Expert Opinion

Determining Triptan Preference for the Individual Patient

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Prescribing a triptan for an individual patient is really conducting a triptan preference trial with an n of 1. With the availability of seven triptans, it would not be practical, however, to give the patient three samples of each oral triptan and have them take each triptan when headaches are of a similar degree of intensity (for a total of 21 trials) and then rate their preferences. This is a challenging problem.

CLINICAL HISTORY

A 30-year-old woman with moderate-to-severe migraine without aura, with mild nausea, but no vomiting does not respond to over-the-counter medications or NSAIDs.

Question.—How can I determine which of the seven triptans might be the best (most effective and tolerable) for her?

EXPERT COMMENTARY

For the sake of limited space for this commentary, I will focus on the question and not speculate over the possible advantage of combining her over-the-counter medications or NSAIDs with an antiemetic. For example, metoclopramide as 10 to 20 mg orally or suppository (20 mg) can be used as antiemetics and ideally, the analgesic should be taken 15 to 20 minutes after administration of the antiemetic drug.[1] Let us instead assume that this woman with migraine without aura needs a triptan for acute treatment of her migraine attacks.

Triptans (5-HT1B/ 1D-agonists) have become the drugs of choice when specific drugs for the acute treatment of moderate-to-severe attacks of migraine are needed.[1-3] In terms of speed of onset, with the exception of naratriptan, the oral triptans provide headache relief within 30 to 60 minutes. Among the available oral triptans, response rates at 2 hours range from 50% to 80%, with 20% to 50% of patients pain-free.[4,5] In placebo-controlled trials and direct comparator studies, rizatriptan, zolmitriptan, and sumatriptan have similar recurrence rates. Naratriptan has a consistently low rate of recurrence across clinical studies, and frovatriptan, which has the longest half-life of any of the triptans (26 hours), has a reported headache recurrence still in up to one-quarter of patients (7% to 25%).[5] The tolerability profiles of rizatriptan, sumatriptan, zolmitriptan, and eletriptan appear to be broadly similar. However, the incidence of treatment emergent adverse events appears to occur less frequently with naratriptan and almotriptan. Although clinical trials may demonstrate significant differences in efficacy and tolerability between triptan tablets, they appear to be very similar when used in clinical practice, particularly after dose adjustments.[5]

Acute migraine treatment should be tailored to the individual patient taking into account available drugs, efficacy versus side effects, contraindications, suitability, convenience, acceptability of route of administration, and costs. Successful treatment requires correct diagnosis, adequate dosing plus choosing the

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optimal route for drug delivery. When oral remedies fail, nasal, rectal, or parenteral therapy may succeed. Most patients with migraine consider that drugs that can be administered orally are most user-friendly.[7] Gastrointestinal absorption may, however, be impaired during migraine attacks as the gastric motility is inhibited and there is a risk that the nausea during the attack will culminate with vomiting.[6] Accordingly, the oral administration is not ideal in the acute treatment of migraine. Furthermore, triptans may, in addition to their antimigraine properties, prolong the gastric-emptying time.[6] For these reasons, the absorption of any triptan taken orally during the migraine attack will be erratic and treatment effects inconsistent. In order to improve the outcome of triptan treatment, patients should be educated in appropriate use of each of the formulations so that reliability of response can be improved. More appropriate use of the formulations may reduce the number of migraine attacks (migraineurs) that do not respond to triptan treatment.[7]

There are at present, no known characteristics of the different triptans that allow prediction of which patients should respond better to which drug, and there appears to be little prospect of such information in the future. However, the use of patient preference as a means of directly comparing the triptans is an approach that is beginning to gain favor.[8] While this method relies on the subjectivity of the patient, it gets to the central issue of which therapy is best for the individual patient. The patient's preference takes efficacy, onset of action, duration, consistency, tolerability, and convenience into an account and eventually provides us with the information about how each individual treatment alternative is perceived by each migraineur. Interestingly, the individual patients may distinguish different characteristics and have a preference for one triptan, dose, or formulation over another.

Within-patient consistency describes the percentage of individual patients who have a response following a triptan during a certain proportion of their treated attacks and is of more clinical relevance than across-attack consistency. The intraindividual consistency of response of the presently available triptans has not been compared in appropriate randomized controlled trials. The subcutaneous injection among all formulations is associated with the highest intraindividual response consistency.[9] The intravenous injection would probably provide an even higher intraindividual response consistency but is not practically useful. Within-patient consistency of response for two of three attacks occurs in 89%, 67%, 64%, and 71% of patients with sumatriptan injection, nasal spray, tablets, and suppository, respectively. Within-patient consistency of response for three out of three attacks occurs in 73%, 35%, 32%, and 41% of patients treated with sumatriptan injection, nasal spray, tablets, and suppository, respectively.[9] The slightly higher intraindividual response consistency (response for three of three attacks occurs in 41%) of the suppository may be attributed to the fact that this route of administration partly avoids presystemic metabolism. Thus, from the perspective of reliability of response to sumatriptan, the injection should be the first choice and the rectal route (suppository) ought to be the obvious second alternative. The nasal spray would be the third choice because the first-pass metabolism is also partly avoided by using this route of administration. In disagreement with the patient's preference, the oral route of administration would rather be the last choice with respect to treatment reliability, ie, intraindividual response consistency.

Within-patient consistency has also been evaluated in a similar way in a subgroup of patients who treated three consecutive attacks with rizatriptan.[10] The pain relief response rates were calculated in the subgroup of patients who treated their first three attacks with rizatriptan, with no prior exposure to placebo. In this subgroup of 125 patients, 75% to 80% had pain relief at 2 hours per attack and 50% had pain relief in all three attacks.

The availability of several triptan formulations provides an opportunity to tailor therapy to individual patient's needs. For the majority of patients, tablets, which offer more or less consistent efficacy within 30 minutes of administration in a convenient dosing form, may be an appropriate choice. Although clinical trials do not demonstrate robust differences in efficacy between triptan tablets, individual patients do distinguish them and often have a preference for one triptan or dose over another. For those having difficulties

in swallowing a tablet, the freeze-dried fast-melting tablet that can be taken without water may be an option. This dosage form dissolves instantly on the tongue, and the active agent is swallowed with the saliva and absorbed from the gastrointestinal tract. For patients who desire particularly rapid relief that cannot be provided by a tablet form, sumatriptan injection with a 10-minute onset of action may be an appropriate choice. Patients with very severe attacks and those with vomiting may also benefit from the injection. For patients with nausea who do not wish to take tablets or who fear injections, a triptan nasal spray with a 15-minute onset of action or a suppository may be appropriate options.

In this particular case, I would inform the woman about pros and cons of different routes of administration and ask her to test two different formulations. I would start the individual titration of preference by prescribing the recommended doses a triptan tablet (eg, sumatriptan 50 mg) and a triptan nasal spray (zolmitriptan 5 mg). In accordance with the concept of patient preference, I would let the patient try the two treatment alternatives in at least two attacks per formulation, and then let her decide for herself, which one of these formulations she would like to use in the future. Alternatively, if her expectations/needs were not met I would, according to the reasons given for this, try to adjust the dose, change formulation, or ask her to evaluate yet another triptan. Under these circumstances, it is quite common that the patient eventually decides to use more than one of the available triptan formulations. For example, the subcutaneous injection of sumatriptan for situations where she wakes up with a fully developed severe migraine attack and the freeze-dried fast-melting tablet of rizatriptan for less severe migraine attacks that develop during the day which enables her to treat earlier. Finally, it can be predicted that this woman does not have to test all available triptans before she finds the triptan and formulation that meets her needs with respect to the acute treatment of her migraine attacks.

REFERENCES

1. Dahlöf C. Integrating the triptans into clinical practice. *Curr Opin Neurol*. 2002;15(3):317-322.
2. Tfelt-Hansen P, Saxena PR, Dahlöf C, Pascual J, Lainez M, Henry P, et al. Ergotamine in the acute treatment of migraine: a review and European consensus. *Brain*. 2000;123(Pt 1):9-18.
3. Goadsby PJ, Lipton RB, Ferrari MD. Migraine-current understanding and treatment. *N Engl J Med*. 2002;346(4):257-270.
4. Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT(1B/1D) agonists) in acute migraine treatment: a meta-analysis of 53 trials. *Lancet*. 2001;358(9294):1668-1675.
5. Dahlöf CGH, Dodick D, Dowson AJ, Pascual J. How does almotriptan compare to other triptans?—a review of data from placebo-controlled clinical trials. *Headache*. 2002;42:99-113.
6. De Ponti F. Pharmacology of emesis and gastrointestinal motility: implications for migraine. *Funct Neurol*. 2000;3:43-49.
7. Dahlöf CGH. Characteristics of different routes of administration. In: Olesen J, Ferrari M, Humphrey PPA, eds. Frontiers in Headache Research—The Triptans: Novel Drugs for Migraine. Oxford: Oxford University Press; 2001:80-90.
8. Dahlöf C. Assessing patient preference in migraine treatment. *Cephalalgia*. 2001;21:791-795.
9. Dahlöf CGH. Sumatriptan: pharmacological basis and clinical results. *Curr Med Res Opin*. 2001;17(suppl 1):35-45.
10. Dahlöf CGH, Lipton RB, Lines CR, et al. Consistency of pain relief over multiple migraine attacks following treatment with rizatriptan. In: Olesen J, Ferrari M, Humphrey PPA, eds. Frontiers in Headache Research—The Triptans: Novel Drugs for Migraine. Oxford: Oxford University Press; 2001:222-227.