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The use of triptans as an effective form of migraine treatment – review

Agata Borkowska, Military Institute of Aviation Medicine, Zygmunta Krasińskiego 54/56, 01-755 Warsaw, Poland
ORCID: https://orcid.org/0009-0008-7347-7762
E-mail: agata.borkowska.ab@wp.pl

Anna Kiełb, 5th Military Clinical Hospital in Krakow, Wrocławska 1-3, 30-901 Krakow, Poland
ORCID: https://orcid.org/0009-0005-3152-5429
E-mail: akielb97@gmail.com

Anna Mich, Independent Public Hospital in Mińsk Mazowiecki, Szpitalna 37, 05-300 Mińsk Mazowiecki, Poland
ORCID:https://orcid.org/0009-0004-6299-5506
E-mail: aniamich97@icloud.com

Klaudia Perkowska, Military Medical Institute, Szaserów 128, 04-349 Warsaw, Poland
ORCID: https://orcid.org/0009-0001-7362-4995
E-mail: dr.kperkowska@gmail.com

Anna Kaźmierczak, 4th Military Clinical Hospital in Wroclaw, Weigla 5, 53-114 Wroclaw, Poland
ORCID: https://orcid.org/0009-0000-8435-6685
E-mail: a.kazmierczak.1998@o2.pl

Patrycja Sornek, Military Medical Academy Memorial Teaching Hospital- Central Veteran Hospital, Stefana Żeromskiego 113, 90-549 Lodz, Poland
ORCID: https://orcid.org/0009-0003-9630-055X
E-mail: sornekpatrycja5@gmail.com

Wiktoria Izdebska, J. Gromkowski Regional Specialist Hospital in Wrocław, Koszarowa 5, 51-149 Wrocław, Poland
ORCID: https://orcid.org/0009-0005-0242-141X
E-mail: wiktoriaxizdebska@gmail.com

Igor Pawlak, Independent Public Hospital in Mińsk Mazowiecki, Szpitalna 37, 05-300 Mińsk Mazowiecki, Poland
ORCID: https://orcid.org/0009-0003-1942-9296
E-mail: igor.a.pawlak@gmail.com

Radosław Ciesielski, Independent Public Hospital in Mińsk Mazowiecki, Szpitalna 37, 05-300 Mińsk Mazowiecki, Poland
ORCID: https://orcid.org/0000-0002-3458-2024
E-mail: radoslaw.ciesielski@yahoo.com

Jakub Stanek, Medical University of Lodz, al. Tadeusza Kościuszki 4, 90-419 Lodz
ORCID: https://orcid.org/0000-0002-9450-7261
E-mail: jakubstanek22@gmail.com

Abstract

Introduction

Migraine, a prevalent neurological disorder, is characterized by recurrent episodes of moderate to severe headache, often accompanied by symptoms such as nausea, photophobia, and phonophobia. Triptans, which belong to the class of serotonin 5-HT1B/1D receptor agonists, are integral to the management of migraine, providing prompt relief from symptoms.

Aim of the study

To clarify how effective triptans are in treating migraines, highlighting their role in symptom relief and improving patients' quality of life

Materials and methods

The article is the result of a comprehensive analysis of present-day scientific literature, which has been collected from PubMed, Scopus, and Google Scholar. The literature was systematically reviewed utilizing specific keywords.

Results

Studies consistently show high efficacy of triptans in treating acute migraines. These pharmaceuticals markedly alleviate pain and symptoms like nausea, photophobia, and phonophobia, providing substantial pain relief. Differences in triptan medications' onset and half-life affect their therapeutic duration and headache recurrence rate. The pharmacokinetic properties of each triptan significantly affect its efficacy and headache recurrence likelihood. Frovatriptan, with its long half-life, showed superior efficacy in reducing migraine recurrence. Conversely, rizatriptan, with its rapid action, offered quick pain relief. In clinical trials, all triptans showed favorable tolerability profiles. Reported adverse effects were generally mild.

Conclusions

Triptans are effective and safe for managing acute migraines. The diverse formulations and swift onset make these treatments essential for migraine management. Choose a triptan based on efficacy, safety, and patient preferences. More research is needed to improve triptan treatments for migraine, focusing on reducing headache recurrence and enhancing patient tolerability.

Keywords: migraine, triptans, sumatriptan, almotriptan.

Introduction

Migraine constitutes a chronic neurological disorder typified by recurrent episodes of headache, which vary in intensity from moderate to severe. These headaches often exhibit a pulsating and unilateral nature and typically endure for a duration ranging between 4 to 72 hours [1]. Given the debilitating nature of migraines, effective treatment options are critical in managing the condition and improving patients' quality of life [2, 3]. In this regard, the use of triptans has emerged as a highly effective therapeutic approach [4, 5]. This paper provides a comprehensive review of various triptans, examining their efficacy and role in the management of migraine [6]. Furthermore, an in-depth exploration of the definition and classification of migraine will be presented, based on the most recent International Classification of Headache Disorders, 3rd edition (ICHD-3) [7, 8].

The clinical manifestation of migraine exhibits variations dependent on the patient's age. In pediatric cases, migraines tend to be of shorter duration and are often accompanied by specific paroxysmal symptoms such as vomiting, abdominal pain, or vertigo. The causes of abdominal migraine in children are not known, but there are certain factors responsible for the onset of pain. These include stress, sleep disturbances, allergies to certain foods, and traveling. Conversely, in the elderly population, there is a notable absence of autonomic signs [9].

The prevalence of migraine in children exhibits variability, contingent on the specific study and the age range of the subjects included, ranging between 2.7% and 10.0%, in younger children (below 7 years of age), there is no significant difference in the prevalence of migraine between girls and boys.[10]

Moreover, migraine is the most common neurological problem in primary care. According to the findings of the most recent Global Burden of Disease study, migraine remains the second leading cause of disability worldwide, particularly ranking first among young women [2,5]. It is a prevalent disorder, affecting 18% of women and 6% of men.

A contributing factor to the increased prevalence of migraine in women, as compared to men, during reproductive years is the withdrawal of estrogen. This hormonal shift serves as a reliable trigger for menstrual migraine attacks in women. [11].

Migraine incidence in women typically decreases post-menopause, further corroborating the impact of hormonal changes on the prevalence of migraines [12, 13]. Furthermore, chronic migraine impacts 2% of the global population, imposing a significant burden on patients, their families, and society at large [1, 2].

The diagnosis is primarily determined through the patient's medical history and a thorough clinical examination. In most cases, imaging techniques are not required [6].

Pathophysiology

The precise pathophysiology of migraine is characterized by a multifactorial nature, encompassing both genetic and environmental influences. The pathophysiology of migraine principally involves the activation of the trigeminovascular system, encompassing the trigeminal nerves and their associated vasculature [14]. During a migraine episode, the trigeminal nerve fibers secrete various neuropeptides, including calcitonin gene-related peptide (CGRP), substance P, and neurokinin A. These neuropeptides induce vasodilation of both cerebral and meningeal blood vessels, resulting in neurogenic inflammation. This inflammatory process is posited to play a pivotal role in the pathogenesis of the throbbing pain that is emblematic of migraines [15]. Moreover, cortical spreading depression (CSD) - characterized by a wave of neuronal depolarization succeeded by a phase of inhibition - is hypothesized to be the underlying mechanism for the aura symptoms encountered by certain individuals suffering from migraines [16].

Calcitonin Gene-Related Peptide (CGRP) plays a pivotal role in migraine pathophysiology by promoting vasodilation and facilitating the transmission of pain signals within the trigeminovascular system [17]. The release of calcitonin gene-related peptide (CGRP) and other pro-inflammatory neuropeptides induces the dilation of blood vessels and sensitization of pain pathways within the brain, thereby contributing to the prolonged and severe pain characteristic of a migraine attack [18].

Triptans, such as sumatriptan, zolmitriptan, rizatriptan, naratriptan, eletriptan, almotriptan, and frovatriptan, classified as serotonin (5-HT1B/1D) receptor agonists, exhibit significant efficacy in the termination of migraine attacks by specifically targeting these pathophysiological mechanisms [4].

Classification of Migraine

The most recent classification of migraine, as delineated in the International Classification of Headache Disorders, 3rd edition (ICHD-3), presents a comprehensive framework for the diagnosis and categorization of various migraine types. Outlined below are the principal classifications of migraines: 1. Migraine Without Aura. This classification is marked by recurrent episodes of headache that typically persist for a duration of 4 to 72 hours. These headaches are generally characterized by a unilateral localization, a pulsatile nature, moderate to severe intensity of pain, and exacerbation due to routine physical activities. Associated symptoms frequently comprise nausea, photophobia, and phonophobia.

Migraine without aura constitutes the most prevalent form of migraine, typically manifesting during adolescence. It is postulated that this phenomenon is associated with genetic predispositions, as there is a tendency for it to manifest within familial lineages. The pathophysiology entails the activation of the trigeminovascular system, accompanied by the release of neuropeptides, including calcitonin gene-related peptide (CGRP). This process results in cerebral inflammation and vasodilation. Effective management frequently involves the utilization of triptans, alongside the implementation of lifestyle modifications aimed at minimizing exposure to triggers. 2. Migraine With Aura. This condition is characterized by transient neurological symptoms that typically precede or accompany the headache. The aforementioned symptoms may encompass visual disturbances, such as photopsia or scotomas, as well as sensory disturbances and impairments in speech or language. The aura typically develops gradually over a minimum duration of five minutes and persists for less than one hour. The phenomenon of aura is posited to result from cortical spreading depression (CSD), which is characterized by a wave of neuronal and glial depolarization, subsequently followed by a suppression of cerebral activity. Patients experiencing migraine with aura may exhibit a heightened susceptibility to ischemic stroke. This risk is notably exacerbated in the presence of additional contributing factors, such as cigarette smoking or the utilization of oral contraceptives. 3. Chronic migrain. This is characterized by the occurrence of headaches on 15 or more days per month over a duration exceeding three months. Of these, at least eight days per month must meet the criteria for migraine with or without aura, as delineated by the International Classification of Headache Disorders, third edition (ICHD-3). Chronic migraine frequently evolves from episodic migraine, with contributing risk factors such as medication overuse, obesity, and elevated stress levels. These factors significantly contribute to the progression of the condition. Migraine, in its most debilitating forms, profoundly affects individuals quality of life and daily functioning. This condition represents one of the most severe impairments within the spectrum of migraine disorders. [1, 7, 14]

Triptans

Triptans, such as sumatriptan, zolmitriptan, rizatriptan, naratriptan, eletriptan, almotriptan, and frovatriptan,, widely employed in the treatment of migraines, primarily achieve their therapeutic efficacy by activating serotonin (5-HT1) receptors. The mechanism of action precipitates several physiological responses that play a crucial role in the mitigation of migraine symptoms. Upon administration, triptans exhibit a high affinity for and selectively bind to specific subtypes of serotonin receptors. Notably, these receptors include the 5-HT1B and 5-HT1D subtypes, which are predominantly located within the cerebral blood vessels. The stimulation of these receptors induces vasoconstriction, leading to the narrowing of previously dilated cerebral blood vessels. This vasoconstrictive action plays a pivotal role in mitigating the intense headache pain associated with migraine attacks. Moreover, triptans are instrumental in mitigating neurogenic inflammation through the inhibition of various pro-inflammatory neuropeptides, including calcitonin gene-related peptide (CGRP). This peptide is critically involved in the transmission of pain signals within the brain [14, 20,22].

Calcitonin Gene-Related Peptide (CGRP) holds a pivotal role in the pathophysiology of migraines. It facilitates vasodilation while sensitizing pain pathways within the trigeminovascular system.

Triptans mitigate the intensity of migraine-associated pain by inhibiting the release of calcitonin gene-related peptide (CGRP) and other neurotransmitters integral to painsignaling mechanisms [15]. The dual mechanism of action, encompassing both vasoconstriction and the inhibition of neuropeptide release, renders triptans exceptionally effective in terminating migraine attacks. This efficacy has established triptans as a fundamental component in the treatment of acute migraine episodes. Numerous clinical studies have demonstrated that triptans are effective not only in alleviating pain but also in mitigating associated symptoms, such as nausea, photophobia (sensitivity to light), and phonophobia (sensitivity to sound). Consequently, they facilitate a quicker return to normal functioning [23]. Although triptans have demonstrated significant efficacy, they may not be appropriate for all patients. For instance, their application is contraindicated in individuals with cardiovascular conditions - such as coronary artery disease - owing to the risk of precipitating coronary vasospasm [24]. In patients exhibiting elevated cardiovascular risk, it is imperative to consider alternative therapeutic strategies, such as the employment of Calcitonin Gene-Related Peptide (CGRP) inhibitors. These inhibitors present a distinct mechanism of action and may offer a viable treatment option [25]. Nonetheless, triptans continue to be among the most frequently prescribed classes of medications for the treatment of migraines. They are efficacious in managing both migraine without aura and migraine with aura. Due to their rapid onset of action and demonstrated efficacy, these agents are the preferred choice for the treatment of acute migraine episodes, and their role in migraine management is considered indispensable [19].

Sumatriptan

Sumatriptan, the inaugural pharmacological agent introduced from the triptan family, represents a notable advancement in the treatment of migraines. As a selective serotonin receptor agonist, sumatriptan primarily targets the 5-HT1B and 5-HT1D receptors. These receptors are integral to the drug's therapeutic effects. By targeting the fundamental mechanisms responsible for migraines, sumatriptan offers precise alleviation of migraine symptoms. The efficacy of this therapeutic agent is predominantly attributed to its capacity to induce vasoconstriction in the cerebral blood vessels, thereby reducing blood flow, and to inhibit the release of neuropeptides associated with pain induction. These mechanisms collectively contribute to the alleviation of symptoms and improved patient outcomes.

The activation of 5-HT1B receptors precipitates the constriction of dilated cranial blood vessels, which constitutes a critical mechanism in the mitigation of throbbing migraine pain. Furthermore, the activation of 5-HT1D receptors by sumatriptan leads to the inhibition of neuropeptide release, including calcitonin gene-related peptide (CGRP), substance P, and neurokinin A. These neuropeptides are recognized for their roles in promoting neurogenic inflammation and the transmission of pain signals within the brain. By inhibiting the release of inflammatory mediators, sumatriptan thereby reduces inflammation and attenuates the perception of pain [14, 21, 22]. Numerous clinical studies have demonstrated that sumatriptan is effective in alleviating headache pain and associated migraine symptoms, such as nausea, vomiting, photophobia (sensitivity to light), and phonophobia (sensitivity to sound). Its rapid onset of action constitutes a substantial advantage, delivering prompt relief to patients experiencing acute migraine episodes.

The availability of sumatriptan in various formulations - including oral tablets, orally disintegrating tablets, subcutaneous injections, and nasal sprays - facilitates flexible treatment options tailored to the individual needs of patients [26, 27]. This variety of delivery methods proves to be particularly advantageous for patients experiencing nausea and vomiting. Such individuals may encounter difficulties in swallowing oral medications. Sumatriptan is typically well-tolerated. Common side effects associated with its use include transient sensations such as tingling, warmth, or pressure. These side effects are generally mild and short-lived. However, it is contraindicated in patients presenting with specific cardiovascular conditions, notably coronary artery disease or uncontrolled hypertension, owing to the associated risk of coronary vasospasm. Meticulous selection and monitoring of patients are imperative to minimize the potential risks associated with its utilization [24, 28, 29]. Despite these contraindications, sumatriptan continues to be a cornerstone in the treatment of acute migraines owing to its well-documented efficacy and safety profile within the general population. Recent laboratory research indicates that sumatriptan may exhibit anti-inflammatory properties in addition to its vasoconstrictive effects. Research suggests that administering low doses of sumatriptan could potentially attenuate the levels of inflammatory markers and alter the signaling pathways implicated in the inflammatory response. These preliminary findings suggest that sumatriptan may have potential applications in the management of other inflammatory conditions, thereby broadening its therapeutic efficacy. As the prototype triptan, sumatriptan has established the benchmark for subsequent advancements in triptan development. Newer agents are designed to enhance efficacy, tolerability, and duration of action. While sumatriptan demonstrates significant efficacy for numerous patients, current research endeavors are concentrated on refining treatment protocols. This includes the integration of combination therapies with additional pharmacologic agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or antiemetics, with the aim of augmenting its therapeutic effectiveness and decreasing the recurrence rates of migraine attacks. Moreover, research into individualized therapy based on genetic markers, as well as personalized medicine approaches, is actively being pursued. This research aims to further refine the application of sumatriptan in the management of migraines. Sumatriptan continues to serve as a fundamental therapeutic agent in the management of acute migraine episodes. The pharmacological agent operates through a dual mechanism - namely, the vasoconstriction of cerebral blood vessels and the inhibition of neuropeptide release - which collectively target the underlying pathophysiological processes associated with migraines. Sumatriptan, demonstrated to be efficacious through various clinical studies, presents itself as a highly valuable pharmacological intervention for the management of migraine symptoms. Its diverse formulations and rapid onset of action further enhance its utility, thereby providing relief to millions of sufferers on a global scale [19, 30, 31].

Zolmitriptan

Zolmitriptan, classified within the triptan group, is extensively utilized for the management of acute migraine episodes, encompassing those with and without aura. Research has demonstrated that zolmitriptan is efficacious in alleviating migraine-related symptoms, which include headache, nausea, photophobia (sensitivity to light), and phonophobia (sensitivity to sound).

Zolmitriptan is accessible in several formulations, such as oral tablets, orally disintegrating tablets, and a nasal spray. The nasal spray formulation demonstrates significant advantages owing to its expedited onset of action. Consequently, it is particularly suitable for patients necessitating immediate relief. This is especially pertinent in cases of severe pain, morning migraines, or migraines accompanied by vomiting [32]. The efficacy of the given treatment has been substantiated through clinical studies, which have included a cohort exceeding 20,000 participants. In these investigations, the administration of a single oral dose of 2.5 mg resulted in headache relief for approximately 30% of patients within a two-hour timeframe. Moreover, higher dosages, specifically 5 mg, demonstrated an even greater efficacy. Zolmitriptan has demonstrated substantial efficacy in achieving pain-free status among patients at 2, 3, and 4 hours post-treatment, in comparison to the placebo group *[33-37].* In a multicenter, randomized, placebo-controlled study, the administration of 5 mg of zolmitriptan nasal spray yielded a significant pain response within a two-hour interval, achieving a response rate of 70.3%, which represented a substantial improvement compared to the placebo group *[38].* In Poland, zolmitriptan is available in tablet form, with dosages of 2.5 mg and 5 mg,as well as in a nasal formulation. Studies comparing the efficacy of zolmitriptan 5 mg with sumatriptan 50 mg have demonstrated that the recurrence of pain is observed less frequently following the administration of zolmitriptan. This phenomenon is likely attributable to zolmitriptan's favorable pharmacokinetic profile. Zolmitriptan demonstrates linear pharmacokinetics and is characterized by a rapid onset of action. Furthermore, it is detectable in the brain within five minutes following intranasal administration. Patients concurrently administered both medications exhibited a pronounced preference for zolmitriptan, thereby underscoring its therapeutic efficacy and the associated patient satisfaction [39, 40]. The safety profile of zolmitriptan is generally considered favorable. Most adverse events associated with this medication are typically mild and transient. However, it is contraindicated in patients with preexisting cardiovascular conditions, such as coronary artery disease or uncontrolled hypertension, due to the potential risk of inducing coronary vasospasm. Scientific evidence unequivocally substantiates the central role of zolmitriptan in the effective management of migraine attacks. Its rapid onset of action, diverse range of formulations, and capacity to deliver prolonged relief render it an essential element in the management of acute migraine episodes. Ongoing research aimed at optimizing dosage and exploring potential prophylactic applications could significantly enhance the therapeutic value of this medication [3, 32].

Eletriptan

Eletriptan is recognized as a highly effective therapeutic agent in the management of migraine disorders. Clinical studies have demonstrated that the administration of 40 mg and 80 mg doses is efficacious in the rapid alleviation of migraine pain. Eletriptan initiates its therapeutic action within approximately 30 minutes following administration. The rapid onset of action is an essential characteristic for patients necessitating immediate relief from pain. In comparative studies, eletriptan has frequently been demonstrated to exhibit equal or, in certain instances, superior efficacy compared to other triptans, such as sumatriptan or zolmitriptan.

In the context of clinical trials, Eletriptan doses of 40 mg and 80 mg were thoroughly evaluated in comparison to sumatriptan at doses of 50 mg and 100 mg, as well as zolmitriptan at doses of 2.5 mg and 5 mg [41, 42].

Eletriptan demonstrated a notably quicker onset of action and provided extended analgesic effects. Furthermore, the safety and tolerability profile of the medication demonstrated equivalence or superiority compared to other pharmacological treatments. Eletriptan is commonly well-tolerated by a substantial proportion of patients. The adverse effects that are generally observed tend to be mild and transient in nature. The most frequently documented adverse effects include dizziness, drowsiness, dry mouth, and nausea. In comparison to other triptans, Eletriptan exhibits a tolerability profile that is either comparable to or superior, thereby positioning it as an attractive therapeutic option for patients. Eletriptan is distinguished by advantageous pharmacokinetic characteristics. The compound exhibits substantial bioavailability coupled with a prolonged half-life, indicating its efficacious absorption into the bloodstream as well as its sustained pharmacological activity. This extended retention guarantees a sustained therapeutic impact, potentially offering significant advantages for patients requiring prolonged analgesic treatment. Eletriptan is primarily metabolized by the hepatic CYP3A4 isoenzyme, whereupon the resultant metabolites are excreted via both renal and fecal pathways [43]. Furthermore, the favorable pharmacokinetic profile of Eletriptan, characterized by high bioavailability and an extended half-life, positions it as an effective treatment option for mitigating the recurrence of migraine episodes. This enables sustained relief for patients suffering from this condition. Eletriptan demonstrates efficacy across a spectrum of migraine subtypes, thereby establishing its versatility as an essential agent in migraine management. Empirical data from real-world applications similarly corroborate high levels of patient satisfaction attributable to the treatment's rapid onset of action and sustained efficacy. Considering the aforementioned characteristics, eletriptan constitutes a significant therapeutic option for the management of acute migraine episodes. This is particularly pertinent for patients necessitating rapid onset and prolonged duration of relief. Its incorporation into clinical practice is in accordance with prevailing guidelines that recommend the utilization of effective and well-tolerated triptans to enhance patients' quality of life by minimizing the impact of migraine symptoms [19, 44-45].

Almotriptan

Almotriptan is accessible over-the-counter in Poland in a standard dosage of 12.5 mg. In a clinical study, a dose of 12.5 mg of almotriptan was evaluated in comparison to 50 mg of sumatriptan. Both pharmacological interventions were administered for the treatment of migraines that varied in intensity from moderate to very severe. Ultimately, the efficacy of both substances was found to be remarkably similar. The study also determined that, in instances where sumatriptan proved to be ineffective, almotriptan could serve as a viable alternative. Based on the aforementioned considerations, it was posited that various types of triptans could be administered to distinct patient populations. The selection of a particular medication should be tailored to the individual patient, with careful attention to the patient's best interests, the drug's efficacy, tolerance levels, and the profile of potential side effects [46-48].

Almotriptan represents the first pharmaceutical agent sanctioned by the United States Food and Drug Administration (FDA) for the treatment of migraines in adults, irrespective of the presence or absence of aura. Research indicates that this intervention is also efficacious for adolescents experiencing migraines that persist for four hours or more in the absence of treatment.

Almotriptan functions by inducing the constriction of cerebral blood vessels, thereby reducing cerebral blood flow and mitigating the transmission of pain signals. The primary metabolic pathway for this compound involves the cytochrome P450 enzyme system. Its metabolites are subsequently excreted in the urine. Consequently, the drug is characterized by a relatively short half-life of approximately three hours. Compared to earlier generations of triptans, such as sumatriptan, almotriptan demonstrates a higher bioavailability of 69.1% and exhibits a favorable safety profile, characterized by minimal differences in side effects when compared to a placebo. Research indicates that a dosage of 12.5 mg is optimal for the treatment of migraine, providing the most favorable risk-to-benefit ratio. Owing to its vasoconstrictive properties, the substance is contraindicated in patients presenting with cardiovascular diseases, including but not limited to coronary artery disease or unmanaged hypertension [48-50]. Almotriptan constitutes a noteworthy therapeutic alternative for the management of acute migraine episodes. It demonstrates efficacy on par with other triptans and is distinguished by a favorable safety profile. The utilization of this intervention should be evaluated within the context of the patient's specific needs in order to enhance the quality of life for individuals experiencing migraines [51].

Rizatriptan

Rizatriptan is distinguished by its notably rapid onset of action among orally administered triptans, exhibiting an approximate time to onset of around 30 minutes. However, its relatively brief half-life of approximately 2 to 2.5 hours may lead to an elevated probability of recurrence of pain within a 24-hour period following administration [52]. Rizatriptan is deemed an efficacious therapeutic intervention for the acute management of moderate to severe migraine episodes. Clinical research has demonstrated that the oral administration of rizatriptan, at dosages of 5 mg and 10 mg, significantly surpasses placebo across numerous clinical parameters. These parameters include pain relief, attainment of pain freedom, reduction of associated symptoms, restoration of normal functioning, and improvement in patients' quality of life. Comparative studies with other triptans, including sumatriptan, have demonstrated that rizatriptan offers more rapid pain relief and a more significant reduction in nausea. Studies have demonstrated that a 10 mg dose of rizatriptan offers more rapid pain relief compared to naratriptan and zolmitriptan. Additionally, a higher proportion of patients achieve complete pain relief and return to normal functioning within two hours when administered rizatriptan. Research has substantiated the long-term efficacy and good tolerability of rizatriptan with extended use. Rizatriptan is typically well-tolerated. The predominant side effects frequently reported are drowsiness, dizziness, a sensation of heaviness, and nausea. Rizatriptan undergoes metabolism primarily through the monoamine oxidase type A (MAO-A) pathway. This process results in the formation of an inactive metabolite, specifically indole acetic acid. Approximately 14% of an orally administered dose is excreted in its unchanged form through the urine. The remaining 51% is excreted as a metabolite, thereby indicating a substantial first-pass metabolism.

Rizatriptan has undergone clinical evaluations within pediatric cohorts, specifically targeting an age range from 6 to 17 years. Research findings indicate that a 5 mg dose of rizatriptan proves effective for pediatric patients whose body weight is below 40 kilograms.For pediatric patients exceeding a body weight of 40 kilograms, the administration of a 10-milligram dosage is advisable. Studies have demonstrated that rizatriptan is both effective and safe in treating acute migraine episodes in this age group, making it a valuable choice in pediatric migraine management [26, 53-54].

Naratriotan

Naratriptan is a pharmacologically efficacious agent utilized for the management of acute migraine episodes. The established therapeutic dosage is 2.5 mg. Clinical studies have demonstrated that this dosage effectively alleviates headaches and facilitates a pain-free state within 2 to 4 hours post-administration [55]. In addition to providing analgesic effects, naratriptan has demonstrated efficacy in alleviating a range of other migraine-associated symptoms, including nausea, photophobia, and phonophobia. It also demonstrates substantial intra-patient consistency and exhibits a low rate of pain recurrence [56]. Naratriptan has demonstrated efficacy as a short-term prophylactic treatment for menstrual migraines (PMM). Research involving women aged 18 and above, who experienced migraines without aura specifically during the perimenstrual period, demonstrated that administering naratriptan at a dosage of 1 mg twice daily, commencing two days prior to the expected onset of menstruation and extending for six days, significantly decreased the frequency of migraine episodes. The majority of patients observed a reduction in the frequency of attacks by a minimum of 50%,. Additionally, there was a notable decrease in the severity of headaches and the associated symptoms [57]. The side-effect profile of naratriptan aligns with that of other triptans and encompasses symptoms such as dizziness, drowsiness, nausea, and fatigue. Nevertheless, the incidence of these symptoms is comparable to that observed with placebo. Naratriptan demonstrates a high degree of tolerability, rendering it a favorable option for individuals in need of acute migraine therapy. In comparison to sumatriptan (100 mg), naratriptan (2.5 mg) demonstrates a slower onset of action and a reduced response rate at the 4-hour mark. However, naratriptan exhibits superior performance in terms of lower recurrence rates and enhanced tolerability [55, 58].

Frovatriptan

Frovatriptan is an oral triptan that has received approval for the acute treatment of migraine in adults, encompassing cases both with and without aura. The precise mechanism of action of frovatriptan remains incompletely elucidated. However, it is known to involve agonism at serotonin 5-HT1B and 5-HT1D receptors. This receptor interaction results in the inhibition of vasodilation in both intracranial and extracerebral arteries, thereby potentially exerting anti-inflammatory and analgesic effects. Frovatriptan demonstrates functional selectivity for 5-HT receptors primarily in the basilar arteries, as opposed to the coronary arteries, which suggests a reduced risk of cardiovascular adverse effects. This characteristic differentiation in receptor activity underscores its potential safety profile in mitigating cardiovascular risks. A notable attribute of frovatriptan is its extended terminal elimination half-life, which is approximately 26 hours.

This prolonged half-life may result in sustained therapeutic effects. Clinical studies have demonstrated the efficacy of an oral dose of frovatriptan 2.5 mg in the treatment of moderate to severe migraine attacks. In randomized, double-blind clinical trials, the proportion of patients attaining pain relief at 2 hours (the primary endpoint) was appreciably higher in the frovatriptan group compared to the placebo group. Frovatriptan was, on the whole, well-tolerated in both short-term and long-term clinical trials. The most common adverse events, observed with greater frequency in the frovatriptan group as compared to the placebo group. In a research study involving patients diagnosed with coronary artery disease or those at elevated risk for developing coronary artery disease, it was observed that frovatriptan did not result in a higher incidence of clinically significant electrocardiogram (ECG) changes or cardiac rhythm disturbances compared to the placebo. In comparative studies evaluating the early administration of frovatriptan during the initial stages of mild headache against a placebo, frovatriptan exhibited superior efficacy. Three crossover studies were conducted to compare the early administration of frovatriptan at a dosage of 2.5 mg with almotriptan at 12.5 mg, rizatriptan at 10 mg, and zolmitriptan at 2.5 mg in patients suffering from migraine. These studies did not reveal significant differences in patient drug preference scores, which served as the primary endpoint, nor in other key endpoints. However, it is noteworthy that in two of the studies, frovatriptan was associated with a lower rate of headache recurrence. These trials did not demonstrate inferior efficacy of frovatriptan compared to the comparator drugs. In conclusion, frovatriptan is a highly efficacious treatment for acute migraine episodes of moderate to severe intensity. It is distinguished by a favorable tolerability profile and demonstrates potential efficacy when administered in the early stages of a migraine attack. Clinical evidence indicates that frovatriptan may exhibit extended therapeutic efficacy and be better tolerated in comparison to certain alternative treatments.Frovatriptan is considered a significant alternative in the management of migraines, especially for patients who encounter adverse effects or frequent recurrences of headaches with other triptans or migraine medications. These patients may benefit from an early intervention strategy. [59-61]

Summary

In summary, triptans, as serotonin 5-HT1B/1D receptor agonists, play a pivotal role in the acute treatment of migraines. Their mechanism of action involves the selective constriction of cranial blood vessels and the inhibition of pro-inflammatory neurotransmitter release, thereby mitigating the symptoms associated with migraine episodes. Studies have demonstrated the efficacy of these treatments in swiftly alleviating headache pain as well as concomitant symptoms, including nausea, photophobia, and phonophobia. The heterogeneity in the pharmacokinetic characteristics of individual triptans, including their duration of action and tolerance profiles, facilitates the tailored customization of therapeutic regimens to meet the specific requirements of patients. Frovatriptan, distinguished by its extended half-life, has demonstrated substantial efficacy in mitigating the recurrence of pain. This characteristic is of particular benefit to patients suffering from chronic migraines. Meanwhile, naratriptan exhibits significant efficacy and a minimal risk of adverse effects, rendering it an appropriate option for the treatment of menstrual migraines. Lastly, eletriptan and zolmitriptan provide swift alleviation, which is particularly critical in instances of acute migraine onset.

Future research ought to concentrate on the long-term efficacy and safety of triptan usage. Moreover, it is essential to examine their impact on patients' quality of life. The advancement of innovative formulations and therapeutic strategies incorporating triptans holds the potential to significantly enhance the management of migraines.

Disclosure

Authors contributions

Conceptualization: Agata Borkowska, Anna Mich
Methodology: Anna Kiełb, Anna Mich and Klaudia Perkowska
Software: Jakub Stanek
Check: Radosław Ciesielski, Anna Mich and Igor Pawlak
Formal analysis: Patrycja Sornek
Investigation: Wiktoria Izdebska and Anna Kaźmierczak
Resources: Klaudia Perkowska
Data curation: Agata Borkowska and Patrycja Sornek
Writing -rough preparation: Agata Borkowska, Anna Kaźmierczak and Wiktoria Izdebska
Writing -review and editing: Radosław Ciesielski, Anna Mich and Jakub Stanek
Visualization: Wiktoria Izdebska
Supervision: Igor Pawlak
Project administration: Agata Borkowska
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