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Different Perspectives for Determining the Optimal Treatment Modality for Gastroesophageal Reflux Disease: Application of the Fuzzy Technique for Ordering Preference by Similarity to Ideal Solution Method

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Abstract

BACKGROUND/AIMS: Gastroesophageal reflux disease (GERD) has spread worldwide over time, impacting most populations in most nations. Therefore, determining the most effective treatment method for GERD is crucial because the most appropriate treatment option must be selected to reduce the effects of GERD and improve the quality of life of patients. This study aimed to introduce a different perspective for determining the optimal treatment modality for GERD.

MATERIALS AND METHODS: To determine the optimal treatment modality in the treatment of GERD, this study has applied the fuzzy technique for ordering preference by similarity to ideal solution (TOPSIS) method to evaluate antacids, histamine blockers, proton pump inhibitors (PPIs), and prokinetics, which are treatment options for GERD against 15 criteria: cost, availability, dose, frequency, allergy, path, safety, efficacy, age, other health condition, GERD stage, treatment duration, success rate, drug-drug interaction, and drug-food interaction.

RESULTS: The closeness coefficients (Ci) of each treatment alternative were used to determine their rankings. The treatment option with the highest closeness coefficient was considered the best. The ranking shows that PPIs are the best treatment for GERD because they had the highest Ci value of 0.642. The treatment option with the lowest Ci value was antacids, which had a Ci value of 0.33.

CONCLUSION: Implementing the Fuzzy TOPSIS method can guide decision-makers in more systematically evaluating complex decisions and choosing the most appropriate treatment modality. Consequently, it is thought that this study will help clinicians make more informed and scientifically based decisions regarding the treatment of GERD.

Keywords: Fuzzy TOPSIS, gastroesophageal reflux disease, proton pump inhibitors, antacids, treatment

INTRODUCTION

The backward movement of acid from the stomach to the esophagus, which is a tube that links the mouth to the stomach, causes a condition known as gastroesophageal reflux disease (GERD) or chronic acid reflux. The lower esophageal sphincter (LESP) is a valve at the end of the esophagus that, when it is healthy and operating well, should shut when food reaches the stomach. If it is not healthy or is not functioning properly, the valve may not close properly. Regurgitation of stomach acid may be a problem for certain people because the valve does not close adequately when it should. When this occurs, the acid backwash travels back up the esophagus, down the throat, and into the mouth, where it leaves a sour taste.[1]

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As of 2019, 783,95 million individuals all over the world were projected to have suffered from GERD. A total of 77.53% more instances were reported between 1990 and 2019, 74.79% more cases occurred, and 77.19% more years of life were lost as a result of impairment. The age-standardized global incidence rate (ASIR) and the global young mortality rate (ASYR) both increased from 0.05 to 0.06 during the study period. Both rates were at a previous level of 0.06. In 2019, Tropical Latin America dominated the rankings for all three age-standardized illness burden metrics, namely ASPR, ASIR, and ASYR. However, East Asia received the lowest score in the ASPR. In every annual category of GERD prevalence and incidence, as well as in every annual category of young-onset GERD prevalence and incidence, females continuously outnumbered males during the entire period of 1990-2019. There was a correlation between having a higher sociodemographic index and having lower GERD-related Acute Symptom Severity Ratings (ASPR, ASIR, and ASYR) in the year 2019.[2]

Histological alterations in the esophageal mucosa may contribute to the development of a variety of potentially diagnosable illnesses, including Barrett's esophagus, reflux esophagitis, and non-erosive reflux disease.[3]

Symptoms of GERD include asthma, a painful throat, persistent coughing, a constant need to clear one's throat, and unexplained chest discomfort.[2] The frequent and bothersome symptoms of GERD and the complications of this disease, such as inflammation of the esophagus, stricture of the esophagus, ulceration of the esophagus, perforation of the esophagus, metaplasia, and esophageal cancer, have a huge negative impact on the quality of life of patients who suffer from GERD in regards to their overall health.[4]

The very high frequency of GERD and the chronic nature of the condition imply that treatment is very expensive, which is a burden for patients, the people who care for them, and the healthcare system as a whole.[5] Clinical management of GERD affects the lives of many and uses up a great deal of healthcare and social services, thereby making them poorer as their resources go toward the treatment of the disease.[3]

Since GERD has far-reaching negative consequences on patients' quality of life, it is crucial to assess current treatments to create more effective options, which will avoid the waste of resources associated with experimenting with different treatment options. Selection of the optimal treatment modality among different treatment methods requires multi-criteria decision-making (MCDM) method. A thorough decision-making process is highly challenging, particularly when dealing with constantly changing information and circumstances. Making decisions while considering several criteria and using multiple decision-makers (DMs) is known as MCDM. The technique for ordering preference by similarity to ideal solution (TOPSIS) is one of the most popular techniques, which was proposed by Hwang and Yoon.[6] It has been widely embraced in several use cases because of its ease of use, flexibility, computing efficiency, and broad mathematical notion. Fuzzy TOPSIS, which is the conventional TOPSIS method's extension to Fuzzy logic, has also been effectively applied in several fields.[7-11]

This study aimed to propose a Fuzzy TOPSIS-based method for selecting the optimal treatment modality among different treatment options for GERD. In the existing literature, the optimal treatment method for GERD has not yet been considered an MCDM problem from this perspective. Thus, determining the optimal treatment modality for GERD will significantly contribute to the literature.

Alternatives to Gastroesophageal Reflux Disease Treatment

Several modalities are available for GERD treatment and these modalities include the following: medications such as antacids, histamine blockers, proton pump inhibitors (PPI), and prokinetic medicines.[12]

Antacids

Given that they have been on the market for consumers to buy for a sizeable length of time, antacids are among the pharmaceutical families that have the largest market share. The widespread use of antacids in the 19th century probably helped those who suffered from stomach troubles find some relief. Antacids are a kind of drug that is used to alleviate hyperacidity by mixing magnesium, calcium, or aluminum salts[13] that elevate the alkalinity of the stomach, neutralize acidity, limit the synthesis of pepsin, and induce the release of bicarbonate and prostaglandin[14] that help reduce the symptoms of GERD. Antacids perform their job by neutralizing acid produced in the stomach, which prevents acid from moving into the duodenum. Pylorospasm, pain, acid-chyme digestion, and corrosion are only a few of the many ailments that an antacid can help. Although the mechanism of action of all antacids includes the binding of hydrogen ions to the stomach, the effectiveness of an antacid may depend on the specific salts used in its manufacturing.

Histamine Blockers

The two main types of anti-ulcer drugs are H2 receptor blockers and H2 receptor antagonists (H2RAs). Both terms refer to the same group of medications.[15] H2RAs prevent the natural ligand histamine from binding to and activating the histamine H2 receptors present in the gastric parietal cells; thus, they are responsible for the reduction in acid production in the stomach. As a result, H2 blockers play the role of an adversary in a context involving competition. In response to food, the stomach enterochromaffin-like cells generate histamine, which binds to histamine H2 receptors in parietal cells and stimulates an increase in acid production. The activation of the enzyme adenylate cyclase results in an increase in the amount of cellular cAMP, which in turn drives the formation of further stomach acid. An enzyme known as protein kinase A (PKA) is stimulated by cAMP. PKA phosphorylates H+/K+ ATPase transporters, which helps them move to the plasma membrane where they can perform their work. There is a greater potential for enhanced acid secretion from parietal cells as a result of a higher concentration of H+/K+ ATPase transporters in the plasma membranes of these cells. Blocking histamine receptors is how H2RAs work to prevent histamine from stimulating acid generation by parietal cells. Therefore, the amount of acid produced in the stomach as a reaction to histamine is decreased.[16] It only takes 60 min for H2RAs to start functioning in the digestive system, and they continue doing so for 4-10 h, making them ideal for the ad hoc treatment of symptoms that only occur occasionally. The anti-acidity effects of H2RAs are reliable and consistent across the board.[17]

Proton Pump Inhibitors

PPIs, also known as proton-pump inhibitors, are a type of medication that is often prescribed to patients with acid-related conditions. In the production of PPIs, the benzimidazole molecule serves as the jumping-

off point.[18] PIs are beneficial because they reduce the amount of acid produced in the stomach. After being absorbed by the body in the top portion of the small intestine, these medications have an effect on parietal cells in the stomach. In parietal cells, PPIs inhibit the activity of the proton-pumping enzyme H+/K+ ATPase. The production of stomach acid is completed with the help of this enzyme, which is the final stage of the process. PPIs are intriguing substances because they are inactive prodrugs. The acidic secretory canaliculi of parietal cells need to cleave PPI to have an impact. They become active as a result of this operation. In the liver, cytochrome P450 enzymes are responsible for PPI breakdown. Although various P450 enzymes are required for the breakdown of different PPIs, CYP2C19 is by far the most important of these enzymes. PPIs, are among the most efficient medications for lowering the production rate of stomach acid.[19,20]

Prokinetic Agents

Pressure in the LESP, is raised by Prokinetics. They also accelerate the rate at which the stomach empties and promote esophageal peristalsis. Some examples are agonists of the GABA-B receptor, dopamine receptor, and agonists for the 5-hydroxytryptamine (5-HT) receptor. The stimulation of the release of acetylcholine from parasympathetic nerve roots is the mechanism by which 5-HT receptor agonists encourage bowel movement and emptying of the stomach.[21,22]

MATERIALS AND METHODS

This study was approved by the Near East University Scientific Research Ethics Committee (approval number: 2023/117-1779, date: 26.10.2023).

This research uses the Fuzzy TOPSIS, which is a well-known method for resolving MCDM issues. Through literature review and consultation with experienced doctors and pharmacists, the study identified 15 criteria that are essential for administering treatments to evaluate the 4 treatment alternatives for GERD, namely, acidic agents, histamine blockers, PPIs, and prokinetic agents. According to expert opinions, cost, availability, dose, frequency, allergy, path, safety, efficacy, age, other health conditions, GERD stage, treatment duration, success rate, drug-drug interaction, and drug-food interaction have been determined as criteria, as shown in Table 1. The treatment alternatives were evaluated against those 15 criteria by three experts: One gastroenterologist and two final-year PhD students in the pharmacy department. Each expert independently evaluates and ranks the criteria in their unique way because they are knowledgeable about the subject matter and consider the relative significance of each alternative and the criteria. For each criterion, the weights allocated by each expert were combined to create a single set. A typical approach in the Fuzzy TOPSIS method is to find the average of the weights assigned by experts.

TOPSIS Idea

The TOPSIS method simplifies the identification of solutions that match criteria by assuming that the utility of each criterion tends to increase or decrease monotonically. Possible suboptimal solutions are proposed, and their Euclidean distance from the best solution is calculated. We can rank alternatives by comparing their relative distances and see how they stack up against one another. Like the ELECTRE technique, In the first step of the TOPSIS approach, the dimensions of the criteria are transformed into non-dimensional criteria.[23] By decreasing the time required to reach both positive and negative optimal solutions, TOPSIS may help users choose the best course of action (NIS). This method ranks criteria and attains peak performance in MCDM. The Fuzzy TOPSIS assessment technique was used to evaluate all qualities by area.[24]

Fuzzy Theory

In mathematics, a fuzzy set can be used as a helpful tool for dealing with ambiguous or erroneous information. The classic set theory approach can be expanded by considering an element's partial membership in a set. In contrast to the binary nature of classical set theory, which holds that an item is either a part of a set or not, fuzzy set theory holds that the degree of membership in a set may vary from 0 to 1, with 0 being the least likely and 1 being the most likely. An element's membership level in a set can have values ranging from 0 (totally not a member) to 1 (totally a member). The membership function assigns a membership degree to an element based on the characteristics of the element.[25]

Table 1. Treatment alternatives and criteria for GERD treatment

Decision makers	Treatment alternatives	Symbol	Criteria
Decision-maker 1 Decision-maker 2 Decision-maker 3	Antacids Histamine blockers Proton pump inhibitors Prokinetic agents	C1	Cost
		C2	Availability
		C3	Dose
		C4	Frequency
		C5	Allergy
		C6	Path
		C7	Safety
		C8	Efficacy
		C9	Age
		C10	Other health conditions
		C11	GERD stage
		C12	Treatment duration
		C13	Success rate
		C14	Drug-drug interaction
		C15	Drug-food interaction

GERD: Gastroesophageal reflux disease.

Fuzzy sets are useful in many areas, such as artificial intelligence, control systems, pattern recognition, and decision-making. This method works effectively with complex and unpredictable systems where it is difficult to obtain reliable data and draw firm conclusions.[26]

Fuzzy TOPSIS

Popular MCDM approaches that use fuzzy set theory to cope with uncertainty and imprecision include the Fuzzy TOPSIS.[25] In 1981, Hwang and Yoon[6] devised a method for selecting the best choice from a group of possibilities. The method involves calculating the distance between each option and the ideal and anti-ideal solutions to determine which option is the best.[27] The characteristics of the most beneficial options are represented by the ideal solution, while the characteristics that are least desired are represented by the anti-ideal solution.[28]

The proposed method goes beyond the traditional TOPSIS approach for managing ambiguities and imprecise data by introducing Fuzzy logic into the decision-making process. Fuzzy logic is a type of artificial intelligence. When ranking alternative solutions, the traditional TOPSIS method considers both the distance from the negative ideal solution and the total number of possibilities. In terms of the positive ideal solution, each criterion is represented by its highest possible potential value. On the other hand, when identifying the negative ideal solution, each criterion is represented by its lowest possible potential value. The use of fuzzy sets in Fuzzy TOPSIS allows for the consideration of uncertainty and ambiguity in both the decision criteria and probable solutions.[6] By comparing how close a solution is to an ideal solution to how far away it is from an ideal negative solution, the classic TOPSIS method assigns a rating to each possible solution. Each criterion value is maximized in the positive ideal solution and minimized in the negative ideal solution. The perfect solution would maximize all of the criterion values. The use of fuzzy sets in Fuzzy TOPSIS allows for the consideration of uncertainty and ambiguity in both the decision criteria and probable solutions.[29] The following steps are applicable to the Fuzzy TOPSIS:

Step 1: Identify various alternatives and criteria: As the starting point for applying the Fuzzy TOPSIS techniques, you must identify the various alternatives and criteria to be used. In this study, 4 alternative treatments for GERD were identified. The treatment alternatives were evaluated against 15 criteria: cost, availability, dose, frequency, allergy, path, safety, efficacy, age, other health conditions, GERD stage, treatment duration, success rate, drug-drug interaction, and drug-food interaction.

Step 2: Establish/form the decision matrix: In the first step, a direct-relation fuzzy matrix is created. In this study, a pairwise comparison of the 3 DMs was conducted. The direct connection matrix is generated by taking the arithmetic mean of the 3 experts' opinions. Before turning into fuzzy integers, the weights were expressed using linguistic variables as part of the Fuzzy TOPSIS technique. After this, the weights are then converted. The preferences of those in charge of making decisions might be reflected in the weights, which could be expressed in the form of linguistic variables. Table 2 shows the Fuzzy scale used in this study.

Step 3: Normalize the decision matrix: Once the criteria and weights were established, the data for each treatment choice were transformed to fit a comparable scale. This goal was achieved using either a linear or non-linear transform. As demonstrated in the following connection, it is possible to construct a normalized choice matrix by making use of both positive and negative ideal solutions:

$$\tilde{r}_{ij} = \left(\frac{a_{ij}}{c_j^*}, \frac{b_{ij}}{c_j^*}, \frac{c_{ij}}{c_j^*}\right) \; ; \; c_j^* = max_i \, c_{ij} \; ; \textit{Positive ideal solution} \tag{1}$$

$$\tilde{r}_{ij} = \left(\frac{a_j^-}{c_{ij}}, \frac{a_j^-}{b_{ij}}, \frac{a_j^-}{a_{ij}}\right) \; ; \; a_j^- = min_i \, a_{ij} \; ; \textit{Negative ideal solution} \tag{2}$$

Step 4: Calculate weighted normalized decision matrix: The weighted normalized decision matrix can be obtained by multiplying the exact weight value for each parameter in the normalized fuzzy decision matrix. The given weights are the weighted normalized matrix. Here, are the steps used for its computation:

$$\tilde{v}_{ij} = \tilde{r}_{ij} . \tilde{w}_{ij} \tag{3}$$

where $\tilde{w}_{ij}$ represents the weight of criterion c_j.

Step 5: Compute the positive and negative ideal solutions (FPIS) and Negative Ideal Solution (FNIS): The FPIS and FNIS of the alternatives are respectively described as follows:

$$A^* = \{\tilde{v}_1^*, \tilde{v}_2^*, \ldots, \tilde{v}_n^*\} = \left\{\left(\max_j v_{ij} \,|i \in L\right), \left(\min_j v_{ij} \,|i \in K\right)\right\} \tag{4}$$

$$A^- = \{\tilde{v}_1^-, \tilde{v}_2^-, \ldots, \tilde{v}_n^-\} = \left\{\left(\min_j v_{ij} \,|i \in L\right), \left(\max_j v_{ij} \,|i \in K\right)\right\} \tag{5}$$

Where $\tilde{v}_i^*$ is the maximum value of i and $\tilde{v}_1^-$ is the minimum value of i for all alternatives. The positive and negative ideal solutions are represented by L and K, respectively.

Step 6: Calculate the separation measures: The separation between each alternative and FPIS, and the separation between each alternative and FNIS are respectively obtained as follows:

$$S_i^* = \sum_{j=1}^n d(\tilde{v}_{ij}, \tilde{v}_j^*) \qquad i=1,2,\ldots,m \tag{6}$$

$$S_i^- = \sum_{j=1}^n d(\tilde{v}_{ij}, \tilde{v}_j^-) \qquad i=1,2,\ldots,m \tag{7}$$

Here, d is the distance between two fuzzy numbers obtained as follows when two triangular fuzzy numbers (a_1, b_1, c_1) and (a_2, b_2, c_2):

$$d_v(\tilde{M}_1, \tilde{M}_2) = \sqrt{\frac{1}{3}[(a_1 - a_2)^2 + (b_1 - b_2)^2 + (c_1 - c_2)^2]} \tag{8}$$

where $d(\tilde{v}_{ij}, \tilde{v}_j^*)$ and $d(\tilde{v}_{ij}, \tilde{v}_j^-)$ represent crisp numbers.

Step 7: Compute the closeness coefficient (C_i) and rank the alternatives: The closeness coefficient (C_i) of each alternative is obtained by the following formula:

$$C_i = \frac{S_i^-}{S_i^+ + S_i^-} \tag{9}$$

Table 2. Fuzzy scale

Code	Linguistic terms	L	M	U
1	Very low	1	1	3
2	Low	1	3	5
3	Medium	3	5	7
4	High	5	7	9
5	Very high	7	9	9

Table 3. Decision matrix

	Cost	Availability	Dose	Frequency	Allergy	Path	Safety	Efficacy	Age	Other health conditions	GERD stage	Treatment duration	Success rate	Drug-drug interaction	Drug-food interaction
Antacids	(1,000, 1,000, 3,000)	(5,667, 7,667, 9,000)	(4,333, 6,333, 8,333)	(5,000, 7,000, 8,333)	(1,000, 1,667, 3,667)	(1,000, 1,667, 3,667)	(4,333, 6,333, 8,333)	(2,333, 4,333, 6,333)	(2,333, 3,667, 5,667)	(1,667, 3,667, 5,667)	(1,000, 1,000, 3,000)	(1,000, 1,667, 3,667)	(1,000, 2,333, 4,333)	(4,333, 6,333, 8,333)	(3,667, 5,667, 7,667)
Histamine blockers	(1,000, 3,000, 5,000)	(4,333, 6,333, 8,333)	(4,333, 6,333, 7,667)	(1,667, 3,667, 5,667)	(1,000, 2,333, 4,333)	(2,333, 4,333, 6,333)	(3,667, 5,667, 7,667)	(2,333, 4,333, 6,333)	(2,333, 4,333, 6,333)	(3,667, 5,667, 7,667)	(1,000, 2,333, 4,333)	(1,000, 1,000, 3,000)	(1,667, 3,667, 5,667)	(4,333, 6,333, 8,333)	(5,000, 7,000, 8,333)
Proton pump inhibitors	(2,333, 4,333, 6,333)	(5,667, 7,667, 9,000)	(1,667, 3,667, 5,667)	(1,000, 3,000, 5,000)	(1,000, 1,667, 3,667)	(1,000, 3,000, 5,000)	(6,333, 8,333, 9,000)	(4,333, 6,333, 8,333)	(1,667, 3,667, 5,667)	(3,667, 5,667, 7,667)	(4,333, 6,333, 8,333)	(1,667, 3,667, 5,667)	(6,333, 8,333, 9,000)	(5,667, 7,667, 9,000)	(5,667, 7,667, 9,000)
Prokinetic agents	(5,000, 7,000, 9,000)	(1,000, 3,000, 5,000)	(1,000, 1,667, 3,667)	(1,000, 1,667, 3,667)	(4,333, 6,333, 8,333)	(2,333, 4,333, 6,333)	(1,667, 3,667, 5,667)	(2,333, 4,333, 6,333)	(5,667, 7,667, 8,333)	(5,667, 7,667, 9,000)	(1,000, 3,000, 5,000)	(1,000, 3,000, 5,000)	(3,000, 5,000, 7,000)	(2,333, 4,333, 6,333)	(5,000, 7,000, 9,000)

GERD: Gastroesophageal reflux disease.

Table 4. Normalized decision matrix

	Cost	Availability	Dose	Frequency	Allergy	Path	Safety	Efficacy	Age	Other health conditions	GERD stage	Treatment duration	Success rate	Drug-drug interaction	Drug-food interaction
Antacids	(0.111, 0.111, 0.333)	(0.630, 0.852, 1,000)	(0.520, 0.760, 1,000)	(0.600, 0.840, 1,000)	(0.120, 0.200, 0.440)	(0.158, 0.263, 0.579)	(0.481, 0.704, 0.926)	(0.280, 0.520, 0.760)	(0.280, 0.440, 0.680)	(0.185, 0.407, 0.630)	(0.120, 0.120, 0.360)	(0.176, 0.294, 0.647)	(0.111, 0.259, 0.481)	(0.481, 0.704, 0.926)	(0.407, 0.630, 0.852)
Histamine blockers	(0.111, 0.333, 0.556)	(0.481, 0.704, 0.926)	(0.520, 0.760, 0.920)	(0.200, 0.440, 0.680)	(0.120, 0.280, 0.520)	(0.368, 0.684, 1,000)	(0.407, 0.630, 0.852)	(0.280, 0.520, 0.760)	(0.280, 0.520, 0.760)	(0.407, 0.630, 0.852)	(0.120, 0.280, 0.520)	(0.176, 0.176, 0.529)	(0.185, 0.407, 0.630)	(0.481, 0.704, 0.926)	(0.556, 0.778, 0.926)
Proton pump inhibitors	(0.259, 0.481, 0.704)	(0.630, 0.852, 1,000)	(0.200, 0.440, 0.680)	(0.120, 0.360, 0.600)	(0.120, 0.200, 0.440)	(0.158, 0.474, 0.790)	(0.704, 0.926, 1,000)	(0.520, 0.760, 1,000)	(0.200, 0.440, 0.680)	(0.407, 0.630, 0.852)	(0.520, 0.760, 1,000)	(0.294, 0.647, 1,000)	(0.704, 0.926, 1,000)	(0.630, 0.852, 1,000)	(0.630, 0.852, 1,000)
Prokinetic agents	(0.556, 0.778, 1,000)	(0.111, 0.333, 0.556)	(0.120, 0.200, 0.440)	(0.120, 0.200, 0.440)	(0.520, 0.760, 1,000)	(0.368, 0.684, 1,000)	(0.185, 0.407, 0.630)	(0.280, 0.520, 0.760)	(0.680, 0.920, 1,000)	(0.630, 0.852, 1,000)	(0.120, 0.360, 0.600)	(0.176, 0.529, 0.882)	(0.333, 0.556, 0.778)	(0.259, 0.481, 0.704)	(0.556, 0.778, 1,000)

GERD: Gastroesophageal reflux disease.

Table 5. Weighted normalized decision matrix

	Cost	Availability	Dose	Frequency	Allergy	Path	Safety	Efficacy	Age	Other health conditions	GERD stage	Treatment duration	Success rate	Drug-drug interaction	Drug- food interaction
Antacids	(0.007, 0.007, 0.022)	(0.042, 0.057, 0.067)	(0.035, 0.051, 0.067)	(0.040, 0.056, 0.067)	(0.008, 0.013, 0.029)	(0.011, 0.018, 0.039)	(0.032, 0.047, 0.062)	(0.019, 0.035, 0.051)	(0.019, 0.029, 0.046)	(0.012, 0.027, 0.042)	(0.008, 0.008, 0.024)	(0.012, 0.020, 0.043)	(0.007, 0.017, 0.032)	(0.032, 0.047, 0.062)	(0.027, 0.042, 0.057)
Histamine blockers	(0.007, 0.022, 0.037)	(0.032, 0.047, 0.062)	(0.035, 0.051, 0.062)	(0.013, 0.029, 0.046)	(0.008, 0.019, 0.035)	(0.025, 0.046, 0.067)	(0.027, 0.042, 0.057)	(0.019, 0.035, 0.051)	(0.019, 0.035, 0.051)	(0.027, 0.042, 0.057)	(0.008, 0.019, 0.035)	(0.012, 0.012, 0.035)	(0.012, 0.027, 0.042)	(0.032, 0.047, 0.062)	(0.037, 0.052, 0.062)
Proton pump inhibitors	(0.017, 0.032, 0.047)	(0.042, 0.057, 0.067)	(0.013, 0.029, 0.046)	(0.008, 0.024, 0.040)	(0.008, 0.013, 0.029)	(0.011, 0.032, 0.053)	(0.047, 0.062, 0.067)	(0.035, 0.051, 0.067)	(0.013, 0.029, 0.046)	(0.027, 0.042, 0.057)	(0.035, 0.051, 0.067)	(0.020, 0.043, 0.067)	(0.047, 0.062, 0.067)	(0.042, 0.057, 0.067)	(0.042, 0.057, 0.067)
Prokinetic agents	(0.037, 0.052, 0.067)	(0.007, 0.022, 0.037)	(0.008, 0.013, 0.029)	(0.008, 0.013, 0.029)	(0.035, 0.051, 0.067)	(0.025, 0.046, 0.067)	(0.012, 0.027, 0.042)	(0.019, 0.035, 0.051)	(0.046, 0.062, 0.067)	(0.042, 0.057, 0.067)	(0.008, 0.024, 0.040)	(0.012, 0.035, 0.059)	(0.022, 0.037, 0.052)	(0.017, 0.032, 0.047)	(0.037, 0.052, 0.067)

GERD: Gastroesophageal reflux disease.

The optimal choice was closest to the FPIS and most distant from the FNIS. The closeness coefficients for each treatment alternative were used to determine their rankings. The treatment option with the greatest closeness coefficient was considered the best.

RESULTS

By applying the Fuzzy TOPSIS method, the alternatives are evaluated in terms of various criteria, and the model results are shown step by step as follows:

Step 2: Form a decision matrix.

Fifteen criteria and 4 alternatives have been evaluated (ranked) using the Fuzzy TOPSIS method. The evaluation was conducted with three decision makers. The matrix below shows the arithmetic means of all of the 3 decision makers, as shown in Table 3.

Step 3: Form a normalized decision matrix.

Based on the positive and negative ideal solutions, the normalized decision matrix presented in Table 4 was calculated from equations 1 and 2.

Step 4: Weighted normalized decision matrix.

Based on the different weights of each criterion, the weighted normalized decision matrix presented in Table 5 was calculated using equation 3.

Step 5: Define the fuzzy positive ideal solution (FPIS, A*) and the fuzzy negative ideal solution ($FNIS, A^{-}$).

The FPIS and FNIS of the alternatives presented in Table 6 were computed from equations 4 and 5.

Step 6: Calculate the distance between each alternative and the FPIS and the distance between each alternative and the FNIS.

The distances between each alternative and the FPIS and the distances between each alternative and the FNIS were computed from equations 6, 7, and 8, as shown in Table 7.

Table 6. Positive and negative ideal solutions

	Positive ideal	Negative ideal
Cost	(0.037, 0.052, 0.067)	(0.007, 0.007, 0.022)
Availability	(0.042, 0.057, 0.067)	(0.007, 0.022, 0.037)
Dose	(0.035, 0.051, 0.067)	(0.008, 0.013, 0.029)
Frequency	(0.040, 0.056, 0.067)	(0.008, 0.013, 0.029)
Allergy	(0.035, 0.051, 0.067)	(0.008, 0.013, 0.029)
Path	(0.025, 0.046, 0.067)	(0.011, 0.018, 0.039)
Safety	(0.047, 0.062, 0.067)	(0.012, 0.027, 0.042)
Efficacy	(0.035, 0.051, 0.067)	(0.019, 0.035, 0.051)
Age	(0.046, 0.062, 0.067)	(0.013, 0.029, 0.046)
Other health conditions	(0.042, 0.057, 0.067)	(0.012, 0.027, 0.042)
GERD stage	(0.035, 0.051, 0.067)	(0.008, 0.008, 0.024)
Treatment duration	(0.020, 0.043, 0.067)	(0.012, 0.012, 0.035)
Success rate	(0.047, 0.062, 0.067)	(0.007, 0.017, 0.032)
Drug-drug interaction	(0.042, 0.057, 0.067)	(0.017, 0.032, 0.047)
Drug-food interaction	(0.042, 0.057, 0.067)	(0.027, 0.042, 0.057)

GERD: Gastroesophageal reflux disease.

Step 7: Compute the closeness coefficient (C_i) and rank alternatives.

The closeness coefficient and C_i of each alternative were obtained from equation 9. The optimal candidate is nearest to the FPIS and most distant from the FNIS. The closeness coefficients of each alternative and their ranking order are presented in Table 8. Based on the implemented method's results, it was observed that PPIs are the best treatment for GERD because they had the highest C_i value of 0.642, as presented in Figure 1. The treatment option with the lowest C_i value was antacids, which had a C_i value of 0.33.

DISCUSSION

Fuzzy TOPSIS, a MCDM approach, was used to assess four treatment alternatives for GERD. After the evaluation of the GERD treatment alternatives by three experts, the ranking showed that PPIs were the number one treatment alternative for GERD, next is prokinetic agents and the least treatment alternative was anticacids. In a study conducted by Gashi et al.[30], to determine whether or not PPIs helped patients with erosive reflux disease by reducing their symptoms and promoting endoscopic repair. This prospective study included 380 individuals with a history of primary symptoms of erosive reflux. The heartburn system score and regurgitation score were used to assess symptoms before and during PPI treatment throughout the three-month period. Approximately 95% of patients had heartburn, 90% had regurgitation, and 70% had epigastric discomfort before PPI treatment. Pyrosis and regurgitation were quantitatively measured in all patients. Patients treated with PPIs showed improvements ranging from 90% to 20% in regurgitation, 70% to 10% in epigastric discomfort, and 95% to 25% in pyrosis. Complete recovery from erosive oesophagitis was observed in 71.67% of patients, with minimal progression observed in 1.05%. Patients with erosive reflux disease treated with PPIs exhibited significant improvement in symptoms and mucosal healing three months after therapy initiation.

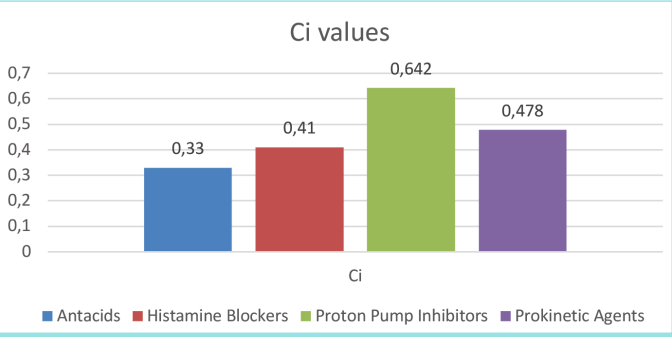

Figure 1. Graph of closeness coefficient values.

Table 7. Distance values of FPIS and FNIS

	Distance from positive ideal	Distance from the negative ideal
Antacids	0.303	0.15
Histamine blockers	0.27	0.188
Proton pump inhibitors	0.163	0.292
Prokinetic agents	0.237	0.217

FPIS: Fuzzy positive ideal solutions, FNIS: Fuzzy negative ideal solutions.

Table 8. Closeness coefficient values of the treatments

	C_i	Rank
Antacids	0.33	4
Histamine blockers	0.41	3
Proton pump inhibitors	0.642	1
Prokinetic agents	0.478	2

According to experts, the 15 criteria used in the study, cost, availability, dose, frequency, allergy, path, safety, efficacy, age, other health conditions, GERD stage, treatment duration, success rate, drug-drug interaction, and drug-food interaction, are very important factors when determining which treatment is suitable for people suffering from GERD. These factors should be considered because they influence the outcome of patient treatment. For example, cost ensures that treatment is accessible and sustainable, while availability ensures that treatment begins and continues on schedule. The correct dose and appropriate dosage increase drug effectiveness and patient compliance. Considering allergies and the path through which the medication is taken, patients do not encounter unfavorable responses and can conveniently consume the medication. Allergy and safety factors may also help prevent possible side effects and complications, while efficacy determines the success of the drug in relieving GERD symptoms. The age criterion is also an important criterion to ensure the suitability of the drug for individual patient profiles. On the other hand, considering other health conditions when choosing treatment for GERD is vital for managing drug interactions and side effects. Although the stage of the disease and duration of treatment also affect the effectiveness and success rate of the treatment plan, drug-drug, and drug-food interactions play an important role in maintaining the integrity of the treatment and the general health of the patient. In short, each criterion used in the study and evaluated by experts is very important.

Castell et al.[31], in their article entitled "Erosive Esophagitis: The Efficacy and Safety of Lansoprazole", a comparison of omeprazole 20 mg, omeprazole 10 mg, omeprazole 5 mg, and placebo was performed with a total of 188 patients with endoscopically confirmed erosive reflux esophagitis who were randomly assigned to receive either lansoprazole 30 mg (n=422), lansoprazole 15 mg (n=218), omeprazole 20 mg (n=431), or placebo (n=213) once daily for 8 weeks. Endoscopic assessments of healing were performed at 2, 4, 6, and 8 weeks. For lansoprazole 30 mg, the success rates at 2, 4, 6, and 8 weeks were 65.3%, 83.3%, 89.4%, and 90.0%, respectively. All active treatments were more effective than placebo, with lansoprazole 15 mg having a 56.3% success rate, omeprazole 20 mg having an 82.0% success rate, and placebo having a 23.9% success rate.

Study Limitations

As with all studies, this study also has limitations. This study was limited to the criteria used in the evaluation of treatment options for GERD. Additionally, the study was limited to experts who evaluated the criteria used in the study.

CONCLUSION

In this study, the Fuzzy TOPSIS method was implemented to select the optimal treatment modality among different treatment options for GERD. In the existing literature, determining the optimal treatment method for GERD has not yet been considered an MCDM problem. We used 15 criteria to evaluate the 4 treatment alternatives (antacids,

histamine blockers, PPIs, and prokinetic agents) of GERD using the Fuzzy TOPSIS technique. The evaluation was performed by one gastroenterologist and two final-year PhD students in the pharmacy department. According to the results, it has been observed that PPIs are the best treatment for GERD because they have the highest C_i value of 0.642, and the treatment alternative with the lowest C_i value of 0.33 is antacids.

Implementing the Fuzzy TOPSIS method would provide DMs with a useful tool to determine the optimal modality for GERD treatment. This approach would provide a more holistic decision-making process, taking into account multiple criteria when evaluating various treatment options. As a result, it is expected that this study will help clinicians make more informed and scientifically based decisions regarding the treatment of GERD. It is recommended to increase the number of criteria for the implemented Fuzzy TOPSIS method in future studies and to compare this method with other MCDM methods.

MAIN POINTS

- The Fuzzy TOPSIS method was implemented to determine the most appropriate treatment method among various treatment options for GERD.
- Determining the optimal treatment method for GERD, which is an MCDM problem, has never been examined before, and this work is the first to do so.
- Proton pump inhibitors are the best treatment for GERD because they have the highest Ci value of 0.642, and the treatment alternative with the lowest Ci value of 0.33 is antacids.
- This approach would provide clinicians with a more holistic decision-making process by considering multiple criteria when evaluating available treatment options for GERD and is believed to help clinicians make more informed and scientifically based decisions regarding the treatment of GERD.

ETHICS

Ethics Committee Approval: This study was approved by the Near East University Scientific Research Ethics Committee (approval number: 2023/117-1779, date: 26.10.2023).

Informed Consent: Patient consent is not required.

Authorship Contributions

Concept: A.F.T., İ.E., N.S., Design: A.F.T., İ.E., N.S., Data Collection and/or Processing: A.F.T., Analysis and/or Interpretation: A.F.T., İ.E., N.S., Literature Search: A.F.T., İ.E., N.S., Writing: A.F.T., İ.E., N.S.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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