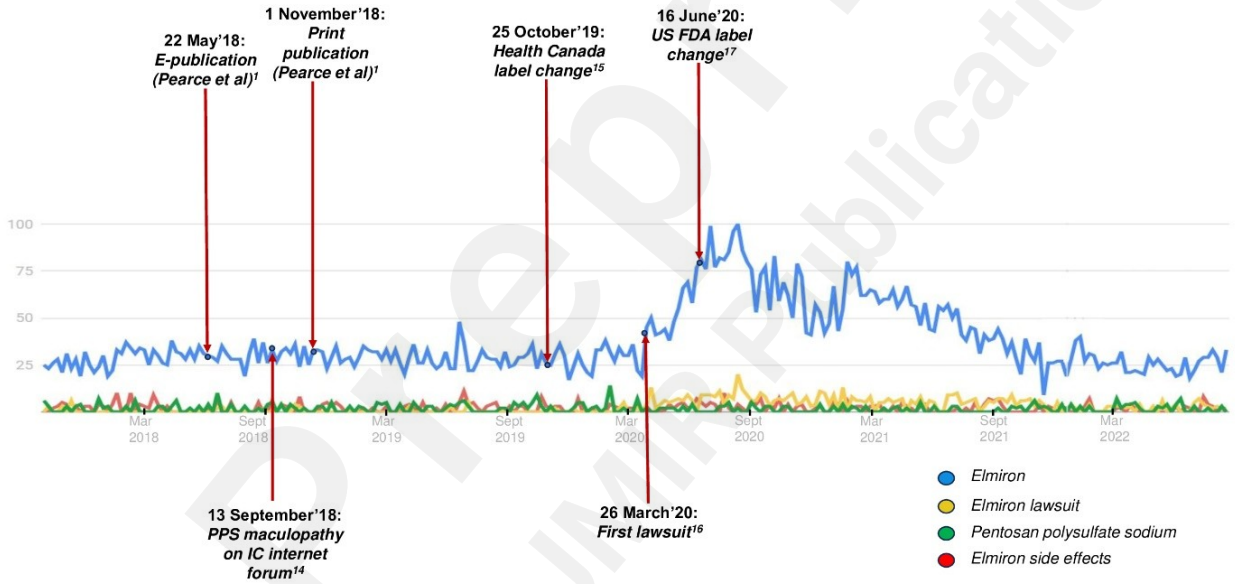

Figure 1: Plot depicting relative search volumes over time for the four search terms, annotated with time stamps depicting pre-specified notable events. (IC = interstitial cystitis; source = Google Trends)

Discussion

The discovery of pentosan polysulfate maculopathy represented a prominent public health issue warranting broad information dissemination to both medical professionals and the lay public. In this study of internet search volumes, we observed a latency between the initial publication on the topic and rise in global internet search volumes.

There was a nearly 2-year gap between the original e-publication by Pearce et al. (May 22, 2018) and an observable and sustained rise in search queries on “Elmiron” (March 2020). The event most closely associated with this rise was the filing of the original lawsuit (March 26, 2020) against the drug manufacturer. Of note, initial lawsuits were accompanied by broad internet, radio, and television marketing campaigns by legal firms in pursuit of clients. In contrast, in the months preceding the initial lawsuit, there were nearly a dozen publications on PPS maculopathy in the ophthalmology and urology literature,[1,18–20] numerous presentations at scientific conferences spanning different medical disciplines, publicly available podcasts on the topic, and engagement with online patient forums.

Of note, while this study demonstrates associations between certain news events and search volumes, we cannot infer a causal relationship. There may be other unidentified events impacting search volumes, and multiple contemporaneous events may have impacted search volumes in concert. Additionally, as we extracted weekly RSV values, we did not assess trends that may have occurred on a shorter time scale. Further, while this study provides general insight regarding lay public awareness of this condition, it is not clear that it reflects awareness among key stakeholders including PPS prescribers and PPS users. Lastly, Google is not universally used as a search engine, and in particular, older audiences may turn to other sources of health information.

In sum, this study provides novel insights into the awareness of PPS maculopathy among the lay public. Publication in traditional scientific media did not appreciably impact internet search volumes, while other ancillary news events were associated with significant rises. These findings may inform future efforts to educate the public regarding time-sensitive health concerns.

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Abbreviations

FDA- Food and Drug Administration
IC- interstitial cystitis
PPS- Pentosan Polysulfate
RSV- relative search volume

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Supplementary Files

Figures

Plot depicting relative search volumes over time for the four search terms, annotated with time stamps depicting pre-specified notable events (IC = interstitial cystitis; source = Google Trends).