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Research Article

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Use of Design of Experiment in the Pharmaceutical Sector

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Abstract

With the recent global pandemic, the world has understood the importance of health. People with chronic respiratory diseases (CRDs) were affected the most. The paper focuses on patients with common respiratory diseases and examines the efficacy of two drugs (namely drug 1 and drug 0) with respect to the adherence level of the patients. It employs full factorial experiments using Pareto Charts for different age groups and gives results for the most significant drug according to each age group. Overall, drug 0 proves to be the most significant according to the study.

Keywords

Design of experiments, Rhinitis, Sinusitis, Upper respiratory infection, Full factorial experiment, Pareto chart

Introduction

In recent years, the world has experienced tragic suffering in Health Sector. It has suffered from the unbeatable COVID-19 and has lost many lives. People having CRDs had the most adverse effects of the recent pandemic. They were at a higher risk of getting COVID due to pre-existing ill-functioning of respiratory organs. Along with such global pandemics, the world also experiences man-made hazards such as increasing pollution, deforestation, building industries without abiding by pollution control rules, and many more. D'Amato et al. discuss that environmental factors and urban air pollution are among the most significant reasons for respiratory allergies [1]. It is important to realize that not only outdoor pollution, but indoor pollution also causes major respiratory diseases. Dhaka was severely affected by indoor pollution leading to enormous distress [2]. A large part of the population suffers from respiratory problems due to these unavoidable factors. The need here is to understand that respiratory diseases should be treated, as it elevates the chances of being prone to more dangerous diseases. Right from teenage to old age people, everyone is affected by chronic problems and each one should be treated with a drug suitable and effective for their age group.

Design of experiments is a structured systematic arrangement of determining the relationship among factors affecting a procedure and its yield. It has major applications in the pharmaceutical sector. Al Saadi shows implementation of a full factorial experiment in optimizing gas chromatographic–mass spectrometric in the pharmaceutical sector [3]. It has been extended to this paper to understand the efficacy of two drugs among the common respiratory problems. This paper attempts to understand the efficacy of two drugs for different age groups in order to suggest the best possible drug for a particular age group suffering from common respiratory diseases. It does that by using the concept of factorial experiments to understand which drug acts most significant by examining the adherence under different age groups for common respiratory diseases. This paper gives a statistical

suggestion to use the best possible drug to recover the affected patients at a faster rate.

Literature Review

The burden of CRDs that affect both adults and children is constantly increasing globally. The mortality and morbidity caused by respiratory diseases is unclear; however, recent statistics published by WHO and other agencies found an estimate of around 400 million people around the globe suffering from mild to moderate conditions of Asthma and COPD alone [4]. The paper aims to give a statistical overview of the best efficient drug for common respiratory diseases such as sinusitis, rhinitis, and upper respiratory infection (URI). It is observed that 28.9 million US adults suffered from sinusitis in 2018 [5]. Also, it was observed that among the 1246 patients in Iran with respiratory symptoms, there were 1084 patients with allergic rhinitis which comes out to be 87% and according to the Global Burden of Disease 2019 study, the URIs reached 17.2 (95% uncertainty interval: 15·4 to 19·3) billion globally in the recent years. The literature clearly shows us that sinusitis, rhinitis, and URI are the most common respiratory diseases which need to be addressed as they affect a major part of the youth worldwide.

The different literature depicts the biological perspective of respiratory diseases. The gap identified in the literature review is that the papers have put in a biological perspective without considering a statistical view of how diseases can be cured at a faster rate by using the most efficient drug for a particular disease with respect to age group. This paper majorly focuses on this idea and attempts to add a new perspective in the medical science field.

Materials and Methods

A secondary data set (Data Source: Confidential) was used to analyze the data which consisted of 18,215 rows and 8 columns, that is, it consists of data of over 18,000 patients. Out of 18,215 patients, 15,276 patients were tested for drug 0 and 2,941 patients were tested for drug 1. It was observed that the same patient was not tested for both the drugs simultaneously. The dataset was collected for different age groups ranging from 11 years old to 65 years old. There were 3,244 patients from the age group 11 - 19 where the upper limit is exclusive. Similarly, there were 13,775 patients for the 19 - 60 age group and 1,199 patients for the 60 - 65 age group. The primary variables are the 3 common respiratory diseases that have been considered in the study. The values of the variables were binary numbers (1 indicates the presence and 0 indicates the absence of the disease). Similarly, the same pattern of values was followed for the usage of drugs among the two. For confidentially, let us consider the two drugs as drug 0 and drug 1, respectively.

In order to achieve the objective of examining which drug is more efficient for which age group and the adherence of patients is checked after the consumption of drugs. For the given dataset, the age group is divided into 3 parts, mainly, Children, Adults, and Senior Citizens. For each of the age groups, a full factorial experiment is performed, considering the three respiratory diseases as the factors and adherence as the response variable. Full factorial experiments are represented using the Pareto chart. Full factorial experiments are designs which consists of two or more factors, where experimental units take all possible combinations of all levels of the factors in order to understand the effect of each factor on the responsible and also the effect of interactions on the response variable. Pareto charts are mostly used to analyze the broad causes by looking at specific components. It uses 80/20 principle where it states that 80% of the effects are due to 20% of the causes. It prioritizes the causes related to a particular effect and highlights the most significant factor. The paper examines the three most common respiratory diseases and examines the efficacy of two drugs. However, it's a granular step toward concluding the efficacy of the drugs. Most importantly, Pareto chart looks at the most significant factor among the rest, and here factorial experiments are used to analyze the disease which shows the most significant result with respect to which drug. The methodology performed in this study is the analysis of pharmaceutical data using the design of experiments.

In figure 1, each step of methodology is represented under each box. In understanding of data, the data is critically scrutinized to understand the further steps that need to be taken to achieve the objective. Next in cleaning of data, the data is examined if there are any outliers. In this paper, box plot was used to detect outliers, but as it is a pharmaceutical, none of the data points can be removed. There were no missing values in the data, hence imputation techniques were not implemented, however in the next step, manipulation of data, the data was structured in order to perform 2^3 factorial experiments. There are three factors as the common respiratory diseases (rhinitis, sinusitis, and URI), each at two levels (0 and 1). Once the data was structured, it was imported to perform the analysis through Pareto charts.

Figure 1: Flow chart representing the methodology.

Results and Discussion

The paper examines the efficacy of the two drugs (drug 0 and drug 1) through the Pareto chart. The age groups were divided into three intervals as mentioned in the methodology section. The Pareto charts for the different age groups with respect to each drug are built to visualize the impact of the two drugs for different age groups.

In figure 2 and figure 3, it is observed that drug 0 is more effective for the disease rhinitis and even for the patients having rhinitis and URI together. It is clearly observed that factor rhinitis crosses the significance level (0.05) in response to the adherence level.

In figure 4 and figure 5, it is observed that drug 0 is very effective for all the diseases individually as well as for patients who have rhinitis and URI together. It can be clearly observed that for drug 0, all the factors cross the significance level, however for drug 1, it doesn't cross the significance level which implies that drug 1 is not effective in adults.

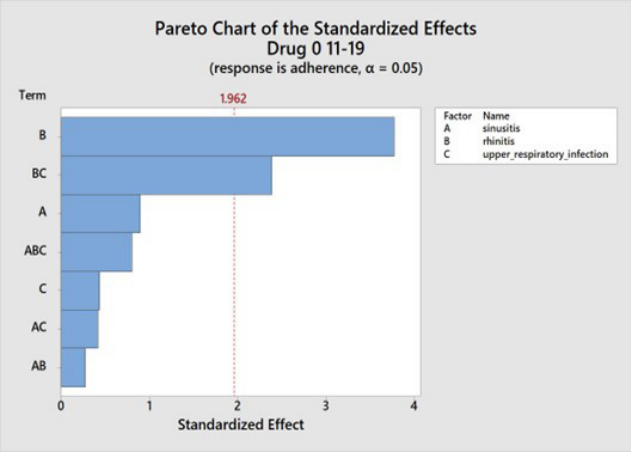

Figure 2: Pareto chart for the age group 11 - 19 with respect to drug 0.

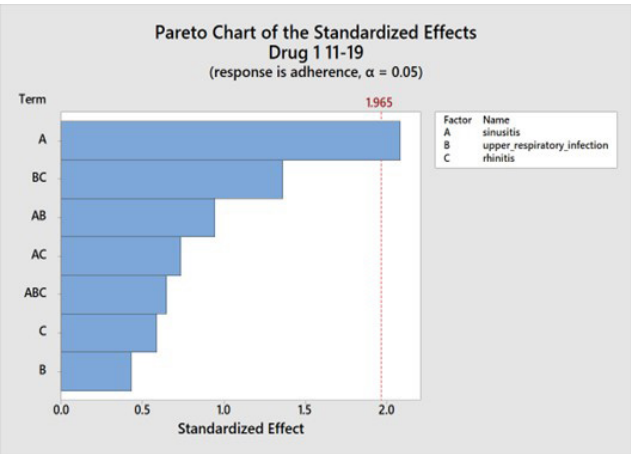

Figure 3: Pareto chart for the age group 11 - 19 with respect to drug 1.

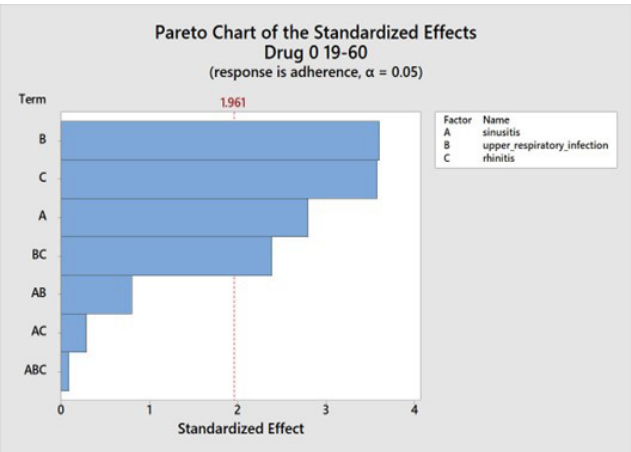

Figure 4: Pareto chart for the age group 19 - 60 with respect to drug 0.

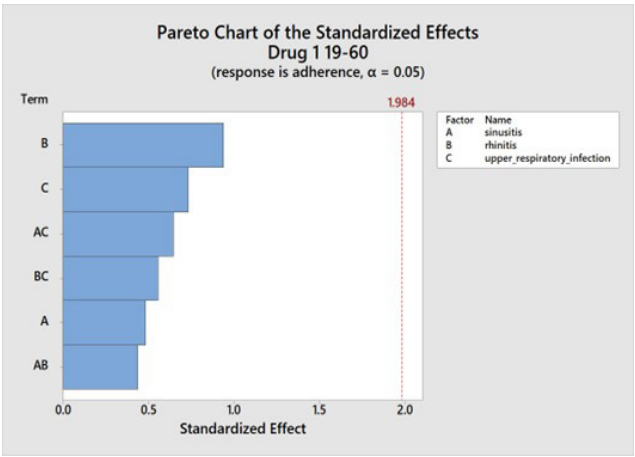

Figure 5: Pareto chart for the age group 19 - 60 with respect to drug 1.

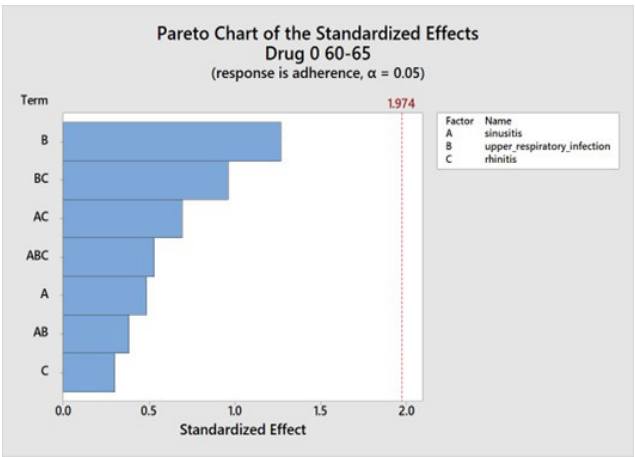

Figure 6: Pareto chart for the age group 60 - 65 with respect to drug 0.

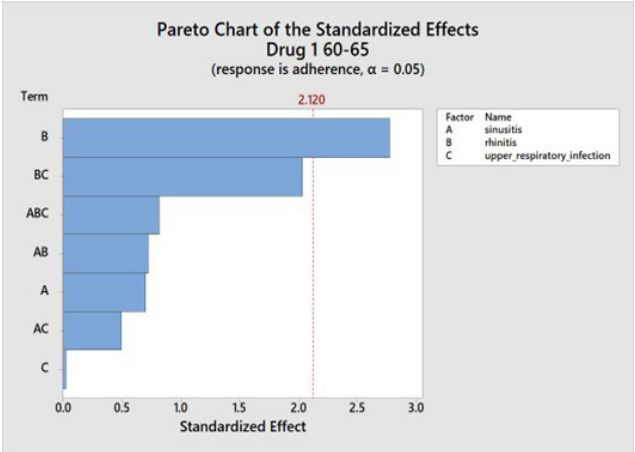

Figure 7: Pareto chart for the age group 60 - 65 with respect to drug 1.

In figure 6 and figure 7, it is insightful to observe that drug 0 is not effective in patients above age 60. However, it can be clearly seen that drug 1 is highly effective for patients suffering from rhinitis. It is discerned that factor rhinitis crosses the significance level (0.05) with respect to the response variable, that is, adherence level.

Overall, it can be noted that both the drugs are efficient for different age groups. Drug 0 is the most consistent, but it doesn't work for older generations, however drug 1 is highly efficient for children and senior citizens. Also, drug 0 helps in curing the adults suffering from all the three respiratory diseases considered in the study.

Conclusion

The study aims to compare the efficacy of two drugs (drug 0 and drug 1). It is observed that drug 0 has remained consistent for different age groups and has been most effective for the disease rhinitis. It is also observed that it is very powerful in curing all the three diseases mentioned in the study for adults. As adults constitute a major part of the population, they can easily be cured with the help of drug 0. However, for older people, drug 1 is effective, it shows that drug 1 must contain ingredients that may not play significantly huge role in adults. Based on the overall comparison, drug 0 is better than drug 1 as even though drug1 is effective but is restricted to only one disease (rhinitis), however, drug 0 is effective for all diseases in adults. Along with comparing the two drugs, the study also aims to convey the implementation of the design of experiments in the pharmaceutical industry to researchers from the biological and pharmaceutical domains with the help of visualizations that will make the concepts easy to understand and implement. It focuses on bridging the gaps between researchers from the biological and statistical domains.

Limitation and Further Scope

The paper focuses on the efficacy of the drugs based on the data collected by a secondary source. It focuses on a small sample of only eighteen thousand patients. The efficacy of the drugs is examined only on the basis of three common respiratory diseases. It can be extended to a wider range by considering a larger sample and examining more significant respiratory diseases. The domain knowledge was limited to the literature survey that was done for analysis. However, the paper gives an overview of the methodology of implementing the design of experiments in the pharmaceutical sector. It will be helpful for researchers to not start from scratch but instead to understand the benefits and utilize for extending it to a wider range.

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Conflict of Interest

The authors assure that they have no known conflict of interests that are relevant to the content of this article.

Credit Author Statement

Barnali Das: Conceptualization, Methodology, Writing - original draft preparation, Writing - review and editing; Pushpak Bhonde: Data analysis, Writing - review and editing; Risha Rodrigues: Data analysis, Writing - review and editing. All the authors read and approved the manuscript.

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