Current Opinions and Recommendations of Healthcare Professionals Regarding local production and bioequivalence study of generic medicines in Saudi Arabia: A cross-sectional study

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ABSTRACT

Objectives: The health practitioners, including doctors and pharmacists, have vital role by preferring to dispense brand drugs and not relying heavily on generic drug, and one reason for this problem may be the lack of knowledge of health practitioners about bioequivalence (BE) study. This study aimed to assess the degree to which medical professionals impose and favour brand-name drugs over generic drugs, as well as the anticipated causes behind this behaviour and measure their knowledge about BE study.

Material and Methods: A multicentre cross-sectional study design, and data were collected using a self-administered structured questionnaire. The study participants were selected from random hospitals, community pharmacy, pharmaceutical industries and research centres around Saudi Arabia.

Results: An online questionnaire was distributed to health practitioners in Saudi Arabia, where 259 participants agreed to participate, while 8 were refused. The percentage of participants who were between the ages of 30-39 was about 39%, 75% of them were males. We asked them whether they know about generic drugs or not, and found that 89% of them answered yes, and 38% of participants do not have a specific preference in dispensing medications, whether brand or generic drugs, while 37% prefer to dispense generic medicines more than brand because they think that it has better quality and more availability. When we asked them about their knowledge about BE study, 64% of them answered yes, and 61% of them believed that there are advantages in conducting BE locally, but 51% of them were not sure whether there is a BE centre in Saudi Arabia or not.

Conclusion: The study's findings demonstrate a generally positive attitude among healthcare practitioners towards locally manufactured medicines. Healthcare professionals recognize that high-quality generic medicines are affordable and have potential to yield significant cost savings. Dispensing of generic medicines is an opportunity to reduce the financial on patients as well as the national expenditure on the pharmaceutical sector, and based on the participants' feedback, it is recommended to increase the establishment of BE centres in Saudi Arabia to ensure higher quality and greater accessibility.

Key words: Drug, generic medication, brand medication, bioequivalence, health professionals

INTRODUCTION

In recent years, the price of medications has been rising worldwide [1]. Saudi Arabia has experienced a notable increase in healthcare costs, primarily attributed to pharmaceutical products. The nation is the largest healthcare spender in the Middle East, with expenditures exceeding USD 37 billion in 2018, of which pharmaceutical costs accounted for United States Dollar (USD) 8.2 billion, approximately 22% of total healthcare expenses [2]. The increased preference of healthcare professionals, especially physicians and pharmacists, for brand-name medications over generic alternatives has led to a rise in pharmaceutical costs in the Kingdom of Saudi Arabia. It is observed that a medicinal framework facilitating the dispensing of generic medications might yield savings above USD 2.67 billion in Saudi Arabia. Brand-name medications are typically costly, contributing to the overall healthcare expenses within a country. Generic medications significantly contribute to the reduction and management of overall healthcare costs [3]. The Saudi Food and Drug Authority (SFDA) is committed to ensuring the safety and efficacy of all pharmaceuticals within the nation. The panel of experts in Saudi Arabia identified the quality of pharmaceuticals as a significant concern. The panel discussion finished with around ten recommendations, identified by experts, that the authority can take to address the quality of generic pharmaceuticals in the country [4]. Pharmacists and physicians are essential in advocating for generic pharmaceuticals, a promotion linked to their quality and the involvement of these healthcare professionals in the initiative. Pharmacists are ideally positioned to advocate for and implement generic substitutes when provided with adequate information [5]. Advocating for and augmenting the utilization of generic medications is regarded as a cost-saving strategy that does not undermine the anticipated quality of healthcare [6].

The primary distinction between brand and generic pharmaceuticals is that the original product developed by a pharmaceutical business is referred to be a branded medication. The corporation is awarded exclusive rights to manufacture and market pharmaceuticals for a specified duration (patent). Currently, no other entity is capable of producing the identical drug [7]. Generic pharmaceuticals are replicas of brand-name products that are marketed following the expiration of patents or other exclusive rights, and they are designed to be more

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affordable. International standards are adhered to in the production of both branded and generic pharmaceuticals. Generic items may be sold under an alternative brand name and may contain fillers, binders, and lubricants that alter its appearance, flavour, aroma, and other attributes [8]. According to the United States Food and Drug Administration (FDA), a generic drug is described as a medication that possesses identical qualities to a branded drug in terms of active ingredient, strength, mode of administration, safety, dosage form, performance, quality, and intended purpose. Generic medications must demonstrate bioequivalence to the branded drug to obtain marketing authorization [9].

The World Health Organization (WHO) states that generic medicines are typically designed to be interchangeable with an innovator product. Given that generic medications are multisource goods, their "interchangeability" with innovator treatments must be validated by the execution of "in vivo equivalence" or "bioequivalence" (BE) studies [10]. Bioequivalence studies are typically conducted to assess whether alternative products, delivered at equivalent molar doses under comparable conditions, exhibit substantial differences in the pace and extent of active component availability at the site of therapeutic action [11]. The lack of evidence on bioequivalence studies and concerns about the quality of available generic drugs diminish the confidence of patients and healthcare providers in these products [12,13].

This study aims to examine the knowledge and perceptions of physicians and pharmacy professionals concerning local manufacture and bioequivalence studies of generic pharmaceuticals, as well as the hurdles and perceived benefits of conducting local bioequivalence studies in Saudi Arabia.

MATERIAL and METHODS

Study design

A cross-sectional study was conducted in Saudi Arabia between March 2024 and July 2024 using an online survey tool to evaluate the knowledge and perceptions of health professionals working in Saudi Arabia regarding local production and BE studies of generic medicines. The barriers and perceived advantages of conducting local BE studies in Saudi Arabia.

Sample size and sampling technique

The sample size was determined using the single population proportion formula with the following assumptions: proportion of participants who prefer local products = 40% (it was selected as there was no previous study and it gives the maximum sample size), 95%confidence interval ($Z_{\alpha/2}$ = 1.96), and margin of error (d=0.05).

$n = (Z_{\alpha/2})^2\, p(1-p) \div d^2$, n= 368

With the assumption of 10% non-and incomplete responses, the final size was calculated to be 405 [14].

Questionnaire tool and data collection

An electronic survey tool was chosen as the instrument for this study. Healthcare professionals and stakeholders were invited to complete an online survey. Managing of this survey by the use of determination designed electronic survey software was therefore considered to be both deliverable and efficient due to suitability of having automated data collection, which saves researcher time, effort and offers cost savings advantages [15]. A previously validated questionnaire was adapted and utilized to achieve the study objectives [14]. The questionnaire was validated on experts working in a hospital, university and a pharmaceutical industry which were not included in the final analysis. Information from the pre-test helped to improve the clarity of some questions and the structure of the questionnaire. The study participants were selected from fifteen hospitals, ten health care centres, six pharmaceutical industries, fifteen community pharmacies, SFDA, National Unified Procurement Company (NUPCO), five universities and the ministry of health. The questionnaire was organised in three major sections. The first section included questions on the respondents' socio-demographic characteristics. The second section solicited information on participants' opinions on generic medicines and their reasons; a list of possible reasons was given for participants to choose from. Additionally, in second section respondents were asked about participants' knowledge of BE, their awareness about the presence of a local BE centre and its perceived advantages. Respondents were asked to choose one or more options from a list of possible answers for questions related to their perceptions on when products can be called bioequivalent, dosage forms that need BE study and advantages of conducting BE studies locally. In the last section, participants were asked about their recommendations on local production and generic substitution and further feedback on the survey.

Participants were advised that all data were held confidentiality and anonymity was assured.

Responses were exported from Bristol survey into MS Excel 2016 and IBM SPSS version 28 for analysis and production of descriptive statistics.

Inclusion and exclusion criteria

Inclusion criteria:

- Healthcare professionals (HCPs) (doctor, nurse, and pharmacist) at hospitals and health care centres.
- Pharmacists at community pharmacy.
- Academics in the pharmacy sector.
- Pharmaceutical industries employees.
- Saudi food and drug administration SFDA employees.
- National Unified Procurement Company employees.

Exclusion criteria:

- General public.
- Healthcare professionals who were not willing to participate in the study.

Statistical analysis

The data for this study was analysed using Statistical Packages for Social Sciences version 28 (SPSS Inc., Chicago, IL, US). The frequency and percentage of categorical data were reported. The data was verified for normality using histogram and normality measures, which revealed that they were normally distributed. The mean (SD) was used to present continuous variables such as the participants' generic medicines knowledge score. The mean generic medicines knowledge score was compared between different demographic groups using an independent sample t-test and a one-way analysis of variance (ANOVA). Fisher's least significant difference (LSD) post hoc test was used to identify the source of significant variation within each group. The mean participants' generic medicines knowledge score (5.9) was used as a cut-off point in the binary logistic regression analysis to determine factors affecting participants' knowledge of generic medicines. A confidence interval of 95% ($p < 0.05$) was applied to represent the statistical significance of the results, and the level of significance was assigned as 5%.

RESULTS

A cross-sectional study was conducted in Saudi Arabia between March 2024 and July 2024 using an online survey tool to evaluate the knowledge and perceptions of health professionals working in Saudi Arabia regarding local production and BE studies of generic medicines. where 259 (97%) of respondents agreed to participate in this study. The percentage of participants who were between the ages of 30-39 about 39%, 75% of them were males. The majority of them worked in hospitals with an experience period of less than 5 years, as shown in Table 1.

Table 1. Socio-demographic characteristic of respondents

Percentage	Frequency	Demographic
Gender		
75%	195	Male
25%	64	Female
Age		
40%	102	20-29
39%	101	30-39
15%	39	40-49
5%	13	49<
Area		
21%	55	Central
13%	34	Eastern
14%	35	West Province
10%	26	Northern
42%	109	Southern
Education		
10%	26	Diploma
56%	145	Bachelor
16%	41	Master Degree
15%	39	PhD Degree
3%	8	The board
Work experience		
39%	102	Less than 5 years
28%	72	5 – 10 years
18%	46	11-15 years
14%	35	More than 15

We asked them whether they know about generic drugs or not, and found that 89% of them answered yes, but 38% of participants do not have a specific preference in dispensing medications, whether brand or generic drugs, While 37% of them prefer to prescribe generic medicines more than brand because they think that it has better quality and more availability, while the people who preferred to prescribe brand form, the majority of them preferred to prescribe Germany and UK products, Even when we asked them if they support current policy of substituting brand-name drugs with generic drugs, 68% of them answered yes, Table 2.

Table 2 . Opinion/ awareness of respondents

Percentage	Frequency	Opinion
Do you aware of generics medicines		
89%	230	Yes
11%	29	No
What do you prefer to prescribe?		
37%	97	Generic
24%	63	Brand
39%	99	No preference
If you have specific preference, what is the reason for your preference?		
18%	55	Cheap price
26%	79	Easily available
30%	91	Better quality
19%	59	More effective
6%	17	Well promoted
If your answer for Question # 8 is 'imported products', which country of origin do you prefer most?		
10%	13	China
33%	43	Germany
27%	36	United Kingdom
21%	28	United State
5%	7	India
3%	4	Other
Do you support the current policy of substituting brand name drugs with generic drugs		
68%	177	Yes
14%	37	No
17%	45	Unsure
Have you heard about BE?		
64%	166	Yes
36%	93	No

We found that 64% of them were knowledgeable about bioequivalence study, and agreed that to be called bioequivalent, products must have/ show similar safety, efficacy and strength, also 65%of respondents believed that SFDA should implement enforcement of BE requirements for locally manufactured immediate release products, and 61% of them think that there are advantages in conducting bioequivalence locally in Saudi Arabia, as shown in Table 2.

Two thirds of respondents agreed that to be called BE, products must be same drug with similar safety, efficacy and have same strength. When we asked them for which dosage forms is BE study necessary, the majority of them said that the tablet (34.0%) and capsule (29.0%) are the most important dosage forms, Figure 1.

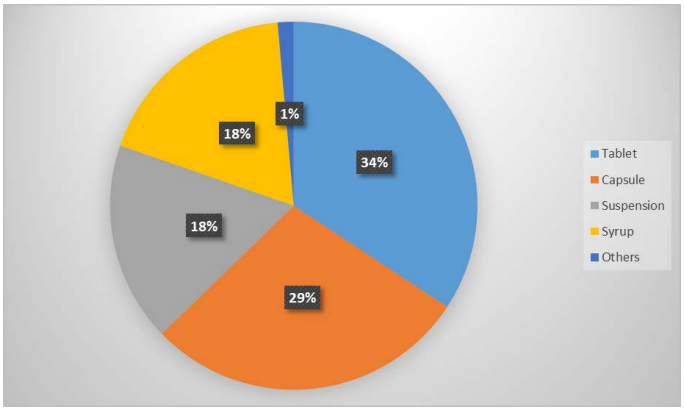

Figure 1. Dosage forms required for the BE study

Around 51.0% of respondants are not sure if there is BE test center in Saudi Arabia or not. After that, we tried to get their opinions where the BE studies center should be conducted, half of them were confused , while 41% said it is better to be locally in Saudi Arabia . As this may help to spread the culture of generic drugs among the companies and people in general. Around 61.0% of the participants reported that BE studies should be conduted locally. This was justified by the following

reasons: more affordable prices, more reliable and dependable findings, being more accessible, and shorter waiting times.

DISCUSSION

Bioequivalence Knowledge and Perceptions of Generic Medicines

The knowledge, attitude, and practice (KAP) of healthcare practitioners toward generic medicine may influence their selection and utilization of therapeutic drugs. The current study revealed that 89% of respondents possessed knowledge of generic medicine, aligning with findings from other studies; however, those studies surveyed patients and discovered that a majority of the public recognized the term "generic medicine" [14]. We inquired whether they wished to prescribe medication and which type they preferred to purchase. We discovered that 39% were uncertain and lacked a specific preference. This confusion parallels findings from another study, where most respondents were indecisive about preferring generic or brand-name drugs [7]. Meanwhile, 37% expressed a preference for prescribing generics, citing superior quality and greater availability compared to brand drugs. This aligns with another study indicating that 70% of participants believed generic medicines do not possess inferior quality compared to brand drugs [15]. Conversely, other studies reported that while generic medicines are more economical and bioequivalent to brand drugs, respondents perceived generics as less effective and less safe [16,17]. However, another study concurred that generic medicines are more affordable, safe, efficacious, and cost-effective than their brand counterparts [18]. We inquired about the preferred country of origin for participants who favoured brand one, and discovered that the majority selected pharmaceutical products from Germany and the UK. While the precise reasons for their preferences remain unclear, we surmise that they are drawn to these products due to their widespread popularity and superior quality. We sought their opinions on the current policy of substituting brand-name drugs with generics; two-thirds responded affirmatively. This aligns with other studies advocating for the substitution of generic drugs for brand-name ones. Furthermore, the FDA maintains that drug products, whether brand-name or generic, which have undergone the approval process, can be dispensed and utilized with the assurance that consumers will receive equivalent clinical benefits [6,19,20]. Nonetheless, the FDA mandates particular criteria that generic products must satisfy before receiving approval [19].

Awareness and Acceptance of Bioequivalence Studies:

In section 3, we inquired whether participants were familiar with the term bioequivalence. Sixty-four percent responded affirmatively, corroborating findings from another study indicating that most pharmacists possess substantial knowledge regarding bioequivalence [7]. Furthermore, the majority concurred that for products to be deemed bioequivalent, they must demonstrate comparable safety, efficacy, and strength. Another study indicated that to guarantee the quality of generics, the government should enhance public trust, which can be achieved by conducting bioequivalence studies of certain medications [21]. We believe that bioequivalence (BE) study centers are essential to establish locally in Saudi Arabia to enhance the education of healthcare practitioners and patients regarding bioequivalence and generic medications. This conclusion is drawn from participant feedback regarding the preferred locations for BE study centers, with 52% advocating for both local and international sites, while 41% emphasized the significance of local centers, citing advantages such as increased accessibility and more reliable results. However, when inquired about the existence of a BE center in Saudi Arabia, 51% of participants expressed uncertainty. When inquiring whether all immediate-release pharmaceutical products necessitate bioequivalence studies, 65% affirmed this requirement. The majority identified tablets and capsules as the most critical dosage forms warranting such studies, likely due to their need for rapid absorption and their prevalence among patients. The subsequent inquiry was whether participants believe that the SFDA should enforce BE regulations for locally manufactured quick release goods; 61% affirmed this stance. Finally, we inquired whether they believe local pharmaceutical plants do BE research. Fifty-three percent responded affirmatively, while those who disagreed cited specific reasons, asserting that the costs associated with BE centers are prohibitive and unattainable.

Policy Recommendations

In this respect, full attention shall be given to both brand and generic medicines, with the realization of their irreplaceable importance, as all drugs should be prescribed by their generic names for clarity and access. Specialized centers should be established for the development of local production to enhance treatment quality and efficiency. More so, the locally produced medicine should be at high standard qualities and must be reasonably priced, and well-packed to ensure reliance on local products is attained. Bioequivalence tests will also be important in the future to stabilize TDM hence ensuring better patient outcome with improvement in the quality of life. Besides, we recommend using treatment guidelines; incentivizing the utilization of generic medicines, including the introduction of tiered payments for branded drugs.

CONCLUSION

The study's findings demonstrate a generally positive attitude among healthcare practitioners towards locally manufactured medicines. General practitioners recognize that high-quality generic medicines are both affordable and have the potential to yield significant cost savings. Increased dispensing of generic medicines presents an opportunity to reduce the financial burden on patients as well as the national expenditure on the pharmaceutical sector. However, based on the participants' feedback, it is recommended to increase the establishment of BE centres in Saudi Arabia to ensure higher quality and greater accessibility. Additionally, there is a need for enhanced education of healthcare practitioners regarding bioequivalence studies to promote this understanding among them and to raise awareness within the broader public.

DATA AVAILABILITY STATEMENT

The datasets generated or analysed for this study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The study protocol was reviewed and ethical approval was granted by the Deanship of the Scientific Research Ethics Committee at Najran University, Najran, Saudi Arabia (Approval No.202403-076-019313-043900). No study activity commenced until all approvals were granted and data was accessed by the study team only. All responses were fully anonymised prior to analysis and all reports accommodated confidentiality requirements.

AUTHOR CONTRIBUTIONS

Conceptualization, H.S.A.; methodology, H.S.A.; software, H.S.A.; validation, H.S.A.; formal analysis, H.S.A.; investigation, H.S.A., B.D., O.A.; resources, H.S.A., B.D., O.A.; data curation, H.S.A.; writing—original draft preparation, H.S.A., B.D., O.A.; writing—review and editing, H.S.A., B.D., O.A.; visualization, H.S.A.; supervision, H.S.A.; project administration, H.S.A.; funding acquisition, H.S.A. All authors have read and agreed to the published version of the manuscript.

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