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ELETRIPTAN AS TREATMENT OPTION FOR ACUTE MIGRAINE

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ABSTRACT

The complex, neurological, and incapacitating condition known as migraine is also marked by a number of autonomic symptoms. The first line of defence against moderate-to-severe headache episodes is the use of triptans, which are selective 5-HT1B/1D serotonin agonists. In this article, we examine the most recent information on the clinical effectiveness, safety, and tolerability of eletriptan as well as any potential clinically significant medication interactions. Eletriptan, a triptan, has a high tolerability profile and consistently considerable clinical effectiveness in the treatment of migraine, particularly in individuals with cardiovascular risk factors but without coronary artery disease. Along with rizatriptan, zolmitriptan, and injections of sumatriptan, it exhibits the best clinical response. In addition, when compared to the other triptans, eletriptan has the most complicated pharmacokinetic/dynamic profile. Since the hepatic enzyme CYP3A4 is principally responsible for its metabolism, the concurrent administration of CYP3A4-potent inhibitors needs to be carefully considered. The co-administration of serotoninergic medications results in a comparatively low incidence of serotonin syndrome. With the exception of ergot derivatives, which shouldn't be provided with eletriptan, no clinically significant interactions have been discovered between eletriptan and medications used for migraine preventative therapy or other acute medications.

Keywords: *Acute Migraine, Efficacy, Eletriptan, Safety.*

Introduction

The prevalence of migraine is believed to be between 10 and 15 % of the population worldwide [1]. Recurrent headache pain is its defining feature, and it may also be accompanied by other autonomic symptoms including nausea, vomiting, and sensitivity to light and sound (photophobia) [2]. Numerous factors, including physical exercise, a certain type of food or drink, hormonal changes, and stress, can make migraines worse [3, 4]. Moreover, the aura, which consists of completely reversible sensory, visual, or dysphasic symptoms, may occur in around one-third of instances prior to headache onset [5]. Finding an effective treatment that is appropriate for each patient should be a top priority because migraines have a significant impact on patients' quality of life. They can lead to short- and long-term disability, reduce work productivity, and negatively impact social relationships and family life [6]. In truth, there are many drugs available for treating acute and preventative migraines, and each patient should have a unique treatment plan based on their clinical characteristics [7]. For moderate-to-severe migraine episodes and mild-to-moderate attacks that did not react to analgesics and anti-inflammatory medications, triptans are the primary preventive therapy [8]. Seven compounds make up the triptan family: sumatriptan, zolmitriptan, eletriptan, naratriptan, rizatriptan, almotriptan, and frovatriptan. Despite their molecular similarities, these molecules each have a different pharmacokinetic and pharmacological profile [9]. Compared to other fast-acting triptans, which show a quick dose-dependent effectiveness with a higher risk of side effects and migraine recurrence, naratriptan and frovatriptan have a delayed beginning of

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action and a more protracted duration due to their longer half-lives [10, 11]. The complex process of choosing the right triptan for each patient should take into account the characteristics of migraine attacks (speed of onset, intensity of pain, and duration of the attack), the drug's onset of action, the patient's individual response and tolerance, the relief of concomitant symptoms, headache recurrence, the consistency of the response, the various delivery systems, and the patient's characteristics (medical history, lifestyle and working habits) [12]. Recently, the importance of inherited and acquired genetic variants in medication response has been recognised, however the selection of a specific treatment is still mostly dependent on the drug's effectiveness and safety profile, and consequently on its pharmacokinetic and pharmacodynamic features [13,14,15]. Eletriptan has the most intricate pharmacokinetic/dynamic profiles of all triptans, as seen in Table 1, suggesting a larger potential for bio- and pharmacological interactions. As new information on eletriptan clinical effectiveness, safety, and tolerability in the treatment of migraines emerges, we will examine these qualities in this review in a methodical manner [16].

Table 1: Triptan's Pharmacodynamic and Pharmacokinetic Features

	Sumatriptan	Eletriptan	Zolmitriptan	Almotriptan	Naratriptan	Rizatriptan	Frovatriptan
Targets	5-HT_{1D} 5-HT_{1B} 5-HT_{1F} 5-HT_{1A}	5-HT_{1D} 5-HT_{1B} 5-HT_{1F} 5-HT_{1A} 5-HT_{1E} 5-HT_{2B} 5-HT_{7}	5-HT_{1D} 5-HT_{1B} 5-HT_{1F} 5-HT_{1A}	5-HT_{1D} 5-HT_{1B}	5-HT_{1D} 5-HT_{1B} 5-HT_{1F} 5-HT_{1A}	5-HT_{1D} 5-HT_{1B} 5-HT_{1F}	5-HT_{1D} 5-HT_{1B}
Enzymes	MAO-A [S]	CYP3A4 [S,Inh] CYP2D6 [S] CYP2C9 [S] CYP2C19 [S] PTGS1 [S] CYP2A6 [Ind]	CYP1A2 [S] MAO-A [S]	CYP3A4 [S] CYP2D6 [S] CYP1A2 [S] CYP2C19 [S] CYP2E1 [S] CYP2C8 [S] MAO-A [S] FMO3 [S]	MAO-A [S]	MAO-A [S] CYP1A2 [S]	CYP1A2 [S]
Transporters	SLCO1A2 [Ind] MRP1 [Inh] ABCG2 [S] SLCO1B1 [S]	MRP1 [S]	-	-	-	-	-
Half-life	2.5 hours	4 hours	3 hours	3–4 hours	5–8 hours	2–3 hours	26 hours
Bioavailability	15%	50%	40%	70%	74%	45%	20–30%
Protein binding	14–21%	85%	25%	35%	28–31%	14%	15%

5-HT, 5-hydroxytryptamine; MAO-A, monoaminooxigenase-A; CYP, cytocrome P450; PTGS, prostaglandines G/H synthase; FMO, dimethylaniline monooxygenase [N-oxide-forming]; SLCO, solute carrier organic anion transporter; MRP, multidrug-resistant protein; ABCG, ATP-binding cassette subfamily G; [S], substrate; [Ind], inducer; [Inh], inhibitor. Pharmacokinetic data for sumatriptan are related to the oral formulation.

Eletriptan Biochemical and Pharmacological Features

Eletriptan is a relatively new medication that the US Food and Drug Administration (FDA) licenced for the acute treatment of migraine in adults on December 26, 2002, whether or not there was an aura. Eletriptan is a member of the group of chemical substances known as indoles and is a methylpyrrolidinyltryptamine derivative replaced with a benzene sulfonyl derivative (Figure 1). Its molecular weight is 382.52 Daltons and its chemical name is (R)-3-(1-methyl-2-pyrrolidinylmethyl)-5-(2-phenylsulphonyl) ethyl-1H-indole.

Chemical Structure:

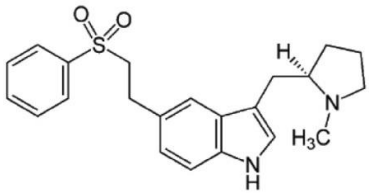

Figure 1: Eletriptan Chemical Structure

High oral bioavailability, fast and consistent absorption, and robust 5-hydroxytryptamine 1-receptor subtype B/D (5-HT1B/1D)-receptor agonist action are all demonstrated [17]. With a strong safety and tolerability profile independent of age or sex, for both short- and long-term treatment, it has a shown effectiveness profile for the acute treatment of moderate-to-severe migraine headache episodes [18]. Eletriptan has been shown to be effective for about 30 minutes after treatment and is commercially available in dosages of 40 mg or 80 mg. Eletriptan (40 and 80 mg) shown higher or equal performance to other triptans in comparative clinical trials, as well as the highest levels of safety and tolerability and the most favourable cost effectiveness when compared to other medications in its class [19, 20, 21].

Pharmacodynamics

Marketed triptans, such as eletriptan, have a strong and highly specific affinity (pKi = 8–9) for 5-HT1B and 5-HT1D receptors that are important in the pathophysiology of migraine (Table 1). In fact, 5-HT1B and 5-HT1D activation inhibits the production of vasoactive neuropeptide by the trigeminal neurons, vasoconstricts painfully dilated cerebral blood vessels, and decreases nociceptive neurotransmission [22]. Eletriptan, like the other triptans, exhibits agonist action for the human 5-HT1F receptor with the exception of frovatriptan and almotriptan (Table 1) [23]. Even though it has been shown that 5-HT1F receptors may block the activation of second-order neurons in the trigeminal nucleus caudalis (TNC), which in turn prevents the transfer of nociceptive information, their functional importance is still not fully understood [24]. Additionally, 5-HT1F mRNA has been discovered in the trigeminal ganglia, human cerebral arteries, and coronary arteries, suggesting that these receptors may play a role in cerebrovascular functioning, dural inflammation, and migraine causation [25]. The pharmacological activity of eletriptan on 5-HT1A, 5-HT1E, 5-HT2B, and 5-HT7 has also been established [26].

No additional pharmacologic targets, such as 5-HT3, 5-HT4, 5-HT5A, 5-HT6, 1, 2, or -adrenoceptors; adenosine A1, dopamine D1, or D2; muscarinic, or histaminic, are clinically important targets for eletriptan (Table 1). The triptan class's excellent level of safety and tolerance is pharmacologically supported by this lack of affinity at other receptors [27]. There are many potential methods by which eletriptan treats migraines: It exerts a vasoconstrictive effect on dilated meningeal blood vessels, suppresses the production of vasoactive neuropeptides in perivascular trigeminal sensory neurons, and decreases pain signal transmission in the trigeminal dorsal horn [28]. The vasoconstrictive activity has been shown in vitro for isolated canine and human arteries, and the isolated human meningeal artery has shown vasoconstriction with potency comparable to sumatriptan (EC50 = 50 nm). Notably, eletriptan is significantly less effective than other drugs at causing isolated human coronary arteries to contract (EC = 4299 nm) [29]. Eletriptan is therefore seen as a selective vasoconstrictor for the intracranial blood vessels in comparison to the other extracranial vessels, particularly the coronary arteries [30].

Pharmacokinetics

Eletriptan is used orally in the form of 20 mg and 40 mg tablets, with a daily dosage cap of 80 mg [31]. Due to eletriptan increased lipophilicity [+0.5 (log D at pH 7.4)], its absorption, central nervous system penetration, and volume of distribution are larger than those of the other triptans [32]. The mean time to maximum concentration (Tmax) is around 2 hours during an acute migraine episode after oral ingestion, which results in fast absorption from the gastrointestinal system. The maximum plasma concentration (Cmax) is between 188 and 234 ng/ml, the protein binding is around 85%, and the half-life is reasonably lengthy. The bioavailability is roughly 50% [33]. The blood-brain barrier efflux mechanism active P-glycoprotein (P-gp), which eliminates lipophilic medicines from the central nervous system, limits eletriptan's ability to penetrate the brain [34]. In reality, it has been shown that the P-gp efflux pump regulates eletriptan oral intake and reduces brain exposure by around 40 times, which helps to explain the high oral dosage that was provided

Age, sex, ethnicity, or the time of the menstrual cycle had no impact on the linearity of the pharmacokinetic characteristics throughout the therapeutic dosage range. About 90% of eletriptan clearance occurs nonrenally and is removed by metabolism (principally hepatic) [35]. Eletriptan is metabolized in the liver via the cytochrome P-450 pathway, principally by the CYP3A4 enzyme and to a lesser extent by the other CYP enzymes. N-desmethyleletriptan, the sole known active metabolite of eletriptan, is produced during hepatic metabolism and has a plasma concentration of around 10–20% of the parent medication.

Eletriptan may interact with the CYP3A4 enzyme's substrates, inhibitors, and inducers. Eletriptan plasma levels may rise or decrease when co-administered with other drugs that might alter CYP3A4 action, increasing the possibility of side effects or decreasing therapeutic effectiveness [36]. Eletriptan and ketoconazole, a powerful CYP3A4 inhibitor, were given together at the highest possible

dosages and were shown to enhance Cmax and area under the curve by 2.7 and 6 times, respectively (AUC) [37]. Eletriptan's Cmax and AUC reduced when it was provided together with weak or moderate CYP3A4 inhibitors, as was predicted (fluconazole, erythromycin, and verapamil). Eletriptan is a substrate, however because it cannot inhibit or induce any CYP enzymes, it has no clinically significant interactions with other drugs [37].

There have also been reports of eletriptan being metabolized by prostaglandin G/H synthase 1 (also known as cyclooxigenase-1) [38]. Because monoamino-oxydase 1 does not metabolize frovatriptan or eletriptan, there is no danger of interactions with medications that inhibit these enzymes (Table 1).

Clinical Efficacy

- **Triptans**

For the treatment of moderate-to-severe acute migraine episodes as well as mild-to-moderate acute migraine attacks with inadequate response to nonsteroidal anti-inflammatory medications (NSAIDs) or combinations of other analgesics, triptans are regarded as the first-line alternative. The main reasons to avoid taking triptans include ischemic heart disease, cerebrovascular illness, peripheral vascular disease, and pregnancy [39]. The outcomes of about 100 double-blind, randomised trials have demonstrated the effectiveness of triptans in treating acute migraine episodes. While the complete response (headache disappearing after two hours with no recurrence in the following 24 hours) is the preferred effect valued by patients, efficacy has primarily been assessed through the parameters "pain free after two hours," "headache response," "sustained pain-free response," and "use of rescue medication" [40]. The International Headache Society (IHS) recommends that a full response be the benchmark by which medications for migraine episodes are assessed [41]. However, important outcomes including the speed and extent of pain relief, improvement in migraine-related symptoms, and the likelihood of side effects also have an impact on how satisfied patients are. The seven triptans that are now on the market have demonstrated alleviation with or without pain elimination after 2 hours and a reduction in the need for rescue medicine if patients are treated when headaches first appear. Additionally, they have demonstrated therapeutic effectiveness in reducing migraine-related symptoms as nausea, vomiting, photophobia, and phonophobia [42].

Patients may also take an extra dosage that is effective in between 15% and 40% of cases if a single administration is ineffective [43, 44].

- **Eletriptan: Efficacy Versus Placebo**

In the treatment of migraines, eletriptan has consistently and significantly increased clinical effectiveness while maintaining a favourable tolerability profile. Multiple trials (head to head and placebo) have evaluated the therapeutic effectiveness of eletriptan at recommended doses for the treatment of moderate-to-severe acute migraine episodes.

Eletriptan was found to be more effective than placebo at all accessible doses (20, 40, and 80 mg) for headache relief at two hours in a placebo-controlled study of one migraine attack treated with it. All of the dosages outperformed the placebo response of 51%, and 20, 40, and 80 mg maintained 64%, 67%, and 76% reductions in headache intensity over two hours, respectively [45]. In a different experiment, eletriptan 20 and 40 mg were compared to a placebo for one treatment of a migraine episode and demonstrated headache-free rates of 35% for 20 mg and 47% for 40 mg at two hours, with a placebo response of 22% [46]. The 40 mg dosage demonstrated a 2-hour headache-free rate of 68% in individuals with mild headaches compared to the placebo's 25%. Another placebo-controlled trial revealed that, compared to a 22% response from the placebo, eletriptan dosages of 20, 40, and 80 mg significantly reduced headache frequency for 2 hours [47]. The results of a second placebo-controlled study using the eletriptan doses of 40 and 80 mg revealed comparable rates of headache relief and freedom after two hours (40 mg: 62% headache relief, 32% headache freedom; 80 mg: 65% headache relief, 34% headache freedom; placebo: 19% headache relief, 3% headache freedom) [48]. Additionally, the three eletriptan dosages were shown to be equally effective and tolerable in patients who had never taken triptans before and those who had. This suggests that the past status of a patient's therapy has no bearing on how well eletriptan responds [49]. Eletriptan 40 and 80 mg were shown to be much more effective than placebo in a recent trial of several attacks (response rate: 72.5% for eletriptan 40 mg, 70% for eletriptan 80 mg, and around 23% for placebo), with minimal rates of adverse events for both dosages [50, 51]. In two meta-analyses of published placebo-controlled trials, eletriptan was determined to be among the most efficient triptans compared to all others [52]. Rizatriptan 10 mg, eletriptan 80 mg, and almotriptan 12.5 mg had the best likelihood of a substantial clinical therapeutic benefit in a meta-analysis

of 53 studies [53]. Additionally, eletriptan 40 mg was found to be superior to all other triptans in the most recent meta-analysis of 74 trials for at least one of the two outcomes that were taken into account (pain-free response at 2 hours, sustained pain-free response at 24 hours, and headache response at 2 hours, sustained headache response at 24 hours). Eletriptan in particular showed the greatest likelihood of patients being pain-free after 2 hours and at 24 hours [54, 55].

- **Eletriptan: Efficacy in Head-to-Head Studies**

Triptan standard doses provided a headache-free response in 42-76% of patients and a sustained headache-free response in 29-50% of patients, with a rescue medication use rate of about 27%, according to a recent systematic review and network meta-analysis of 133 randomised controlled trials that compared triptans with placebo-controlled or active migraine treatments [56]. Triptan standard dosages performed equally well or better than NSAIDs, aspirin, and acetaminophen when the goal was a headache-free response at two hours (responses of 42-76% and 38%, respectively) [56, 57]. Additionally, among all triptans, eletriptan tablets demonstrated the best results, followed by sumatriptan subcutaneous injection, rizatriptan, and zolmitriptan [56]. When evaluating the 2-hour headache-response result in comparison to zolmitriptan, eletriptan 80 mg, but not 40 mg, demonstrated a substantial advantage. However, during a 24-hour period, eletriptan 40 mg demonstrated a much-decreased recurrence rate and requirement for rescue treatment [58]. When compared to naratriptan, eletriptan (40 mg) also shown higher clinical effectiveness (while maintaining the same tolerability profile) (2.5 mg). In fact, the eletriptan group had greater 2-hour pain-free response and sustained headache-free response scores and used fewer rescue drugs [59]. Three trials comparing sumatriptan (50 or 100 mg) with eletriptan at various dosages have been conducted (20, 40, or 80 mg). These studies' findings repeatedly shown that eletriptan's (40 and 80 mg) clinical effectiveness and beginning of action were superior to oral sumatriptan (100 mg) when compared. Eletriptan and sumatriptan were both well tolerated with few side effects [60]. Additionally, eletriptan has been shown to be successful in treating acute migraine in individuals who had previously failed to react to sumatriptan or were intolerable to the drug (as compared to placebo) [61]. Other triptan-switch trials revealed that eletriptan 40 mg was effective in treating migraine sufferers who did not benefit from rizatriptan plus NSAID therapy [62]. After three consecutive migraine episodes, patients who did not respond well to low doses of eletriptan were able to respond at a 2-hour response rate of 42.5–60% when the dosage was increased to 80 mg. Therefore, even if a person does not respond to three successive assaults at a lower dose, a dose increase should be thought of as a successful technique in about 50% of cases [63].

Tolerability and Safety

The different triptans' differing 5-HT receptor affinities may not be significant to their antimigraine effectiveness, but they may have an impact on their tolerability profile. Additionally, each drug's pharmacokinetic characteristics, including bioavailability, lipophilicity, and metabolism, are important for safety and tolerability. Triptan-family medications frequently cause side symptoms such as drowsiness or weariness, difficulties thinking, tachycardia, and dizziness [64]. Literature has described eletriptan as a medication that is both safe and acceptable. The most frequent side effects are often brief and connected to the central nervous system (CNS) action of eletriptan, including dose-related somnolence, dizziness, asthenia, and nausea [65]. No appreciable changes in vital indicators or important clinical changes in chemistry have been associated with eletriptan therapy in patients. A typical side effect of eletriptan administration is a brief rise in mean systolic and diastolic blood pressure after 1 hour, which corresponds to the drug's Cmax. It has been demonstrated that the dosage of eletriptan is connected to the rise in diastolic blood pressure, but not as strongly to the rise in systolic blood pressure [66]. The majority of reported serious adverse events—cardiovascular acute illnesses such acute myocardial infarction, arrhythmias, and cerebrovascular events—were infrequent, especially in individuals with a history of cardiovascular disease. To the best of our knowledge, it is a singular case, but myocardial infarction caused by eletriptan overdose in a patient without coronary artery disease has just been documented. Notably, eletriptan has been shown to cause coronary constriction in rats at a dosage that is four times higher than that of sumatriptan [67]. In individuals with cardiovascular risk factors but without coronary artery disease, it stands in as the triptan of choice. In any event, patients should be taught to recognise the early clinical signs of angina and not to exceed the recommended dose [68].

According to Sandrini and colleagues, the incidence of adverse events for eletriptan 20 and 40 mg and placebo were identical (with a minor rise for the 40 mg), however the rate for the dose of 80 mg was greater compared to the dosage of 40 mg (1–7%) [69]. Additionally, the incidence of discontinuation due to the occurrence of adverse events was observed to range between 0.2% (40 mg) and 1.6% (80

mg) in previous trials [70, 71]. Eletriptan 20 and 40 mg had a similar frequency of adverse effects to sumatriptan 50 and 100 mg, however eletriptan 80 mg has a slightly greater incidence. Adverse effects that are severe and severe are rare. Eletriptan has a consistent tolerability for long-term therapies, and the frequency of side effects may go down over time [70].

Triptans with a greater frequency of central side effects include frovatriptan, rizatriptan, zolmitriptan, and eletriptan; this may be because of the existence of their active N-desmethyl metabolites. The increased lipophilicity of N-desmethyl eletriptan may be connected to its capacity to pass the blood-brain barrier, even if information on the role of active metabolites of eletriptan to its tolerability profile is not yet available. N-desmethyl eletriptan may be able to interact with 5-HT or other receptors linked to CNS adverse effects in addition to the parent drug's allegedly increased brain concentration [72]. The FDA has noted a serotonin-syndrome risk when triptans and serotonergic antidepressants are used together in therapy. No major adverse effects were reported in a study of seven studies with a large number of patients receiving eletriptan, with 306 individuals also receiving serotonin-reuptake inhibitors [73]. Additionally, when administered alone, serotoninergic antidepressants may seldom cause serotonin syndrome. Due to the substantial overlap of migraine with anxiety and depression, triptans and selective serotonin reuptake inhibitors (SSRIs) are commonly administered together. Since there aren't many accounts of serotoninergic syndrome in the literature, it's likely that this adverse occurrence is quite uncommon [73]. Eletriptan is classified as pregnancy category C by the FDA (i.e. despite the absence of controlled data in human pregnancy, some previous studies carried out in animal models have shown evidence of toxicity with regard to the foetal development). As a result, prescribing eletriptan to pregnant migraineurs should only be done when all other options have been exhausted. Additionally, there is no prior data linking triptan usage during pregnancy to an increased risk of congenital abnormalities, while triptan use during the second or third trimester of pregnancy has been linked to a somewhat incremental increase in the risk of atonic uterus and bleeding. Eletriptan concentrations in human breast milk, however, were shown to be significantly lower than those in maternal serum, and as a result, it is unlikely to have a deleterious effect on newborns.

Additionally, adjustments to the eletriptan effectiveness profile should be made in light of the drug's metabolism and the rise in CYP3A4 activity during pregnancy [74].

Bio and Drug Interactions of Clinical Significance

When migraine is often prescribed as a multiple-drug treatment, especially in its chronic form, there is an increased chance of clinically significant medication interactions (DDIs). Particularly, triptans or other analgesics are typically used during an acute attack in individuals who have received preventative medication for chronic conditions. The selection of a combination therapy with a low rate of clinically relevant DDIs is complicated by the large range of both preventive and acute medications and their potential pharmacological interactions [75]. Eletriptan is predominantly metabolised in the liver, where cytochrome P450 3A4 plays a significant role (CYP3A4). Eletriptan treatment results in an increase in peak plasma concentration (Cmax, 18%) and systemic exposure (AUC, 34%) in individuals with mild-to-moderate hepatic impairment. In certain people, dosage modification might not be required. Eletriptan is not advised for usage in individuals with severe hepatic impairment since it has not been evaluated in this population. The interaction between eletriptan and medications metabolised by the same cytochrome CYP3A4, which has the most exclusive metabolism, has been examined. Drugs that are contraindicated with eletriptan in the EU labeling fall within the category of strong CYP 3A4 inhibitors (inhibitory constant (Ki)) in vitro of 25 mol or less. Some of the powerful CYP3A4 inhibitors include ketoconazole, itraconazole, erythromycin, clarithromycin, josamycin, ritonavir, nelfinavir, and indinavir [76]. There have been reports of clinically significant pharmacokinetic interactions between eletriptan and a number of these medications, including verapamil and fluconazole. Eletriptan use is not advised in the US prior to 72 hours following treatment with a powerful CYP3A4 inhibitor due to the possibility of an increase in plasma concentration. Eletriptan and CYP3A4 inhibitor co-administration did not seem to affect the incidence or severity of side effects, though [69]. In a large study of patients receiving triptan treatment, it was shown that almost half of the patients also got CYP3A4-metabolized coprescriptions. This finding is likely due to the vast range of medications that CYP3A4 can metabolise. In particular, triptans and powerful CYP3A4 inhibitors were co-prescribed for 5% of the patients, and eletriptan for 6% of them particularly [77]. Concomitant prescriptions are not advised due to the increased clinician knowledge of eletriptan, which may be helpful in preventing potential adverse effects brought on by CYP3A4-based pharmacokinetic interactions. There has been no information provided concerning interactions that could affect the effectiveness or side effects of eletriptan with migraine prevention drugs (beta-blockers, tricyclic antidepressants, SSRIs, methysergide and flunarizine). Propranolol treatment enhanced eletriptan exposure in clinical tests (AUC, 33%); nevertheless, the result is

not regarded as clinically significant because any rise in blood pressure or other negative effects were linked to co-administration as compared to eletriptan administration alone. One and two hours after eletriptan, consumption of cafergot (caffeine and ergotamine) was associated with slight elevations in blood pressure, which is expected given the pharmacodynamics of the two medications [78]. Dihydroergotamine or methysergide, which are ergot-type or ergotamine-containing drugs, should not be used within 24 hours after taking eletriptan, and vice versa. According to population pharmacokinetic analysis of clinical research, beta-blockers, tricyclic antidepressants, SSRIs, estrogen-based hormone replacement therapy, estrogen-containing oral contraceptives, and calcium-channel blockers had no impact on the pharmacokinetic characteristics of eletriptan [79]. Additionally, as eletriptan is not metabolised by monoamine oxidase (MAO), there is no anticipated interaction between eletriptan and MAO inhibitors.

Conclusion

The choice of a triptan for a certain patient is a nuanced procedure that should include a number of clinical, pharmacological, and personal factors. Among its pharmacological attributes, eletriptan has very little vasoconstrictive activity on coronary arteries and is a selective 5-HT1 vasoconstrictor for intracranial blood vessels in comparison to other extracranial vessels. Eletriptan is largely metabolised by hepatic cytochrome P450, which accounts for the increased likelihood of bio and pharmacological interactions. Pharmacokinetic characteristics are linear across the therapeutic dosage range. Clinical trials using eletriptan have shown it to be effective in comparison to placebo-controlled and head-to-head tests. Together with rizatriptan, zolmitriptan, and sumatriptan subcutaneous injection, it had the most positive clinical results of any triptan. It is regarded as the preferred triptan in people with cardiovascular risk factors but without coronary artery disease since it is a safe and well-tolerated medication. The incidence of adverse events may go down over time, and severe and major adverse events are infrequent. With the exception of ergot derivatives and cafergot, no clinically significant interactions have been shown between the other first- and second-line preventative medicines or other acute treatments for migraine, despite the fact that CYP3A4 undergoes hepatic metabolism. It is important to carefully assess if eletriptan should be prescribed along with other serotonin-related medicines including powerful CYP3A4 inhibitors.

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