CONSUMER REPORTING OF PSYCHIATRIC DRUG EFFECTS ACROSS THE INTERNET: IMPROVED METHODS FOR UNDERSTANDING DRUG HARMS

Shannon Hughes[1]

[1]School of Social Work, Colorado State University, Fort Collins, USA

Abstract

Despite extensive clinical testing, much is unknown about psychiatric drugs' safety upon market release wherein millions of consumers might use the drug within a relatively short period of time. Existing online social networking sites populated by drug consumers, as well as mobile health technologies, offer promising opportunities to collect patient-reported harms data that could more quickly and accurately illuminate drugs' safety profile. This study assessed the viability of using online consumer-reported harms data in this way by conducting a grounded theory textual analysis of 960 randomly selected online consumer reviews from 4 websites (Webmd, RevolutionHealth, AskAPatient and CrazyMeds) for a popularly prescribed antipsychotic (quetiapine, n=480) and antidepressant (escitalopram, n=480) medication. Consumers taking escitalopram or quetiapine most frequently reported adverse effects related to fatigue/tiredness (23.8% and 33.1%), weight gain (13.1% and 22.5%), and symptom worsening (15.8% and 10%). Multiple quantitative and qualitative discrepancies appeared between consumer-reported effects and the approved drug label. For example, while 22.5% of consumers in this sample reported weight gain as an adverse effect of quetiapine, the drug label cites only a 4-6% incidence of weight gain across clinical studies. While professional literature explains that "drowsiness" is a "less severe side effect" of quetiapine, consumers described "extreme sleeping," "coma-like sleep," and being "unwakable – for the next 12 or more hours." Online consumer-reported drug experiences contribute valuable additional perspective and context for fully understanding the range and severity of drugs' potential harms and undesirable effects. Consumers' ability to contribute to the construction of harms-related drug information could be facilitated through the development of mobile applications designed to prospectively collect and organize real-time data from consumers who are newly initiating or changing medications.

Keywords

psychotropic drugs, safety surveillance, patient-reported outcomes, internet

Introduction

Psychiatric drugs, such as those in the antipsychotic and antidepressant classes, rank among the highest-selling prescription drugs globally and are prescribed for myriad indicated and off-label, psychiatric and non-psychiatric uses [1-3]. Poor safety monitoring is an extensively documented problem [4-5] that is particularly salient in psychiatric drug research and clinical use because, as psychoactive substances, these drugs produce a wide range of sometimes-unpredictable physical, psychological, emotional, and behavioral effects [6]. Deficiencies in safety assessment and reporting in the context of clinical trials, and recent large settlements resulting from lawsuits against pharmaceutical manufacturers for minimizing or concealing drug harms [7] highlight the fact that some drug effects remain unrecognized at the time of drug approval and too tardily recognized after a drug has reached the market. The result is a distorted benefit-to-harm ratio and a serious obstacle to evidence-based decision-making. There is, therefore, a critical need to develop new platforms and methods for the systematic collection of data that captures the full range of psychiatric drugs' varied effects. Existing online social networking sites populated by drug consumers, as well as mobile health technologies, offer promising opportunities to collect patient-reported harms data that could more quickly and accurately illuminate drugs' safety profile.

The objective of this study was to assess the viability of using spontaneously contributed psychotropic drug reports on the Internet to improve understanding of the scope and severity of drugs' effects. Recommendations are made for increasing the effectiveness and efficiency of collecting and utilizing consumer-reported data.

Methods

Sample

Websites were purposively selected to represent a range of social communities around psychotropic drug use. Two websites (AskAPatient and CrazyMeds) reflect primarily consumer-driven websites where most or all of the content is contributed by users. These websites are neither monitored or edited my medical or health professionals. Two websites (WebMD and RevolutionHealth) reflect reputable commercial health information portals intended for a general audience. These sites also provide dedicated space for users to rate and provide brief commentary on a treatment experience.

Escitalopram (Lexapro, Cipralex) and quetiapine (Seroquel, Xeroquel, Ketipinor) were selected as points of entry for this study because both were top-selling drugs in the antidepressant and antipsychotic classes, respectively, at the time of this research [8-9]. All consumer ratings and commentary about the two drugs from the four websites through the end of February 2009 were imported into QDA Miner 3.2 data analysis software. Each individual consumer was considered a single case. Data collection resulted in a sampling frame of 6,998 consumer cases. A stratified simple random sample of 120 consumer cases per drug per website (13.7% of the sampling frame) resulted in a coding sample of 960 cases (escitalopram, n=480; quetiapine, n=480).

Additional sources of drug information were used as a point of comparison for consumer-reported drug effects. These sources included the approved drug label, professionally derived health information found on WedMD and RevolutionHealth, and the peer-reviewed literature (i.e., systematic reviews, meta-analyses, and clinical studies of escitalopram and quetiapine).

Online consumer reviews were regarded in this study to be part of the public domain [10] and no personally identifiable information was collected. The Florida International University Office of Research Integrity approved this study.

Coding and Analysis

Grounded theory methods of initial and focused line-by-line coding were used to analyze reported drug effects. Initial coding aimed to condense and capture literal descriptions of drug effects, preserving as much as possible the actual language of the consumer. For example, consumers' exact descriptions, such as "extreme sleepiness," were used as code names instead of standard professional or regulatory codes such as "drowsiness" or "somnolence." Focused coding aimed to refine the initial codes into broader categories and groupings of drug effects. The final codebook identified 70 drug effects grouped into 11 categories

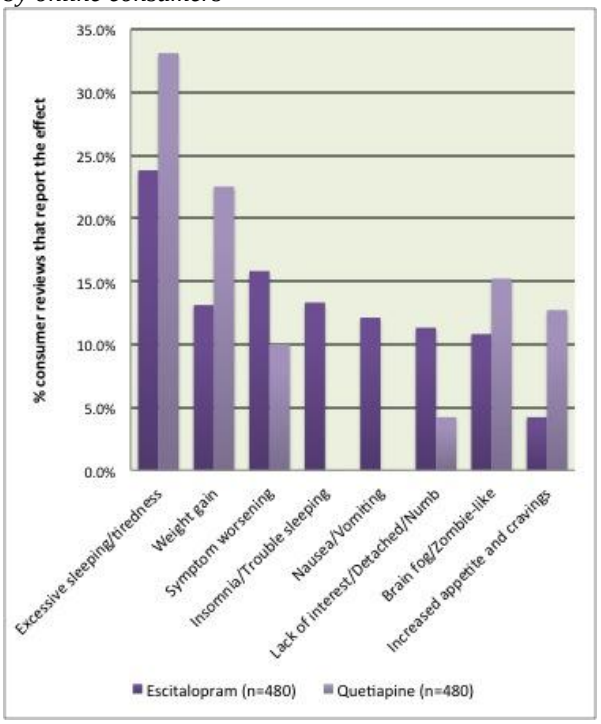
A coding agreement analysis was conducted by S.H. and a second independent coder on 191 (20%) randomly selected cases. Inter-coder agreement was calculated for each category of effect on the level of code occurrence within a case using Scott's pi (>0.70 pre-specified to indicate acceptable inter-coder agreement). All disagreements were resolved by discussion.

Descriptive statistics summarize consumer-reported drug effects, and textual excerpts illustrate differences in consumer-reported descriptions and the professional literature.

Results

Consumers taking escitalopram or quetiapine most often reported effects that impacted their mental state or mood (61.7% and 52.9% of consumers), and sleep effects (36% and 60.6%). Figure 1 details the most frequently reported adverse effects for each drug. Excessive sleeping and tiredness, weight gain, worsening symptoms (i.e., new or worsened depression, anxiety, irritability, or other psychological/behavioral conditions), and brain fog were frequently reported effects of both drugs.

Fig. 1: Most frequently reported adverse drug effects by online consumers



Multiple quantitative and qualitative discrepancies appeared between consumer-reported effects and the professional literature (i.e., the approved drug label, health information on WebMD and RevolutionHealth, and published clinical drug studies). For example, while 22.5% of consumers in this sample reported

weight gain as an adverse effect of quetiapine, the drug label cites only a 4-6% incidence of weight gain across clinical studies. While the health information provided on WedMD and RevolutionHealth explains that quetiapine "may cause drowsiness" and that this is a "less severe side effect" of the drug, consumers describe "extreme sleeping," "coma-like sleep," and being "unwakable – for the next 12 or more hours." This effect was interpreted by consumers as both desirable and undesirable, depending on individual need and circumstance:

"helped very, very effectively with sleep: 30 minutes max after taking (it), I am out for good" (#808)

"I like what this drug does to me (sleepy bye bye land)" (#613)

"So while it does provide me sleep…it's the kind of sleep that wouldn't allow me to be woken, even if my house is on fire. That scares me." (case #515)

"You'll sleep until next Tuesday. Of course, that could be a good thing, depending on how your life is at this moment" (#1084)

Table 1 provides additional examples of differences between consumer reports and the professional literature using common effects of escitalopram.

Tab. 1: Contrasting rates and descriptions of frequently reported effects of escitalopram

Drug Effect	Consumer Reviews from Present Study (n=480)	FDA-Approved Drug Label	Clinical Studies
Sleepiness	23.8%	6-13%	Mild, mixed sedative and stimulant properties
Weight Gain	13.1% "out of control; no relief even with exercise"	"no clinically important changes in body weight"	"Weight changes" – "less serious"
Sexual Dysfunction	20.2%	2-7%	20-80%

Consumer reviews in general discussed a broad range of physical, mental, emotional, and behavioral effects disrupting daily routines. Health information on WebMD and RevolutionHealth, in contrast, primarily emphasized physical adverse drug effects, such as dizziness, nausea, and blood-related changes, giving less attention to the range of other types of effects. The exception to this pattern was the frequent mention in both consumer and professional text of new or worsening psychiatric symptoms. Descriptions of this adverse effect, however, were qualitatively different between sources. Professionally-delivered health information cautioned repeatedly about "unusual behavior changes" and "unusual or severe mental/mood changes." Consumers offered more specific descriptive detail and situational context:

"(I) had some hypomania then extreme agitation then suicidality. The agitation was awful, felt like I was going to jump out of my skin" (#172)

"2 hours of alternating panic attacks/crying jags" (#130)

"I seemed to become more aggressive and assertive. I would just speak my mind whenever I got angry, and had no fear" (#41)

"I had my first manic experience which lasted about 30 minutes of complete reckless driving, I probably should have gotten arrested. And a few minutes later I came down into deep depression" (#258)

Discussion

Principal findings

Consumer drug reviews on the Internet report many of the same effects that already appear in the professional literature, but often at an apparently higher frequency and with greater precision and descriptive detail. Frequency estimates of "uncommon" or "infrequent" found on WebMD and RevolutionHealth were not proportional to the rate of consumers discussing the effect in their online commentaries, especially for sleep effects of quetiapine and sexual effects of escitalopram. Similarly, a large gulf exists between severity ratings of "less serious" in the professional literature and consumer descriptions of "the worst," "appalling," and "out of control" for many weight and sexual effects. However, the high incidence of an effect among consumer reviews may reflect its subjective burden on consumers more than its actual incidence in the drug using population or its severity in terms of potential health complications. Nevertheless, these important differences suggest that consumer-reported drug experiences contribute valuable additional perspective and context for fully understanding the range, severity, and impact of drugs' effects.

The professional literature and online consumer-reports are most clearly and prominently differentiated by the rift between listing drug effects and describing drug experiences. Language used to list effects in professional literature tended to be vague (i.e., "drowsiness") and fixed (i.e., "less severe"). The information was homogenized and the diversity of experiences was erased, making room for more simple and straightforward treatment decisions. The information reported by consumers represented a greater diversity of perspectives, and effects were presented in a more specific and relatable manner with situational examples. Although this finding is of little

surprise considering the respective sources of data, the significance of this finding should not be underestimated. For example, what can be learned from consumers is that "drowsiness" caused by quetiapine can sometimes translate to "coma-like sleep" or having to miss work or school because of the inability to stay awake. This drug effect was not always interpreted by consumers as necessarily "adverse," as some found this effect desirable – perhaps even their primary reason for taking the drug. For "new or worsened symptoms," the professional literature summarized in list form the adverse mental or mood effects cited in warnings on the drugs' labels. Consumers reported these same effects, but with many examples of how they can manifest in various combinations and with varying degrees of severity. Consumers' experiential data provides the context that is absent from fixed lists of effects found in professional sources of drug information and thus facilitates more fully informed treatment decision-making.

In sum, it appears that both sources of understanding and information (i.e., scientific data from clinical studies and experiential data from drug consumers) each have advantages that offset the other's limitations. Both sources should be cultivated and integrated into standards of drug assessment in order to construct a comprehensive and accurate knowledge base.

Future research – Going mobile

Online consumers in this sample offered full and descriptive accounts of drug effects, but the usability of this information is limited by the volume of data (i.e., thousands of single, dispersed comments) that require sorting and analyzing. Additionally, while one-third of Internet users report consulting consumer-generated content for aiding treatment decisions, only 6% of users contribute this content [11]. Consumers of psychiatric drugs who use the Internet and contribute their treatment experiences are a special population of drug consumers that likely do not represent the majority of the drug using population.

Consumers' ability to more effectively and deliberately contribute to the construction of harms-related drug information could be facilitated through the development of mobile applications designed to prospectively collect and organize real-time, naturalistic data from drug consumers. This technology would need to be capable of collecting a variety of structured and unstructured data on physical, psychological, emotional, and behavioral drug effects, as well as other variables potentially relevant to clinical outcomes, such as treatment expectancy and attitudes towards drug use. A mobile technology could also provide users instant feedback in case an important safety issue is signaled by the user's input.

Such technology would contribute to a more comprehensive appraisal of psychiatric drug effects and increased diligence and speed in identifying potential safety concerns. Beyond enhancing individual patient safety in outpatient care, this technology could be introduced into clinical trials as an improved methodology for collecting harms data and, if adopted on a wider scale, also supplement passive safety surveillance mechanisms. Integrating mobile technology for consumer-reported drug effects into standard clinical practice and research protocol could thus introduce a much-needed new paradigm for psychiatric drug monitoring and assessment.

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Shannon Hughes, Ph.D.
School of Social Work
College of Health and Human Sciences
Colorado State University
1586 Campus Delivery, Education 119
Fort Collins, Colorado, USA 80523
E-mail: shannon.hughes@colostate.edu
Phone: +01 970 491 5654