Retrospective study: Ubrogepant vs. Triptans in Treating Migraine in Jeddah, Saudi Arabia

By
Ahmad Ali Abdullah Fallata*
MD, FRCPC
***Assistant Professor of Internal Medicine (Neurology)**
Movement disorders Consultant
Electromyographer/ Neuromuscular consultant
Consultant General Neurology , University of Tabuk
Room 222- Faculty of Medicine, University of Tabuk, Tabuk, Saudi Arabia, Tabuk 71491 /Tel: 014 427 3022

Abstract- The present study aims to compare between two medications of migraine, ubrogepant and eletriptan (triptans), in terms of general characteristics, efficacy, and special considerations of use. Topics of discussion in the study include the following: overview of migraine, types of pharmacological treatments of migraine, overview of ubrogepant, considerations in the use of ubrogepant for treating migraine, overview of triptans, and considerations in the use of triptans for treating migraine. The study also involves conducting a descriptive study to compare the efficacy of the two medications on a sample of (56) patients at three large general hospitals located in the city of Jeddah, Saudi Arabia. Findings of the study do not show significant differences between the two medications in terms of efficacy and duration before feeling improvement, measured by extent of improvement. Sample members from both study groups also reported using similar additional medications. However, one significant aspect of difference between the two study groups concerns the reported side effects, although the incidence of such effects was rare in both groups. In the light of the findings, the researcher recommends conducing further research, on larger scale, to investigate, in more detail, the potential side effects of using ubrogepant or eletriptan in migraine treatment.

Keywords: Ubrogepant, Triptans, Eletriptan, Migraine.

Introduction:

Migraine is a common neurovascular disorder with an incapacitating and chronic nature. It is characterized by severe headaches, impaired functioning of the nervous system, and, in many cases, other neurological problems. Several symptoms and manifestations characterize migraine. Patients with migraine typically experience episodes of headache often occurring in a throbbing pattern and unilateral concentration, and in many cases pain can be severe. Typical symptoms of migraine include vomiting, nausea, and sensitivity to sensory stimuli. If left untreated, migraine symptoms may last for a period ranging in length from 4 to 72 hours (Goadsby et al., 2002, 257).

Effective treatment of migraine requires accurate diagnosis, identification of potential factors underlying the condition, and appropriate responding to the disorder's impact in the patient. It is also important that treatment plans take into careful consideration any comorbid or coincidental conditions that the patient may have. Pharmacological treatments are commonly used for addressing the needs of patients with migraine. Such treatments can be either acute or preventing. For patients with severe migraine symptoms, both types of treatment are often needed (Silberstein, 2015, 973).

Several pharmacological products are available for addressing the needs of patients with migraine. Notable among these products is ubrogepant, which is used for acute treatment of migraine. Its underlying mechanism revolves around interacting with calcitonin gene-related peptide (abbreviated as CGRP) and blocking its receptor. Clinical evidence shows that the medication is characterized by safety, tolerability, and efficacy. Moreover, evidence shows that the use of ubrogepant is linked to other positive outcomes, such as higher patient satisfaction, reduction of functional disability, and improvement in overall functioning (Adams et al., 2023, 2).

Another type of pharmacological treatment for migraine is a class of medications known as triptans, which are also abortive medications. Triptans do not treat pain, but they impact the occurrence of the migraine attack itself as well as the symptoms. Although these medications are efficacious in stopping migraine attacks, they cannot prevent their occurrence (Cologno et al., 2012, S193).

Understanding Migraine:

Migraine can be described as a chronic medical condition, characterized by the symptom of headaches happening in a recurring manner and with intensity ranging between moderate and severe. The intensity of pain associated with migraine headaches is so potent that they can have debilitating effects on an individual's functioning. In many cases, the headaches can be incapacitating to the extent that an individual will need bed rest. The duration of lasting for a migraine headache ranges in period length between a part of the day to several days (Spierings, 2003, 255).

The headache pain characterizing migraine is often associated with other symptoms, such as vomiting, nausea, and higher sensitivity to sensory stimuli. Migraine is believed to be

among the most prevalence neurological disorders, as the prevalence rate of migraine is estimated to range between 12 and 15% globally. Migraines of severe degrees are considered by the World Health Organization (WHO) to be among the medical conditions with the most potent effects on patients (Dighriri et al., 2023, 1).

Types of Pharmacological Treatments of Migraine:

Treatments of migraine are classified into two main categories, which are abortive and preventive treatments. Abortive treatments are used for the purpose of complete and fast relief of pain resulting from migraine. On the other hand, the purpose of preventive treatment is the reduction of severity, duration, and frequency of migraine attacks. Choosing the right preventive treatment requires taking multiple factors into consideration, such as the medication's efficaciousness and side effects, the patient's needs and response to other medications, and the presence of any comorbidity (Bordini et al., 2005, 388).

Several medications have been developed for treating migraine. Table 1 below presents a brief list of the most common medications for treating the disorder, with the explanation of medication classes, primary uses, and tolerability, side effects of each of these medications.

Table 1. The main types of medications used to treat migraine (Dighriri et al., 2023, 8).

Medication class	Medication	Primary use	Tolerability/side effects
Triptans	Sumatriptan, rizatriptan	Acute migraine treatment	Generally well-tolerated; sensations of tightness in chest, neck, jaw, etc. Contraindicated for specific cardiovascular conditions.
Ergotamines	Ergotamine, dihydroergotamine	Counteract migraine-related dilation	It can lead to medication overuse, headaches, and nausea. Potential for vasoconstriction complications.
Beta-blockers	Propranolol, metoprolol	Preventive migraine treatment	Fatigue, depression, cold hands and feet. Contraindicated in asthma or certain cardiovascular conditions.
Anticonvulsants	Topiramate, valproic acid	Migraine prevention	Weight loss, cognitive side effects, tingling in hands and feet.
Onabotulinumtoxin A	Botox	Preventive for chronic migraines (every three months)	Generally well-tolerated; injection site reactions; rare spread of toxin effects.
CGRP monoclonal antibodies	Erenumab, fremanezumab	Preventive for episodic or chronic migraines	Generally well-tolerated injection site reactions.
	Ubrogepant	Acute treatment for episodic migraine	Generally well-tolerated. Mild side effects (nausea, somnolence, dizziness) indicate good tolerability and likely acceptability.

Figure 1 below illustrates the underlying physiology of migraine and how medications of multiple commonly accepted medication classes mitigate migraine symptoms.

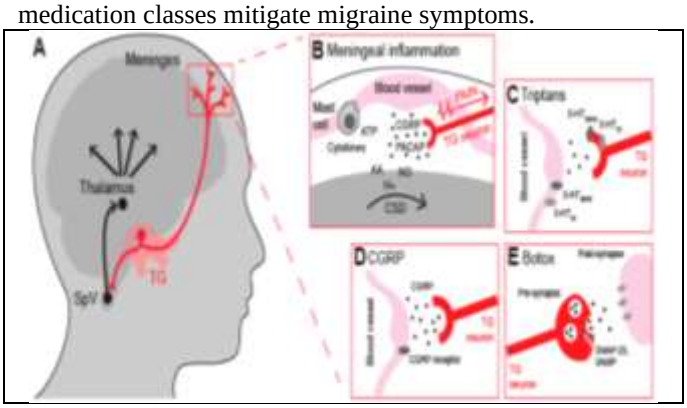

Figure 1. The underlying physiology of migraine and how medications of different classes treat the symptoms (Cohen et al., 2023, 2).

Below is a brief explanation of the main sections of Figure 1:

- (**A**): the axis of migraine-induced pain, which encompasses parts of the central nervous system, such as thalamus and spinal trigeminal nucleus (abbreviated as SpV), as well as peripheral sites in the brain, such as meninges and the trigeminal ganglia (abbreviated as TG).
- (**B**): meningeal inflammation results from the release of nociceptive and inflammatory neuropeptides, triggered by cortical spreading depression (abbreviated as CSD). These neuropeptides are released by trigeminal terminals, which are responsible for the process of innervating the meninges as well as their associated blood vessels.
- (**D**): the mechanism by which calcitonin gene-related peptide (abbreviated as CGRP) contributes to the underlying physiology of migraine.
- (**C**): depiction of the action mechanism of triptans against migraine.
- (**E**): depiction of the action mechanism of Botox against migraine.

Overview of Ubrogepant:

Ubrogepant is a CGRP receptor antagonist used a medication for treating migraine. It is undergoing clinical trials for proving its efficaciousness as treatment (Dodick et al., 2019, 2). The chemical composition of the drug is illustrated in Figure

Drug name	Ubrogepant
Phase	Registered
Indication	Acute Migraine
Pharmacology description	Calcitonin gene-related peptide receptor antagonist
Route of administration	Oral
Chemical structure	

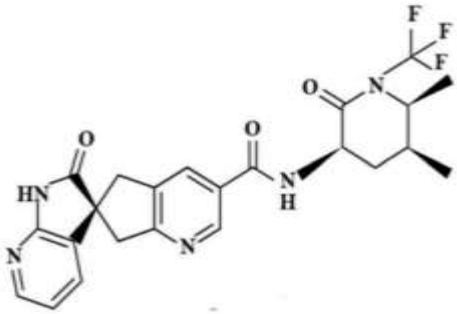

Figure 2. The chemical composition of ubrogepant (Dodick et al., 2019, 2).

Findings of long-term and pivotal safety trials show that ubrogepant is characterized by efficacy, tolerability, and safety as

an acute treatment for the symptoms of migraine. It has been found that the use of ubrogepant has the potential to improve levels of patient satisfaction and ameliorate the debilitating effects of migraine symptoms on the patient. Ubrogepant is used, both in trials and clinical practice, in the treatment of breakthrough migraine (Lipton et al., 2024, 70).

Ubrogepant is classified as an "acute treatment" drug for migraine. Thus, it differs from other drugs that are purely prophyiactic (preventive) or those with mixed acute/prophyiactic therapeutic effects (de Vries et al., 2021, 976). Figure 2 below illustrates how Ubrogepant compares in that regard.

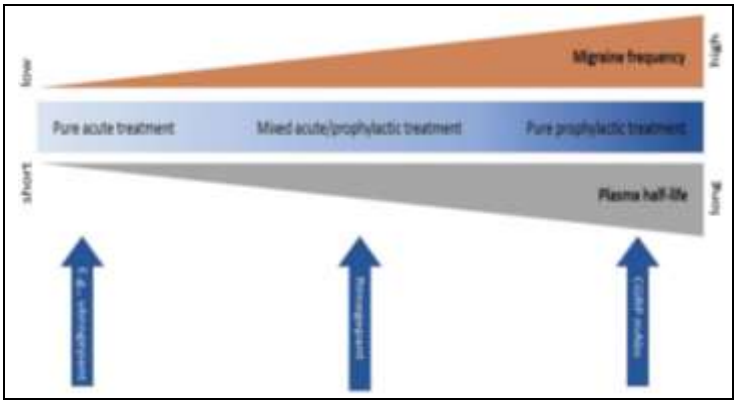

Figure 3. Continuum-based comparison of ubrogepant with other drugs with different therapeutic approaches (de Vries et al., 2021, 976).

The mechanism by which ubrogepant mitigates the pain associated with migraine is illustrated in Figure 3 below.

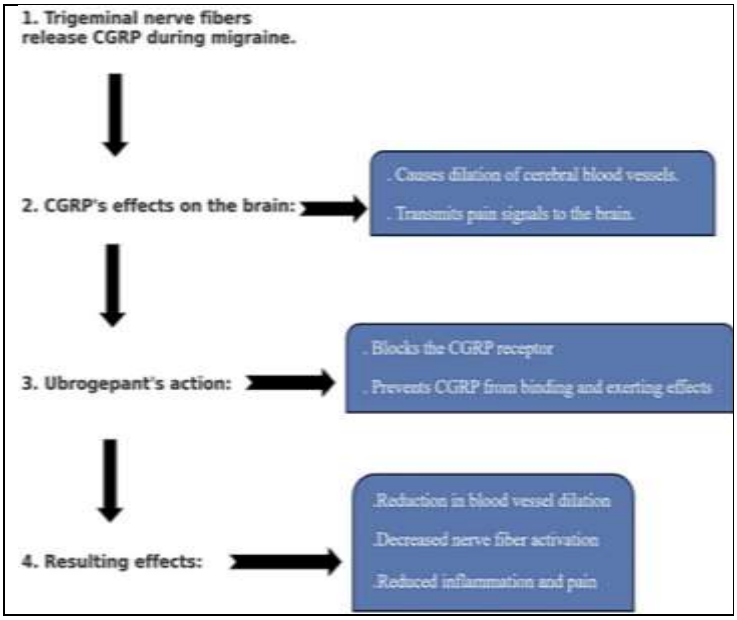

Figure 4. The mechanism by which ubrogepant mitigates the pain associated with migraine (Dighriri et al., 2023, 4).

Considerations in the Use of Ubrogepant for Treating Migraine:

- **General Factors:**

The effectiveness of ubrogepant in treating migraine is influenced by a number of factors. The most influential of these factors are listed in Table 2 below.

Table 2. Factors that influence the effectiveness of ubrogepant in treating migraine (Dighriri et al., 2023, 9).

Factor	Details
Adverse effects	The most commonly reported adverse effects of ubrogepant include nausea, dry mouth, and dizziness. These tend to be mild to moderate in severity.
Drug interactions	CYP3A4 metabolizes ubrogepant. Drugs that inhibit or induce CYP3A4 can affect ubrogepant levels and potentially increase side effects.
Underlying conditions	Patients with severe hepatic or renal impairment may have increased side effects with ubrogepant due to reduced clearance. Dose adjustments may be needed.
Food intake	Food does not have a clinically meaningful impact on ubrogepant pharmacokinetics or side effects. It can be taken without regard to meals.
Dosage	Higher doses of ubrogepant are associated with higher rates of adverse events. Proper dosing is essential to balance efficacy and tolerability.

- **Contraindications:**

In addition to the aforementioned factors, certain contraindications prevent the use of ubrogepant in treating migraine. The most notable of these contraindications are listed in Table 3.

Table 3. Contraindications prevent the use of ubrogepant in treating migraine (Dighriri et al., 2023, 10).

Contraindication	Description and reasoning
Hypersensitivity	Risk of severe allergic reactions due to hypersen
Severe hepatic impairment	The liver metabolizes ubrogepant; higher blood l risk of adverse effects.
Co-administration with potent CYP3A4 inhibitors	Potent CYP3A4 inhibitors can significantly increa effects.
Pregnancy and breastfeeding	Limited safety data in pregnancy and excretion in
Uncontrolled hypertension	Ubrogepant can cause transient increases in bloo patients.

Overview of Triptans:

Triptans are potent serotonin 5-$HT_{1B/1D}$-receptor agonists that can be used for the purpose of acute treatment of migraine. The mechanism of action by which triptans mitigate the effects of migraine focuses on the constriction o blood vessels, inhibition of neurotransmission, stabilization of sensory terminals, and inhibition of the release of calcitonin gene-related peptide CGRP with is fundamentally linked to the pathophysiology of migraine. Seven triptans are available for

medical use, and each of them is distinctive and unique in terms of tolerability and efficacy.

A significant issue associated with the use of triptans in treating migraines is the risk of what is known as medication overuse headache, which is a disorder in which the patient experiences migraine attacks in a pattern characterized by increased intensity and frequency (Davidsson et al., 2021). The chemical composition of reach of the seven triptans available for medical use is illustrated in Figure 5 below.

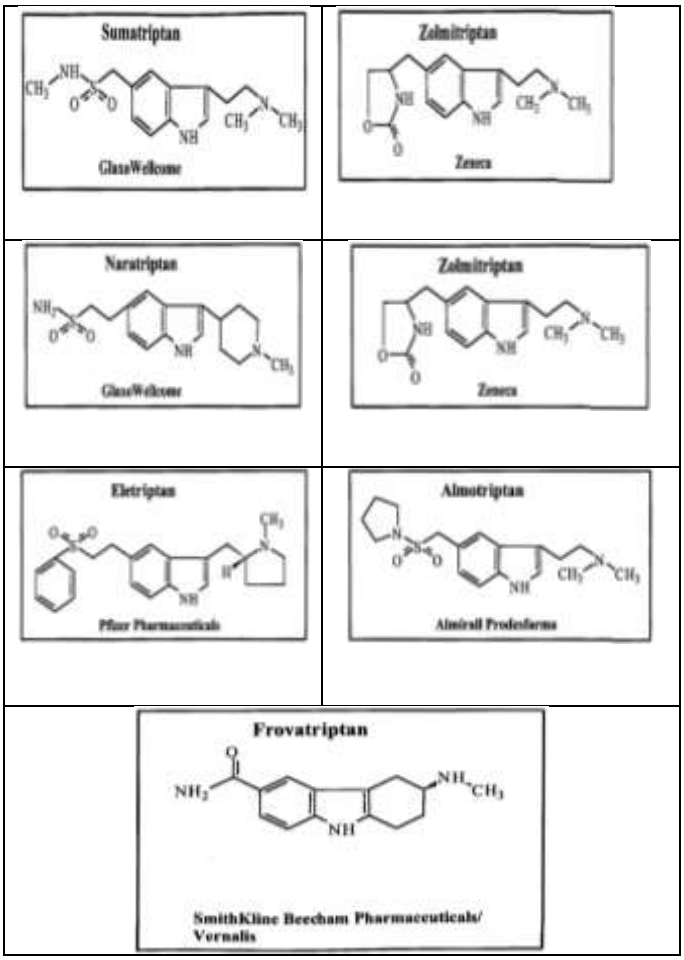

Figure 5. Chemical composition of reach of the seven triptans available for medical use (Saxena & Tfelt-Hansen, 2001, 4).

Considerations in the Use of Triptans for Treating Migraine:

- **Potential Mistakes in Administering:**

The use of triptans for treating migraine should be done while talking certain considerations into account. The most important of these considerations are discussed below.

- **Triptans Should Be Used Early in the Migraine Attack:**

Triptans are most efficacious when used early in the migraine. It should not be used when the pain progresses to a subsequent more intense phase (e.g., aura phase). It is important to take into account the following (BPAC, 2007, 31):

1. Clinical trials in which triptans were tested during the aura phase showed no significant therapeutic superiority compared to the placebo condition.
2. In many cases, the patient's phase of migraine may not be apparent. This is especially so among patients with complex manifestation of symptoms of the aura phase.

- **Repeated Doses Should Be Avoided:**

As a general rule, the triptan dose should not be repeated if the patient perceives no improvement after the first dose. On the other hand, if the first dose results in relief, the dose should be repeated, with accordance to the requirements of administering each individual triptan (BPAC, 2007, 31-32). Table 4 illustrates the different recommended arrangements for repeating doses in the use of four commercially available triptans, which are sumatriptan, rizatriptan, zolmitriptan, and naratriptan.

Table 4. The different recommended arrangements for repeating doses in the use of a list of commercially available triptans (BPAC, 2007, 31-32).

Triptan	Dose	Instructions
Sumatriptan	Oral: 50 mg (some patients may require 100 mg)	Dose may be repeated after at least two hours if migraine recurs; maximum 300 mg in 24 hours
	Subcutaneous: 6 mg	Dose may be repeated once after at least one hour if migraine recurs; maximum 12 mg in 24 hours
Rizatriptan	Oral: 10 mg	Dose may be repeated after at least two hours if migraine recurs; maximum 30 mg in 24 hours. If prescribing the wafer formulation, advise patient that it should be placed on the tongue and allowed to dissolve.
Zolmitriptan	Intranasal: 5 mg into one nostril	Dose may be repeated after at least two hours if migraine recurs; maximum 10 mg in 24 hours. N.B. this advice is from the UK datasheet for zolmitriptan nasal spray; the New Zealand datasheet does not include information about repeat dosing.
Naratriptan	Oral: 2.5 mg	Dose may be repeated after at least four hours if migraine recurs; maximum 5 mg in 24 hours.

- **Avoidance of Use for 10 Days or More a Month:**

The use triptans for 10 days more a month can result in medication overuse headache. Therefore, in order to prevent the risk of medication overuse headache, the use of triptans for 10 days or more should be avoided. The characteristic symptom of medication overuse headache is a daily headache similar to that associated with tension or attacks of headaches similar in fashion to migraine. Withdrawal of triptans results in improvement in headache symptoms within two months, although symptoms

often initially worsen until improvement of symptoms actually occurs (BPAC, 2007, 32).

- **Safety Precautions and Considerations:**
  - **Cardiovascular Health:**

There have been frequent reports of serious cardiovascular health issues, even leading to death, associated with the use of triptans among patients with cardiovascular conditions. The use of triptans in the case of patients with high cardiac arrest risks should carefully assessed before using a triptan-based migraine therapy. Moreover, the use of triptans is contraindicated in patients with patients with certain medical conditions, such as ischaemic heart disease, severe hypertension, coronary vasospasm, stroke, and myocardial infarction; the risk of using triptans in these groups of patients is attributed to the vasoconstrictive effects associated with their medical conditions (BPAC, 2007, 33).

  - **Pregnancy and Breastfeeding:**

Migraines are far more common in females than in males. The age range within which migraines are most common is between 25 and 55 years. Therefore, ensuring the safety of using in women during periods of pregnancy and breastfeeding is an important issue of consideration (BPAC, 2007, 33).

Clinical trials have not shown that migraines pose a risk factor for other adverse outcomes in women during periods of pregnancy or breastfeeding. However, it has been reported that pregnancy is possibly linked to certain conditions such as pre-eclampsia and pregnancy induced hypertension. On the other hand, it has been reported that the period of pregnancy can witness reduced frequency of migraine attacks; this effect is believed to be a result of sustained levels of estrogen during pregnancy. Despite the inconclusive findings, it is important to pay attention to providing treatment and help to pregnant women who experience migraine attacks in order to avoid adverse outcomes that may affect their overall health status and well-being. Examples of such outcomes include increased stress, poor nutrition (largely due to nausea and vomiting), and sleep deprivation (BPAC, 2007, 33).

  - **Interaction with Other Medications:**

The decision whether to use triptans for treating migraine should be taken while considering the potential risks associated with taking other medications. The most notable of these medications are listed below (BPAC, 2007, 35):

1. Monoamine oxidase inhibitors (MAOIs): the use of triptans should be avoided in the cases of patients who are currently using MAOIs. Evidence shows that using MAOIs causes significantly increased bioavailability of triptans as well as of other MAOIs, thereby potentially leading to unexpected/undesired outcomes of using triptans.
2. Selective serotonin reuptake inhibitor (SSRIs): the use of triptans with SSRIs is associated with a risk of serotonin syndrome. However, this risk is insignificant as interaction between the two classes of medications is shown to be rare by clinical evidence.
3. Ergot derivatives: the combination of triptans and ergot derivatives is associated with a potentially significant risk of coronary vasoconstriction and theoretical risk of additive vasoconstriction. However, the two medications can be taken but with taking careful consideration of the necessity of adequate temporal separation between the timings of taking the medications; in general, the use of triptans should avoided for 24 hours SSRIs, while the use of SSRIs should be avoided for six hours after using triptans.

Methodology:

- **Research Design:**

This study adopts a comparative descriptive research design. It is similar to the simple descriptive design; however, a key difference between the two designs is that the former has the advantage of allowing the researcher to comparing findings obtained from different research groups (Hlungwani, 2017, 33). The present study uses qualitative data (collected using questionnaires) and analysis in order to compare the efficacy of ubrogepant and triptans for treating migraine in a sample of patients in Jeddah, Saudi Arabia.

- **Population and Sample of the Study:**
  - **Population of the Study:**

The target population of the study consisted of patients with migraine who visited three large general hospitals in the city of Jeddah during January 2024. The study focused on patients who were prescribed and either ubrogepant or triptans and used the medication for at least 14 days. A sample from that population was invited to complete a questionnaire during follow-up visits.

  - **Sample of the Study:**

From among the target population of the study, a sample of 56 patients was selected for data collection. The sample consisted of two groups:

1. Ubrogepant group: this group included 23 patients.
2. Eletriptan (triptan) group: this sample included 33 patients.

- **Sampling:**

The present study used the random sampling method for selecting the research sample. With the use of this technique, all members of the target population have equal changes of being selected in the final sample for data collection. The purpose of using the random sampling method was to avoid bias in sampling and collect data in a manner that allows for deriving general conclusions on the entire target population of the study.

- **Data Collection:**
  - **Research Instrument:**

For the purposes of the present study, the researcher designed a semi-structured questionnaire encompassing both quantitative and qualitative items. The questionnaire focuses on the treatment outcomes listed below:

1. Personal perception of improvement resulting from using the medication (quantitative; expressed in percentage).
2. Duration between taking the medication and feeling change/improvement (quantitative; expressed in minutes/hours).
3. Whether other medications are used (qualitative; answers are open ended).
4. Whether any side effects are felt after taking the medication (qualitative; answers are open ended).

  - **Data Collection Procedures:**

Data collection was conducted during February 2024. Three large general hospitals located in Jeddah, Saudi Arabia, were visited for questionnaire distribution. Senior management of each hospital was contacted and informed of the purpose of the study and the ethical considerations intended to be implemented. Data was collected from patients doing follow-up visits after using prescribed medications for at least two weeks. Informed consent was obtained from all patients who participated in the study.

- **Data Analysis Techniques:**

The researcher used a combination of quantitative and qualitative analysis techniques to analyze the quantitative and qualitative data collected from sample members, respectively.

Results and Analysis:

- **Demographic Attributes of the Sample:**

The demographic attributes of the sample are summed up as follows:

1. Mean age: 42 years.
2. Gender distribution: 14 (25%) males, and 42 (75%) females.

- **Personal Perception of Improvement:**

Table 5 illustrates the distribution of sample members' responses on the personal perception of improvement after taking the medication.

Table 5. Sample members' responses on the personal perception of improvement after taking the medication.

Study Group	Do You Perceive Improvement as a Result of the Medication?	
	Yes	No
Ubrogepant	19	4
Eletriptan	25	8

Table 5 shows that the majority of sample members in both groups expressed their perception of improvement of migraine symptoms as a result of the medication received. Sample member vary in terms of their perceptions of the potency the medications their received.

- **Degree of Responsiveness on the Efficacy of Medication:**
  - **Ubrogepant Group:**
    1. Only four patients perceived the drug as fully eliminating the symptoms of migraine.
    2. Degrees of responsiveness for the rest of group members who believed the medication to be effective (n = 14) ranged between 60 and 80%.
  - **Eletriptan Group:**
    1. Only four patients perceived the drug as fully eliminating the symptoms of migraine.
    2. Degrees of responsiveness for the rest of group members who believed the medication to be effective (n = 21) ranged between 60 and 75%.
- **Duration before Feeling Improvement:**
  - **Ubrogepant Group:**

According on sample members' perceptions, the mean duration between taking the medication and feeling improvement is three hours.

  - **Eletriptan Group:**

According on sample members' perceptions, the mean duration between taking the medication and feeling improvement is two hours.

- **Other Medications Taking Alongside Migraine Treatments:**
  - **Ubrogepant Group:**

Three patients reported using paracetamol or NSAID alongside ubrogepant.

  - **Eletriptan Group:**

A total of 12 patients reported using paracetamol or NSAID alongside eletriptan.

- **Side Effects Felt After Taking the Medication:**
  - **Ubrogepant Group:**

Only one patient reported feeling dizziness after the use of ubrogepant.

  - **Eletriptan Group:**

Only three patients report heaviness in the neck and tongue.

Conclusion:

This study has compared between two of the most prominent medications used for the treatment of migraine, which are ubrogepant and eletriptan (triptan). Topics of discussion in the study included overview of migraine, types of pharmacological treatments of migraine, overview of ubrogepant, considerations in the use of ubrogepant for treating migraine, overview of triptans, and considerations in the use of triptans for treating migraine.

Findings of the study do not show significant differences between the two medications in terms of efficacy. Most sample members from both study groups perceived the migraine medication they were taking as highly effective in mitigating the pain, with some of them expressing their feeling that taking the medications fully eliminates migraine symptoms. Only a very small proportion of the sample believes the medications to be ineffective. The difference between the two medications in the length of duration needed for the medication's effect to be felt is insignificant. However, it is noticed that the number of sample members taking additional medications is significantly larger in the eletriptan group. A finding that warrants careful attention concerns the other symptoms felts after taking the medications; although the number of patients who experienced other symptoms is very small, the reported experienced symptoms are noticeably different. Therefore, the researcher recommends conducing further research, on larger scale, to investigate, in more detail, the potential side effects of using ubrogepant or eletriptan in migraine treatment.

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