SciMedCentral

Journal of Urology and Research

Short Communication

Rates of Patient-Reported Side Effects for PDE5 Inhibitors Prescribed on a Direct-to-Consumer Telehealth Platform

Lauren Broffman[1]*, Michael Eisenberg[2], and Melynda Barnes[1]

[1]*Ro, New York, USA*

[2]*Department of Urology, Stanford University School of Medicine, USA*

***Corresponding author**

Lauren Broffman, Ro, New York, 116 West 23rd Street, 4th Floor, New York, NY 10011, USA, Tel: 7167134178; Email: Lauren.broffman@ro.co

Submitted: 04 August 2020

Accepted: 30 September 2020

Published: 02 October 2020

ISSN: 2379-951X

Keywords

- Erectile dysfunction; Telehealth; PDE5 inhibitors; Side effects; Health technology

Abstract

Direct-to-consumer telehealth is becoming increasingly common for the treatment of erectile dysfunction, but little is known about rates of side effects for patients being treated with prescription medication through these platforms. In this study, EHR and customer service data from a random sample of 10,000 DTC erectile dysfunction telehealth patients receiving treatment on one of the largest telehealth platforms in the U.S. was analyzed for instances of patients' experiencing side effects. We report the incidence rate of patient-reported side effects for sample patients that were prescribed PDE5 inhibitors and compared them to published literature. Rates of side effects were much lower than what was reported in clinical trials, but they align with published rates of discontinued use. Further, the distribution of the kinds of side effects experienced reflects results from other studies. Findings suggest that the experience of side effects is not drastically different for patients being treated on a DTC telehealth platform than in other settings. Similar distribution and rates of side effects for men most bothered these medications indicates that treatment for ED on a DTC telehealth platform does not lead to unsafe, or even unexpected, numbers of experienced side effects.

ABBREVIATIONS

DTC: Direct to Consumer; PDE5: oral phosphodiesterase type 5; ED: Erectile Dysfunction; EHR: Electronic Health Record

INTRODUCTION

The medical community has begun to debate the implications of direct-to-consumer (DTC) telehealth, especially in light of its proliferation during the COVID-19 pandemic as a crucial delivery platform for essential health care. Research has shown that patient satisfaction with DTC telehealth is high, [1] and evidence is emerging that certain conditions can be effectively managed in this way [2,3]. However, uncertainties remain: a recent editorial published in the Journal of the American Medical Association (JAMA) notes positives of the DTC health care model, including increased access and decreased costs but also flags the lack of literature on "the prevalence of adverse events related to the sale of prescription drugs [4]."

One organization operating a DTC telehealth platform is Ro. a U.S.-based DTC health company whose digital health clinic for men, Roman, offers treatment for men with erectile dysfunction (ED). With recent reports citing a current valuation of 1.5 billion dollars [5], they are one of the largest and most prominent players in the DTC health care space. Patients seeking ED treatment on Ro's platform start by engaging in an adaptive online intake process that captures their demographics, current symptoms, health history, and other relevant clinical information in a structured format. Depending on their preference and/or state laws regulating telehealth, patients are then connected to a U.S. licensed provider via video call, phone call, or through the secure, asynchronous exchange of medical information and messages."

Their Ro-affiliated provider then determines which, if any, course of treatment is appropriate. Following their visit, patients are able to communicate continuously with their physician over Ro's secure platform. Patients are able to ask questions, and, if necessary, report side effects.

Given the noted literature gap on relative prevalence rates of reported side effects from medication prescribed on a DTC telehealth platform, a team of researchers at Ro analyzed electronic health record (EHR) and customer service data on men that were prescribed treatment for ED. The aim of this study, the first of its kind in DTC telehealth platform, is to compare rates of patient-reported side effects from medication prescribed on a DTC telehealth platform to existing research on rates of side effects reported via clinical studies.

MATERIALS AND METHODS

The design of this study was approved by the Biomedical

Research Association of New York Institutional Review Board. To assess rates of side effects prescribed via telehealth, we randomly selected 10,000 men from a larger pool of patients who were treated virtually on Ro's DTC telehealth platform starting in 2018. This ensured that patients had been taking medication long enough for any possible side effects to arise. We limited the sampling frame to those who were prescribed one of the two most commonly prescribed medications used in ED treatment, and randomly selected 5,000 patients that were prescribed tadalafil (the active ingredient in Cialis) and 5,000 that were prescribed sildenafil (the active ingredient in Viagra). These medications are classified as oral phosphodiesterase type 5 (PDE5) inhibitors, the standard pharmacologic treatment for ED. Patients taking these medications were selected because their use is widespread and rates of side effects for both sildenafil and tadalafil are well-studied, allowing us to compare rates of side effects reported on Ro's platform to rates of side effects published in the literature.

We assessed rates of patient-reported side effects by analyzing two sets of records. We define "patient reported" as an unprompted communication initiated by the patient to inform either their Ro-affiliated provider or Ro's patient relations team that they experienced a side effect from a prescribed medication. To do this, we first reviewed messages between patients and their Ro-affiliated providers from initial treatment sometime in 2018 through September 2019. This chat interaction data undergoes consistent quality review every two weeks by a quality assurance team to ensure that it accurately reflects the information exchanged between a given patient and their provider. To ensure that the data was extracted correctly from the database, the SQL code used to pull the study sample underwent a standard verification process in which the pull was repeated by a second analyst and assessed for overlap. To further ensure that all side effects experienced by patients in the sample were accurately captured, we then reviewed a second set of data: separate records maintained by Ro's patient relations team tracking patients who contacted them with medical questions. We found there were no instances of side effects reported to the patient relations team that were not relayed to the provider, who then followed up with patients. Thus, reports of side effects captured in patient relations team data were also consistently reflected in our main data source, the patient-provider messages.

To analyze the rates of patient-reported side effects, a PhD level scientist reviewed the text exchange for each patient in the sample, flagging any records where patients reported side effect, and categorized the side effect by type. Most were obvious, e.g., "the medication gave me a headache." Less-than-clear reports were discussed by the research team with a Ro physician researcher adjudicating final decisions.

RESULTS AND DISCUSSION

Overall, 1.4% of patients reported a side effect from a PDE5 inhibitor: 1.8% of patients taking sildenafil, and 1.0% of patients taking tadalafil (Table 1), with headache, flushing, rhinitis, and dyspepsia being the most common. Side effects in the "other" category include rashes and ringing in ears for tadalafil and bloody stools for sildenafil. We also observed that most patients (>90%) who initiated a conversation with their Ro-affiliated provider to report side effects requested and received a change in dose or medication.

Table 1: Patient-reported side effects from PDE5 inhibitors prescribed via telehealh.

	% Overall (n)	% Sildenafil group (n)	% Tadalafil group (n)
Any side effect	1.4 (143)	1.8 (92)	1.0 (50)
Headache	47.9 (68)	55.7 (44)	55.8 (24)
Flushing	23.2 (33)	34.2 (27)	14.0 (6)
Rhinitis	20.4 (29)	26.6 (21)	18.6 (8)
Dyspepsia	12.0 (17)	13.9 (11)	14.0 (6)
Vision-related (blurring/itchiness in eyes)	6.3 (9)	10.1 (8)	2.3 (1)
Back or muscle pain	4.9 (7)	1.3 (1)	11.6 (5)
Dizziness	2.1 (3)	0.0 (0)	7.0 (3)
Other	4.2 (6)	3.8 (3)	7.0 (3)

This study represents the first published set of data from a large DTC telehealth platform on medication side effects. Of note, our results are derived from proactive patient reports in a real-world setting rather than trial-directed protocols of standardized adverse event collection. Because of this, our study unsurprisingly shows that the incidence of reported side effects are significantly lower than rates from clinical trials [6,7]. However, the distribution of side effects types observed is consistent with the reported literature: headaches, dyspepsia, flushing, and rhinitis are the most common [8,9].

Notably, our overall incidence rates are similar to published rates of discontinued use due to side effects for both drugs (0-6%), [8-10], aligning with our observation that proactive patient side effect reporting was accompanied by requests for prescription changes, i.e., discontinued use. More patients may have experienced mild side effects tolerable enough to not report and continued use of the medication at current dosages. Though the purpose of this study was not to compare rates of side effects for sildenafil and tadalafil, we note that the overall side effect rate was higher in sildenafil, which contradicts some comparative studies of both drugs [11].

One of the limitations of this study is that we cannot be entirely certain that a patient who experienced an intolerable side effect communicated it to their Ro-affiliated provider or the patient relations team, and thus it is possible that the incidence rate of side effects is artificially low. However, it is not uncommon in the in-person care system for a provider to be unaware when their patient receives care in other settings, so this limitation is not unique to a telehealth setting. Further, these results might not be generalizable to other DTC telehealth platform or telehealth more broadly.

CONCLUSION

More research is needed on the association of telehealth platforms and side effects for other prescription drugs. Limitations notwithstanding, similar distribution and rates of side effects for men most bothered by either sildenafil or tadalafil suggests that treatment for ED on a DTC telehealth platforms1) does not lead to unsafe, or even unexpected, numbers of experienced

side-effects; and, 2) supports prompt and coordinated physician responses to requests for medication changes when intolerable levels of side effects do occur. Further, structured renewal visits that prompt patients to report any side effects and automated data collection of DTC telehealth platforms, like Ro, provide numerous opportunities beyond traditional treatment models for understanding treatment side effects and improving patient safety.

ACKNOWLEDGEMENTS

We are indebted to Ro employees Kevin Stern for the aggregation and cleaning of electronic health record data, and to Adam Greenberg, Amy Westergren, Meghan Pianta, Dr. Tzvi Doron, and Zachariah Reitano for their feedback on the manuscript.

CONFLICT OF INTEREST

No direct funding was supplied for this study; however, the study was conducted at Ro, with whom all three authors are affiliated. As Drs. Broffman and Barnes are directly employed by Ro and were engaged at all levels of the study, Ro, as the de-facto sponsor organization, was involved in the design and conduct of the study, collection, management, and analysis of data, preparation, review and approval of the manuscript, and the decision to submit for publication.

Dr. Broffman is a full-time employee at Ro and has stock options in the company

Dr. Eisenberg serves as an unpaid advisor on Ro's medical advisory board and has stock options in the company

Dr. Barnes is a full-time employee at Ro

REFERENCES

1. Polinski JM, Barker T, Gagliano N, Sussman, Brennan TA, Shrank WH. Patients' Satisfaction with and Preference for Telehealth Visits. Journal of general internal medicine. 2016; 31: 269-275.
2. Rothberg MB, Martinez KA. Influenza Management via Direct to Consumer Telehealth: an Observational Study. Journal of General Internal Medicine. 2020; 1-3.
3. Rastogi R, Martinez KA, Gupta N. Management of Urinary Tract Infections in Direct to Consumer Telehealth. Journal of general internal medicine. 2019: 1-6.
4. Jain T, Lu RJ, Mehrotra A. Prescriptions on Demand: The Growth of Direct-to-Consumer Telehealth Companies. Jama. 2019; 322: 925-926.
5. Farr C. Ro, a 3-year-old online health provider, just raised a new round that values it at $1.5 billion
6. . 2020.
7. Coward RM, Carson CC. Tadalafil in the treatment of erectile dysfunction. Therapeutics and clinical risk management. 2008; 4: 1315.
8. Moore R, Edwards J, McQuay H. Sildenafil (Viagra) for male erectile dysfunction: a meta-analysis of clinical trial reports. BMC Urology. 2002; 2: 6.
9. Moore RA, Derry S, McQuay HJ. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. BMC Urology. 2005; 5: 18.
10. McMurray JG, Feldman RA, Auerbach SM. Long-term safety and effectiveness of sildenafil citrate in men with erectile dysfunction. Therapeutics and clinical risk management. 2007; 3: 975.
11. Moreira Jr SG, Brannigan RE, Spitz A, Orejuela FJ, Lipshultz LI, Kim ED. Side-effect profile of sildenafil citrate (Viagra) in clinical practice. Urology. 2000; 56: 474-476.
12. von Keitz A, Rajfer J, Segal S, Murphy A, Denne J, Costigan T, et al. A multicenter, randomized, double-blind, crossover study to evaluate patient preference between tadalafil and sildenafil. European urology. 2004; 45: 499-509.

Cite this article

Broffman L, Eisenberg M, Barnes M (2020) Rates of Patient-Reported Side Effects for PDE5 Inhibitors Prescribed on a Direct-to-Consumer Telehealth Platform. J Urol Res 7(2): 1122.