Information about benzodiazepines: what does the internet offer us?

Abstract This study analysed the quality of information published on the internet regarding 4 benzodiazepines that are widely used in Brazil: alprazolam, bromazepam, clonazepam and diazepam. This choice is justified by the fact that these drugs are widely used and can generate chemical dependency, and the internet is an important source of information about them. We analysed 20 sites for each drug. More than half (56.3%) of the sites were classified as deficient or very deficient. The most frequent problems with the sites were the absence of a description of the person responsible for the site (60%), incomplete information (62.5%), the absence of a contact for additional information (45%) and the absence of the last date the site was updated (82%). These results reinforce concerns regarding the quality of the health information published on the internet, which has already been noted in the literature, and the need to adopt minimum quality criteria for this information.

Key words Internet, Drug, Information
Introduction

The advent of the Internet has revolutionized both the access to information and health relations. Internet access has increased significantly, reaching just over four billion users in 2018, accounting for 55.1% of the world’s population. In Brazil, continuous National Household Sample Survey (PNAD) data from 2016 showed that there was internet use in 48.1 million households visited, which represented 69.3% of households.

The health-related information is becoming increasingly available on the websites and pages of public and private institutions. Easy access to information assists in the day-to-day life of both health professionals and users, directly influencing the doctor-patient relationship. In Brazil, the Internet has already reached the 75 million users mark, taking the country to fifth place in the search for health information on the Internet.

Silvestre et al. interviewed patients in the 18-60 age group in a waiting room for outpatien
t care in the city of Tubarão, Santa Catarina, and observed that 50% of the interviewees used the Internet to access health information were individuals between the ages of 31-45 and were women.

Moretti et al. interviewed 1,828 individuals and observed that the internet has been a source of health information with great relevance to the population, predominantly being used by women seeking information for their own health (92%). For most of these women (86%), the internet is one of their main sources of health information. The authors report that 69% of respondents acknowledge the impact of the internet on their relationship with physicians and that 16% and 10% of them asked the doctor to prescribe a specific drug or to change the prescribed drug, respectively, after an online consultation. Fifty-two percent of these people stated that doctors have met these requests.

Sinclair et al. interviewed 284 pregnant women and observed that 39% of them were using medication when they found themselves to be pregnant. Of these women, 79% used the internet to seek information about the safety of these drugs during pregnancy.

Pereira Neto et al. analysed the profile of online information consumption by young people from a popular community in a waiting room for medical consultation in a primary care clinic linked to the Unified Health System and observed that although these young people searched for in-
formation on the network, they continued to use the doctor as their main source of information.

However, the quality of health information on the Internet is still a challenge worldwide. Often, health information on the Internet is inaccurate, incomplete, or incomprehensible to readers, posing risks to users. Several studies have addressed the evaluation and qualification of websites on the internet. An instrument that is widely used in evaluating the quality of health pages is proposed by the Health On the Net (HON) Foundation, a Swiss nongovernmental organization. The HON Foundation grants a certificate of quality to pages that comply with its code of conduct, which has seven basic principles: authorship, complementarity, confidentiality, attribution, justifications, transparency and publicity honesty.

In Brazil, several authors have proposed the development and use of mechanisms to evaluate the quality of information on health pages. The Sanitary Surveillance Center (CVS) of the state of São Paulo has translated and adapted a document from the World Health Organization (WHO), entitled the Guide to Finding Safe Information, with the objective of providing users with criteria for evaluating site content, such as the name and contact information of the person responsible, publication dates, identification of funders and the objectives of page. The Regional Council of Medicine of the State of São Paulo also published a manual with ethical principles for medical and health websites.

An alternative evaluation model was created by Pereira Neto et al., with a proposal of three dimensions for evaluation: content, usability and readability, subdivided into indicators to which weights are assigned. These added values allow one to create a page ranking, making it possible to identify weaknesses and strengths of each site, in addition to pointing out how accurate the information on the proposed theme is.

Benzodiazepines are among the most prescribed drugs in the world. According to data from the National Controlled Products Management System, of the five active substances with greatest consumption in Brazil between 2007 and 2010, three are benzodiazepines. Two drugs in this class are included in the list of the 100 most marketed drugs in 2017 in the country. Several authors point to the high prevalence of these drugs in the Brazilian population, even without a medical prescription.
net regarding the 4 benzodiazepines that are the most widely used in Brazil: alprazolam, bromazepam, clonazepam and diazepam. This choice is justified by the fact that these drugs can generate chemical dependence, and the internet is an important source of information about them.

Methods

The identification of the sites occurred through a search on Google, the main search engine in use in Brazil, using the common Brazilian denomination (DCB) of medicines as a keyword. We used the DCB of each drug because it allows the recovery of both the sites that treat the product by the trade name and those that exclusively refer to benzodiazepines with this name. For each drug, the first 20 sites recovered were selected. The exclusion criteria were official sites of public agencies or sales sites that did not provide information about the product. Official sites from public agencies were excluded because, in principle, they are not directly influenced by commercial interests or groups of users and are usually developed by trained professionals.

The choice of evaluation criteria (Chart 1) was based on the work of Pereira Neto et al.\(^2\)\(^3\) in terms of content and design. Regarding the content, the accuracy and comprehensiveness of the information, the name and other data of the owner / the party responsible for the site information, as well as their references and the date of the last update, were considered. To assess the accuracy, which involves the degree of agreement between the information available and the available scientific evidence\(^4\), the content of the site was compared to the technical data available in the bulletin of the National Sanitary Surveillance Agency\(^3\). The ANVISA bulletin was taken as a parameter, once it was approved by the Brazilian regulatory agency, due to its official character. The same text was used to analyse the comprehensiveness of the information, defined by Pereira Neto et al.\(^2\)\(^3\)\(^4\), such as the degree of the coverage of the information. The information specified, in addition to the indications, the contraindications of the product, the indication of the need for professional follow-up regarding the use of the product in the body of the site information, and the DCB for the medicine. To evaluate the existence of financial interests, both where the product could be purchased and expressions of suggested use or that offered information such as dose were considered. In terms of the design, the existence of distractions, such as animations, advertisements and the presence of images, for example, was considered, as well as the language used (Chart 1).

Each site was independently evaluated by two team members. If there was disagreement between the analyses of any indicator, a third individual performed the analysis, and the opinion of the majority prevailed.

Sites that scored higher than 80 were considered to have good quality information, those with scores less than 80 but greater than or equal to 50 were considered regular, those with scores less than 50 but greater than or equal to 30 were considered deficient, and those with scores lower than 30 were considered very deficient.

The data from the evaluation were stored in a spreadsheet from the Microsoft Excel 2010 software. For the analysis of the results, descriptive

<table>
<thead>
<tr>
<th>Chart 1. Aspects considered in the evaluation of sites.</th>
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<tbody>
<tr>
<td><strong>Aspect</strong></td>
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<tr>
<td><strong>Content</strong></td>
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<tr>
<td></td>
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<tr>
<td><strong>Design</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>
statistics tools were used with the aid of the same software.

In addition, the sites that had the HON Foundation seal of quality were evaluated. The clarity and adequacy of the site language was also analysed, and the use of technical terms that could make it difficult to understand the text and the type of language adopted (technical or lay) was taken as a parameter.

The Kruskal–Wallis test was used to evaluate the difference in scores obtained by different types of sites (blogs, sales sites and discussion sites) and between the different drugs.

Results

In total, 80 sites were analysed (twenty for each drug), and the majority were blogs (40%), sales sites / companies (27.5%), sites that had drug inserts (21.2%) and discussion sites (2.5%).

The sites analysed had a lower score and, therefore, more problems in relation to the presentation of the site manager (60%), incomplete information (62.5%), contact for additional information (45%) and date of update (82%). (Figure 1).

In general, the presence of user distraction elements, such as images and videos, was observed in advertisements on almost half of the sites (47.5%), especially on those related to the drugs bromazepam (65%) and alprazolam (50%). The suggestion of where to buy the product was observed on 31.2% of the sites, while contraindications were absent on 37.5% of them.

For clonazepam, alprazolam, 90% of the sites were regular or deficient (mean score = 45, fashion = 40). For bromazepam, the majority (55%) were considered deficient (mean score = 48.5, fashion = 40) (Table 2). 60% of the sites were deficient or very deficient (mean score = 47, fashion = 40), and for diazepam, 50% were considered good or regular and 50% deficient (mean score = 52, fashion = 40) (Table 2).

Information about where to have access to the drug was present on 40% of the clonazepam and diazepam sites and was present on only 25% and 20% of the alprazolam and bromazepam sites, respectively. The need for professional counselling for consumption was absent in 45% of clonazepam and bromazepam sites, which may influence consumption by self-indication. The absence of a contact for additional information was observed on 85% of the sites for clonazepam.

All websites of sales companies exhibited the “banned internet sale” indicator, as determined by ANVISA.

More than half (56.3%) of the sites were classified as deficient or very deficient (Table 3). Only two sites (2.5%) had the HON seal at the time of analysis. One of these sites was considered to have the best score for both alprazolam and bromazepam but was classified as regular for bromazepam and clonazepam. The information provided in the second site, however, was considered deficient for all 4 medications.

Comparing the scores obtained by the different medications showed no statistically significant differences at a significance level of 5% (p = 0.7168). There was also no statistically significant difference between the scores of the different site types for each drug: alprazolam (p = 0.9933), bromazepam (p = 0.8932), clonazepam (p = 0.8378) and diazepam (p = 0.6866). However, when considering the complete set of sites analysed, the difference between the scores obtained by the different site types was statistically significant (p = 0.0018), with sites with the package insert format having a better score. There was no statistically significant difference between the results of company websites and blogs (p = 1), and both were inferior to the package insert sites.

For sites that spoke about diazepam, the main source for additional contact was by telephone (50%), followed by question and answer mechanisms (37.5%) and e-mail (18.75%). For bromazepam, question and answer mechanisms was the predominant form of additional contact on 45% of sites, while the telephone represented 55% of the contact options. For clonazepam, on the 3 sites that presented additional contact information, the predominant mode was by telephone. For alprazolam, only 45% of the sites had an additional form of contact: 55% used question and answer, and 22.5% each used either telephone or email.

The use of lay language was observed on 55% of sites involving alprazolam and bromazepam, 45% of diazepam sites and 40% of clonazepam sites. The imbalance between indications of use and the presentation of contraindications and care was observed on 36.5% of all sites analysed.

Discussion

Of the 80 sites analysed, 56.3% were classified as deficient or very deficient. This result is in agreement with that found by Pereira Neto et
Figure 1. Global performance of analysed sites (N = 80), 2018.

Table 1. Percentage of indicators present on the sites analysed for each drug, N=80, Niterói, 2018.

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Alprazolam</th>
<th>Bromazepam</th>
<th>Clonazepam</th>
<th>Diazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Content Is the site explicitly responsible?</td>
<td>35</td>
<td>35</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Is the information about the medicine complete and according to ANVISA's bulletin?</td>
<td>35</td>
<td>7</td>
<td>7</td>
<td>40</td>
</tr>
<tr>
<td>Are the contraindications presented?</td>
<td>55</td>
<td>11</td>
<td>65</td>
<td>13</td>
</tr>
<tr>
<td>Does it indicate the need for professional follow-up?</td>
<td>70</td>
<td>14</td>
<td>55</td>
<td>11</td>
</tr>
<tr>
<td>Does it use Brazilian common denomination (DCB)?</td>
<td>100 *</td>
<td>20</td>
<td>95**</td>
<td>19</td>
</tr>
<tr>
<td>Does it contain the date of the last update?</td>
<td>10</td>
<td>2</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Is there a contact for additional information?</td>
<td>45</td>
<td>9</td>
<td>60</td>
<td>12</td>
</tr>
<tr>
<td>Does it have suggested use guidelines?</td>
<td>25</td>
<td>5</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Is there a suggestion for where to get the medicine?</td>
<td>25</td>
<td>5</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Design Is there any element of distraction?</td>
<td>50</td>
<td>10</td>
<td>65</td>
<td>13</td>
</tr>
</tbody>
</table>

* Two sites used both DCB and the product’s trade name. ** Two sites used both DCB and the product’s trade name. *** Four sites used both DCB and the product’s trade name.
al., who, when evaluating 8 NGO sites related to HIV/AIDS, observed that only one site presented content that was in accordance with what was expected from at least 50%. A similar result was observed by Neumark et al.14 when analysing 29 Hebrew sites about contraceptives based on HON codes. The average accuracy rating of the sites was 50.9%.

Paolucci et al.15 evaluated the quality of information on tuberculosis on Brazilian sites and showed that no site obtained more than 65% compliance with the quality criteria adopted in the evaluation. Del Giglio et al.32 evaluated the quality of information related to diabetes mellitus, systemic arterial hypertension and acute myocardial infarction, also on national sites, and observed that the information was often inadequate and insufficient.

Yoon et al.18 analysed Korean sites on inflammatory bowel disease and concluded that the quality of the information was not ideal and varied significantly both in relation to the type of site but also in the search tool used. The authors also noted that the quality of the information was not related to the position in which the site appears in the search results.

The absence of responsible content (60%) and the date of update (82%) in most of the analysed sites directly affected the reliability of the site, as noted by Newmark et al.14, Mendonça and Pereira Neto2 and Molino and Melo33. In addition, the lack of these features makes taking responsibility for the information provided unfeasible. These results are in agreement with other studies34,35. In contrast, Hirata et al.36 identified a description of the person responsible for 79.3% of the 4 Brazilian sites on coronary disease analysed.

The incomplete information observed on 62.5% of the sites is in agreement with the literature4-14,35,37,39 and compromises the possibility that the user can adequately analyse the safety and feasibility of using the product or the health problems treated by the site. The imbalance in information, also noted by several authors1,35,38, highlighting the benefits and omitting the contraindications, is another aspect that may expose the user to risk by leading him or her to consume unnecessary or inappropriate products. This same strategy is observed in media pieces advertising drugs, such as in advertisements for drugs broadcast on radio stations40 and those arranged in pharmacies and drugstores41. A similar strategy was observed in scientific journal articles in a magazine that is highly circulated in Brazil13.

The concern with the quality of the information made available specifically on psychoactive drugs, such as benzodiazepines, in advertisements was also noted by Mastroianni et al.38. The authors note that these pieces presented incomplete, summarized, inconsistent and different information from the studies cited in the scientific text, always favouring therapeutic indication, efficacy, safety and the cost of the products.

The internet will continue to grow as a health information provider, but the means by which this information reaches the patient should not compromise characteristics such as accuracy, credibility, quality and comprehensibility of information42. In this context, engaging those responsible for sites that provide health information with codes of conduct or quality standards is important43-45. Varady et al.44 analysed sites containing information on osteoarthritis in several countries and found that HON-certified sites or those using the DISCERN instrument, which is

<table>
<thead>
<tr>
<th>Medication / Site classification</th>
<th>good</th>
<th>regular</th>
<th>deficient</th>
<th>very poor</th>
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<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>45</td>
</tr>
<tr>
<td>Bromazepam</td>
<td>3</td>
<td>15</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>2</td>
<td>10</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>Diazepam</td>
<td>4</td>
<td>20</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>11.25</td>
<td>26</td>
<td>32.5</td>
</tr>
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</table>
used for consumers to assess the quality of written information about treatment choices obtained significantly higher scores than those without certification. A similar result has been indicated by other studies.

In this sense, the low number of sites on benzodiazepines with HON certification (2.5%) is worrying. The percentage of sites with HON certification varied significantly between different studies, with 4% to 60% of certified sites being found. Equally relevant is the fact that, even on the sites with HON certification, problems of information quality were observed. This result is in agreement with Grohol et al. The statistically significant difference in the evaluation of the 80 sites analysed according to the type of site is in agreement with the results observed by other authors. Yoon et al. observed superior quality in institutional sites. Support sites (maintained by support groups, users, etc.) had the lowest scores in terms of quality assessment. Grohol et al. observed superiority in the quality of the sites with the HONCode seal and without commercial interests. The variation in relation to the search tool pointed out by these authors, however, was not analyzed in this work.

Another relevant aspect is the fact that benzodiazepines are identified, by some authors, as the main drugs involved in exogenous intoxications in Brazil. It is reasonable to assume that the ease of access to information about these products on the internet and the low quality of this information may be factors that contribute to the irrational use of these products. In addition, in Brazil, even medications that require the presentation of a medical prescription are easily purchased on the market. Several authors point to the indiscriminate use, including self-medication, of benzodiazepines, and their consequences for the population’s health.

Conclusion

Despite the limited number of sites analysed, i.e., only sites in the Portuguese language that were retrieved by a single search tool, in addition to the use of the ANVISA bulletin as a parameter for comparing product information, which is the main limitation of this study, the results show the poor quality of information available on the internet regarding benzodiazepine medicines. In this way, these results reinforce the worldwide discussion on the need to regulate health-related content available on the Internet.

The low percentage of sites that have a quality label, such as HON certification, for example, shows the low level of concern the developers of these pages have for offering a reliable parameter of evaluating the content of the site for users. This lack of concern is reinforced by the lack of basic information such as identification of those responsible for the available content, the references used and the date of updating the content, which are all relevant to the reliability of the information provided.

In this way, the regulation of the information presented on these sites and the application of quality stamps in Brazil are crucial for the user to know what information can be trusted, thus avoiding the irrational use of medicines and the serious health problems that could result from the use of medicines due to a lack of or low quality information provided.
Collaborations

SR Castilho participated in defining the methodology, analyzing the results and writing the text. TB Ramos, LC Bokehi, EB Oliveira and MSA Gomes participated in the discussion of the methodology, collected the data, participated in the analysis of the data and the writing of the text. JR Bokehi participated in the discussion of the methodology, data analysis and text review.

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