Evaluation of physicians’ practices, attitude and perceptions towards biosimilars usage among patients

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Citation

ABSTRACT

Objective: This study evaluated the current practices, attitude and perceptions towards biosimilars among physicians in Saudi Arabia.

Methods: A cross-sectional study was conducted using the convenience sampling method to collect data among physicians in Saudi Arabia. Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 24.0 were used to analyze data using descriptive and inferential statistics. A p-value of <0.05 was considered to interpret the obtained results as statistically significant.

Results: According to the findings of the study, most of the physicians had positive attitude and good perceptions about biosimilars usage, safety, efficacy and overall effectiveness. Among the study participants, some of the physicians were already practicing prescribing biosimilars to their patients. Statistically, a significant association (p-value <0.05) and positive correlation were also observed among attitude questions and perceptions of the physicians about overall biosimilars’ information and their efficacy and effectiveness.

Conclusion: This study concluded that the studied physicians had positive attitude and good perceptions about biosimilars in Saudi Arabia.

Keywords: Biosimilars, physicians, practices, attitude, perception, Saudi Arabia
1. INTRODUCTION
These days, for numerous life-threatening and debilitating diseases, biologic therapies are often used however their therapeutic effectiveness can further be improved if access of patients to these medications is well-controlled (Braun et al., 2016). Numerous biological medications have a competitive version, produced from other cell lines by other manufacturers, known as biosimilars or biosimilar medicines (Kurki et al., 2017). They are not identical, but have structural and functional similarities, which should be reflected in their efficacy, clinical properties and safety (Tsiftsoglou et al., 2013; Jarrett et al., 2015).

Biosimilars are novel medicines that were first approved in 2006 by the European Medicines Agency (EMA) (Stanhope et al., 2010). According to EMA, biosimilarity of a medicinal product means its higher similarity in terms of its efficacy, structure, biological activity, immunogenicity to the original product and safety (Sieczkowska et al., 2018; EMA, 2020). However, biosimilars are complex proteins and as a result, these medicines will never be an identical duplicate of the original, due to their heterogeneous nature, batch-to-batch variability, complexity and high molecular weight (O’Callaghan et al., 2017). Compared to generic medicines, biosimilar drugs are more complex and require extensive investigation to obtain a marketing authorization (Cohen et al., 2017).

These new drugs have nowadays become a big part of pharmacotherapies and used by many practitioners in the treatment of several diseases, like rheumatoid arthritis, cancer, Crohn’s diseases, colitis, diabetes mellitus, osteoporosis, anemia, immunologic disorders and other ailments, both in adults and in children (Cohen et al., 2017; USFDA, 2015). The regulatory framework applicable to biosimilar medications is well-defined both by European Medicines Agency (EMA) and the Food and Drug Administration (FDA) (Lucio et al., 2013; EMA, 2014). FDA approved Zarxio as a first biosimilar in March 2015 and the last approved biosimilar is Avasol that was approved in December 2019 (FDA, 2020). The approval of biosimilar products can increase the number of medication options with lower costs.

Healthcare providers could play a key role in the introduction and managing of biosimilars into healthcare systems in terms of their appropriate usage. Healthcare providers like physicians, pharmacists and nurses’ awareness about biosimilars is vital in biosimilars’ clinical adaptation and usage in patient care practices (Stevenson et al., 2017). This study aimed to assess physicians’ practices, attitude and perceptions towards biosimilars in Saudi Arabia.

2. MATERIALS AND METHODS

Study design, duration and research instrument
A cross-sectional study was conducted among physicians of various healthcare setups in Saudi Arabia. A self-developed research tool which was validated using the content and face validity was used to collect the data from May 2019 to August 2019. Stratified convenience sampling method (as non-probability form), was used to approach practicing physicians. Attitude of studied physicians was observed as negative, neutral and positive. Perceptions about biosimilars were observed as Yes and No for correct and incorrect answers respectively.

Statistical analyses
Descriptive statistics were used to evaluate the demographic and personal characteristics of the study physicians. Categorical variables were presented as percentages and frequencies and continuous variables were presented as means and standard deviations. Spearman’s correlation coefficient test was used to determine differences among study participants regarding attitude and perceptions about biosimilars. A p-value of <0.05 was considered to interpret the obtained results as statistically significant.

3. RESULTS
Data from a total of studied physicians were collected. The physicians were from different specialties as shown in figure 1.

Regarding the prescribing of biosimilars, the physicians mainly prescribed adalimumab (8%), sulfasalazine (7%), and azathioprine (7%), followed by others. The results are illustrated in figure 2.

This study showed that around 22% of the physicians were familiar with biosimilars. Mixed findings were observed regarding their familiarity regarding reference biologics. And about 32.4% of the physicians were not familiar with general (local) rules and regulations regarding prescribing biosimilars in Saudi Arabia. The study findings are denoted in table 1. Table 2 represents physicians’ attitude towards biosimilars. The studied physicians were generally comfortable prescribing biosimilars to their patients (44%) and only 4% were not comfortable with it. Table 3 denotes that only 7.6% of the physicians were not familiar with the basic information regarding biosimilars. But as a whole, the majority of the physicians were quite familiar with positive perceptions about biosimilars.
Figure 1 Study physicians with their specialties

![Pie chart showing specialties of physicians]

Figure 2 Prescribed biosimilars to patients by the physicians (%)

![Bar chart showing prescribed biosimilars]

Table 1 General familiarity of physicians about biosimilars in Saudi Arabia

<table>
<thead>
<tr>
<th>Statements</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familiarity of biosimilars</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not familiar</td>
<td>45</td>
<td>42.9</td>
</tr>
<tr>
<td>Somewhat familiar</td>
<td>37</td>
<td>35.2</td>
</tr>
<tr>
<td>Familiar</td>
<td>11</td>
<td>10.5</td>
</tr>
<tr>
<td>Very familiar</td>
<td>12</td>
<td>11.4</td>
</tr>
<tr>
<td>Familiarity of reference biologics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference biologics are generic versions of biosimilars</td>
<td>32</td>
<td>30.5</td>
</tr>
<tr>
<td>Reference biologics are somewhat similar to biosimilars</td>
<td>26</td>
<td>24.8</td>
</tr>
<tr>
<td>Reference biologics are identical copies of biosimilars</td>
<td>31</td>
<td>29.5</td>
</tr>
</tbody>
</table>
I do not know & 16 & 15.2  

**Familiarity of local rules and regulations regarding biosimilars**

<table>
<thead>
<tr>
<th>Familiarity</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not familiar</td>
<td>34</td>
<td>32.4</td>
</tr>
<tr>
<td>Somewhat familiar</td>
<td>42</td>
<td>40.0</td>
</tr>
<tr>
<td>Familiar</td>
<td>22</td>
<td>21.0</td>
</tr>
<tr>
<td>Very familiar</td>
<td>7</td>
<td>6.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statements</th>
<th>Negative</th>
<th>Neutral</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am generally comfortable prescribing biosimilars to my patients.</td>
<td>4 (3.8)</td>
<td>57 (54.3)</td>
<td>44 (41.9)</td>
</tr>
<tr>
<td>If a biosimilar has good efficacy and effectiveness it should be approved to prescribe.</td>
<td>4 (3.8)</td>
<td>28 (26.7)</td>
<td>73 (69.5)</td>
</tr>
<tr>
<td>In my view, biosimilars are exact replacement of generic drugs.</td>
<td>20 (19.0)</td>
<td>32 (30.5)</td>
<td>53 (50.5)</td>
</tr>
<tr>
<td>I believe it is difficult to obtain information about clinical efficacy and safety for biosimilar products.</td>
<td>8 (7.6)</td>
<td>28 (26.7)</td>
<td>69 (65.7)</td>
</tr>
<tr>
<td>In my view, biosimilars’ clinical trial data must be included in labeling of biosimilars to further guide prescribers and patients.</td>
<td>2 (1.9)</td>
<td>18 (17.1)</td>
<td>83 (79.0)</td>
</tr>
<tr>
<td>In my opinion, details of clinical effectiveness of biosimilars are imperative to know before prescribing to patients.</td>
<td>0 (0.0)</td>
<td>14 (13.3)</td>
<td>91 (86.7)</td>
</tr>
<tr>
<td>I believe, biosimilars would have high side effects than their reference products.</td>
<td>6 (5.7)</td>
<td>36 (34.3)</td>
<td>63 (60.0)</td>
</tr>
<tr>
<td>Biosimilars must undergo a rigorous post-marketing surveillance, to know their exact efficacy.</td>
<td>4 (3.8)</td>
<td>12 (11.4)</td>
<td>89 (84.8)</td>
</tr>
<tr>
<td>In my view, biosimilars are an excellent addition in clinical practice which will have a greater impact on disease management in upcoming years.</td>
<td>4 (3.8)</td>
<td>49 (46.7)</td>
<td>52 (49.5)</td>
</tr>
<tr>
<td>I am comfortable in prescribing biosimilars to my patients only if their efficacy, safety and effectiveness are established and are approved by SFDA.</td>
<td>4 (3.8)</td>
<td>57 (54.3)</td>
<td>44 (41.9)</td>
</tr>
</tbody>
</table>

**Table 3 Perceptions of physicians about biosimilars N (%)**

<table>
<thead>
<tr>
<th>Statements</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biosimilars are developed without a strict comparison to reference products.</td>
<td>8 (7.6)</td>
<td>97 (92.4)</td>
</tr>
<tr>
<td>Biosimilars are therapeutic proteins that may have clinically significant differences in formulation, doses/dosing regimen, efficacy, safety, and immunogenicity.</td>
<td>34 (32.4)</td>
<td>71 (67.6)</td>
</tr>
</tbody>
</table>
Biosimilar are biologics that are altered to achieve high drug safety, efficiency and efficacy than reference products. 22 (21.0) 83 (79.0)

Biosimilars are biological medicinal products that contain high similarity to their reference biologics. 22 (21.0) 83 (79.0)

I do not know about efficacy and effectiveness of biosimilars. 18 (17.1) 87 (82.9)

As demonstrated in table 4 and figure 3-5, statistically a significant association ($p$-value < 0.05) and mild to moderate correlation (0.155-0.477) were observed between the some of the attitude questions and perception of physicians regarding their attitude and perception that biosimilars are biological medicinal products that contain high similarity to their reference biologics.

Table 4 Correlation between attitude and perceptions of physicians about biosimilars

<table>
<thead>
<tr>
<th>No.</th>
<th>Statements</th>
<th>$r$-Value</th>
<th>$p$-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Biosimilars are biological medicinal products that contain high similarity to their reference biologics. vs I am generally comfortable prescribing biosimilars to my patients.</td>
<td>0.155</td>
<td>0.026*</td>
</tr>
<tr>
<td>2</td>
<td>If a biosimilar has good efficacy and effectiveness it should be approved to prescribe.</td>
<td>0.291</td>
<td>0.019*</td>
</tr>
<tr>
<td>3</td>
<td>Biosimilars are biological medicinal products that contain high similarity to their reference biologics. vs I am comfortable in prescribing biosimilars to my patients only if their efficacy, safety and effectiveness are established and are approved by SFDA.</td>
<td>0.317</td>
<td>0.008*</td>
</tr>
</tbody>
</table>

* Statistical correlation is significant at 0.05 level

Figure 3 Correlation of statement 1 with statement 2
4. DISCUSSION

Until December 2019, USFDA had approved about 26 biosimilars which include 5 adalimumab products, 5 trastuzumab products, 4 infliximab products, 3 pegfilgrastim products, 2 rituximab product, 2 bevacizumab product, 2 etanercept product, 2 filgrastim product, 1 epoetin-alfa product. This study was especially aimed to evaluate the current practices, the attitude and perceptions of the physicians about biosimilars practicing in various parts of the country. This study was novel in its types as there was no study evident in literature from Saudi Arabia. When considering licensure of a biosimilar product, USFDA reviews the whole data including the foundation of detailed analytical characterization, in vivo studies, clinical pharmacology and other comparative clinical studies if needed (USFDA, 2020). For approval, USFDA requires both biosimilar and reference biological products meet its approval standards so that both patients and health care specialists can rely on the safety and effectiveness of the biosimilars. This all done to mitigate prescribers’ apprehensions that after approval by FDA there will be no clinical and meaningful differences exist between a biosimilar with its reference product (USFDA, 2020; Calvo et al., 2015). The USFDA issued a book known as “Purple Book” lists biological products, including any biosimilar and interchangeable biological products approved and licensed under the Public Health Service Act (USFDA, 2020; Calvo et al., 2015).
In current study findings, about 34 (32.4%) of the physicians were not familiar with general rules and regulations regarding prescribing biosimilars in Saudi Arabia. Only about 31 (29.5%) of the studied physicians answered correctly the question that “reference biologics are identical copies of biosimilars” which shows that their familiarity about the difference between biosimilar and reference products was not that good. Biosimilars are identical copies or similar to their reference biologics. On the other hand, around 45 (42.9%) were not familiar with general information and details of biosimilars. Similar results were reported in a study among physicians in Russia (Karateev et al., 2019). The majority of studied physicians showed a positive attitude in prescribing biosimilars to the patients if their safety and efficacy is evidenced by the SFDA. Approximately, 73 (69.5%) of the physicians were of the view that if efficacy and effectiveness of a biosimilar is established then it should be approved to prescribe and practice among the patients by the physicians in Saudi Arabia has well it should be approved to prescribe. On the other hand, a total of 91 (86.7%) of the physicians believed that the details of clinical effectiveness and safety of biosimilars are imperative to know before prescribing them to patients. Around 89 (84.8%) of the physicians also showed a very positive attitude about another question that biosimilars must undergo a rigorous post-marketing surveillance, to know their exact efficacy before prescribing to the patients. Our study findings are also similar to another study conducted in Russia, where physicians generally had a positive attitude towards biosimilars (Karateev et al., 2019).

In perception of the physicians about biosimilars, overall good perception was noted among physicians in Saudi Arabia about biosimilars. A total of 97 (92.4%) reported that they perceive that biosimilars are not developed without a strict comparison to reference products. In terms of concept that biosimilars are biological medicinal products that contain high similarity of their reference biologics, the majority of the physicians perceived positive (83 (79.0%). Similar results were observed by two other studies done by Karateev et al in Russia and Teeple et al. in United States (Karateev et al., 2019; Teeple et al., 2019). In opposition, just 18 (17.1%) of the studied physicians were not fully aware about efficacy and effectiveness of the biosimilars. Our study results were also in line to another study conducted in Maltese physicians where they determined that biosimilars’ perception amongst Maltese clinicians was also positive (Cassar et al., 2016).

Overall, the results show that there was not good familiarity and awareness shown related to biosimilars among physicians in Saudi Arabia. On the other hand, there was a greater positive attitude was observed among majority of the physicians towards biosimilars. There are two limitations associated with this study; firstly the participants were not analyzed by the physicians’ expertise, educational level and their total practicing experience. Secondly the results reported in the study are the self-response and self-assessment of the physicians which may not reflect their actual clinical practice, attitudes and perceptions about biosimilars in Saudi Arabia.

5. CONCLUSION

The results of this study emphasize that better and extensive medical education and awareness is required to advance physicians’ understanding about prescribing biosimilars to their patients and to improve their overall attitude and perceptions towards biosimilars. Improvement and advancement of the medical education can be done in the form of continuous professional development (CPDs) and continuous medical education (CMEs) using different methods like workshops, lectures, webinars and conferences.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

Ethical approval

All research and ethical procedures were performed in accordance with the ethical standards of the department research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards (Ethical approval # 04/19/CP/02).

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