Review Article

Patient Preferences and Values in Decision Making for Migraines: A Systematic Literature Review

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Received 12 March 2021; Revised 31 July 2021; Accepted 28 August 2021; Published 17 September 2021

Objective. To comprehensively summarize the evidence on the preferences and values of migraine patients.

Methods. We searched PubMed, Embase, Web of Science, China National Knowledge Infrastructure, Sino-Med, Chongqing VIP, and Wanfang Data for studies on the preferences and values of migraine patients. A qualitative review was performed, but no quantitative synthesis.

Results. Twenty-one studies were finally included, involving a total of 8701 participants. Patients expected a cure, to be symptom-free, a reduction in frequency of headaches, a reduction in severity of headaches, and an improved quality of life from their preventive treatment. Patients expected rapid pain relief, complete pain relief, return to normal activities, no recurrence, and no adverse events from their acute symptomatic treatment.

Conclusion. Efficacy is the primary consideration in the treatment of migraine. Specifically, the most important embodiment of patient preferences and values is the reduced frequency of attacks with preventive treatment as well as prompt analgesia with acute symptomatic treatment.

1. Introduction

Patient preferences and values are mostly convergent with those of healthcare workers, but there are also differences [1]. As direct recipients in the process of disease diagnosis and treatment, the preferences and values of patients cannot be ignored [2]. Patients themselves have expressed interest in the decision-making process, and their adherence to treatment can be simultaneously improved when they participate in the decision-making process [3, 4]. Evidence-based medicine states that optimal clinical decisions should take into account the experience of clinicians, clinical research evidence, and patient preferences and values [5]. Furthermore, evidence of patient preferences and values has also been emphasized in the development of guidelines [6–10].

Migraine is the third most prevalent disorder and the first cause of disability [11]. Current mainstay of migraine treatment is drugs, including prophylactic and analgesic drugs [12]. The use of prophylactic drugs aims to lessen the frequency and severity of the migraine attacks, and the common prophylactic drugs include antihypertensives (e.g., β-blockers, calcium channel blockers, and angiotensin-converting enzyme inhibitors), antidepressants, anticonvulsants, and antihistamines [12]. The use of analgesic drugs aims to prevent a migraine attack or to stop it once it starts, and the common analgesic drugs include triptans, nonsteroidal anti-inflammatory drugs, acetaminophen, combination (acetaminophen, caffeine, and aspirin), and narcotics [13]. Other treatments such as application of pressure, cold, or heat, acupuncture, and surgical treatment have also gradually attracted attention in recent years, but evidence support is still lacking [14].

According to the Grading of Recommendations, Assessment, Development, and Evaluation approach, patient preferences and values refer to the relative importance of the patient for the outcome or health state of interest [9]. Based on the experience of guideline experts [10], we defined patient preferences and values as the perspectives, expectations, and goals of patients regarding treatment attributes. Treatment attributes were divided into treatment process...
attributes and outcome attributes. Among them, treatment process attributes included treatment strategy, duration, route of administration, formulation, and cost; treatment outcome attributes included treatment benefits and side effects [10]. There had been a significant increase in the number of studies investigating the preferences and values in patients with migraines; to comprehensively summarize the evidence, we carried out this systematic literature study.

2. Methods

2.1. Eligibility Criteria. Inclusion criteria were as follows: studies related to patient preferences and values for migraine therapy, both the preventive treatment and the acute symptomatic treatment; studies that examined the context of the consideration of migraine therapy and how patients value alternative health states and experiences with treatment; and studies that examined the choices patients make when presented with decisional aids for management options regarding migraine therapy. The exclusion criteria were reviews, letters, posters, case reports, and case series.

2.2. Data Sources and Search Strategy. PubMed, Embase, Web of Science, China National Knowledge Infrastructure, Sino-Med, Chongqing VIP, and Wanfang Data were searched from their inception to August 2020. Search terms included migraine, patient preferences, patient values, and health attitude. Table 1 provides a search strategy for the Embase database.

2.3. Study Selection and Data Extraction. Two investigators independently read titles, abstracts, and full text to identify eligible studies. Any conflicts were adjudicated through discussion. According to the characteristics of the included studies, we extracted the following basic information using a standardized data extraction form: the first author, year of publication, date of study conduction, type of study, number of patients, and their demographics (mean age, gender), treatment protocol, methods used for evaluating patient preferences and values, outcomes assessed, main results, and methodological characteristics.

2.4. Quality Assessment. An evaluation of the quality of the included studies was performed with the instrument recommended by the Agency for Healthcare Research and Quality (AHRQ) [15]. There were 11 items in the AHRQ checklist, and each item was evaluated using three evaluation options, yes (scored “1”), unclear (scored “0”), or no (scored “0”). The quality was classified into three levels: low quality = 0–3; moderate quality = 4–7; high quality = 8–11 [16].

2.5. Statistical Analysis. A qualitative review was performed, but no quantitative synthesis. The results are presented in tabular form.

3. Results

3.1. Results of Included Studies. A total of 3774 articles were acquired from the electronic search, and 405 duplicates were excluded. After screening the titles and abstracts, 3259 articles were excluded. Afterwards, the full texts of the remaining 110 articles were read for further evaluation, and 89 articles were excluded. Finally, a total of 21 studies [17–37] were ultimately included. The selection process is shown in Figure 1.

Characteristics of the studies, including date of study conduction, country, study design, simple size, migraine status, treatments, methods of stated-preference assessment, and methodological quality of the studies, are shown in Table 2. The most commonly used methods for evaluating patient preferences and values are described briefly in Table 3.

3.2. The Preventive Treatment for Migraine. Preferences and values for preventive treatment were reported in seven studies [17–23]. In general, all patients attached great importance to the preventive treatment of migraine. For treatment process, therapies with higher response rates, fewer adverse events, less frequent dosing regimens, and higher convenience were preferred [17, 18, 20, 22]. For treatment outcome, patients expected a cure, to be symptom-free, a reduction in frequency of headaches, a reduction in severity of headaches, and an improved quality of life from their treatment [18, 20, 21]. Efficacy was the most important aspect of outcome in preventive treatment; some patients even did not mind taking more than one preventive agent at one time if greater efficacy could be achieved [22]. The preventive treatment for migraine was important; however, not all patients actually used this treatment [19]. More details are shown in Table 4.

3.3. Acute Symptomatic Treatment for Migraine. Preferences and values for acute symptomatic treatment were reported in 14 studies [24–37]. For treatment process, therapies with a faster onset of action, a longer duration of the effects, fewer adverse events, and lower price were preferred [26–35, 37]. Triptans were the most commonly used drugs, and the order of priority for dosage form of triptans was tablets, nasal spray, and subcutaneous injection [24, 27, 30]. For treatment outcome, patients expected rapid pain relief, complete pain relief, return to normal activities, no recurrence, and no adverse events from their treatment [24, 27–37]. More details are shown in Table 5.

4. Discussion

A literature search yielded several published studies on preferences and values among patients with migraines. In this research, we systematically evaluated studies reporting the preferences and values of patients with migraines, thus providing summarized evidence for clinicians.
4.1. Summary of Main Findings. In this review, 21 studies enrolled 8701 participants were final included. In summary, evidence from these included studies suggested that the efficacy was the primary consideration in the treatment of migraine. For preventive treatment, therapies with higher response rates, fewer adverse events, less frequent dosing regimens, and higher convenience were preferred. Patients expected a cure, to be symptom-free, a reduction in frequency of headaches, a reduction in severity of headaches, and an improved quality of life from their preventive treatment. For acute symptomatic treatment, therapies with a faster onset of action, a longer duration of the effects, fewer adverse events, and lower price were preferred. Patients expected rapid pain relief, complete pain relief, return to normal activities, no recurrence, and no adverse events from their acute symptomatic treatment. Moreover, triptans were
| Study                  | Date                  | Country          | Study design    | Simple size | Migraine status | Drug                                                                 | Treatment           | Usage                      | Duration | Cost       | Side effect | Method | Score |
|------------------------|-----------------------|------------------|-----------------|-------------|----------------|------------------------------------------------------------------------|---------------------|----------------------------|-----------|------------|-------------|--------|--------|
| Cowan et al. [17]      | 2016–2017             | American         | Cross-sectional | 417         | ≥1 d/m         | A new class of biologics                                               | Subcutaneous injection | Administer monthly or quarterly | Once/m, once/d, twice/m | Disregarded | Unclear    | Ranking 9 |
| Mansfield et al. [18]  | February and May, 2017| American         | Cross-sectional | 100         | ≥6 d/m         | Injection or oral pill                                                   |                      |                              |           |            | Yes         | SG     | 10     |
| Kol et al. [19]        | 2008^a                | Netherlands      | Cross-sectional | 151         |                | Triptans, analgesics, β-blockers, calcium channel blockers, antidepressants, antiepileptics, neurotoxins |                      |                              |           |            | Yes         | SG     | 9      |
| Peres et al. [20]      | 2007^a                | American         | Cross-sectional | 250         | ≥12 m/y        |                          |                      |                              |           |            | Yes         | SG     | 10     |
| Kelman [21]            | 2006^a                | American         | Prospective study | 1750       |                | Analgesic, natural therapy                                              |                      |                              |           |            | Yes         | Interviews 8 |
| Rozen [22]             | 2006^a                | American         | Cross-sectional | 150         |                |                          |                      |                              |           |            | Yes         | Ranking 9 |
| Wenzel et al. [23]     | September to November, 2002 | American | Cross-sectional | 22          |                | Over the counter                                                       |                      |                              |           |            | Yes         | Ranking 9 |
| Lipton and Stewart [24]| 1998                  | American         | Cross-sectional | 688         |                | Capsule, subcutaneous injection Disintegrating tablet, conventional tablet. |                      |                              |           |            | Yes         | Interviews 7 |
| Adelman et al. [25]    | January to June, 1999 | American         | Prospective study | 367         |                | Rizatriptan                                                           |                      | 10 mg/d, 6 m                      | Interviews 8 |
| Pascual et al. [26]    | 2001^a                | Spain            | Case-control study | 94          |                | Sumatriptan, zolmitriptan                                              |                      | Oral tablet, 50 mg, 2.5 mg | Ranking 8 |
| Weidmann et al. [27]   | 2003^a                | American         | Case-control study | 33          | 2–6 d/m        | Sumatriptan                                                           |                      | Oral, intranasal, subcutaneous | $45       | Yes        | Ranking 9 |

Table 2: The preventive treatment of migraine.
| Study            | Date       | Country     | Study design            | Simple size | Migraine status | Drug                   | Usage                          | Duration     | Cost          | Side effect | Method | Score |
|------------------|------------|-------------|-------------------------|-------------|-----------------|------------------------|--------------------------------|--------------|---------------|-------------|--------|-------|
| Dahlöf et al.    | 2002–2003  | Sweden      | Case-control study      | 232         | Acute attacked  | Zolmitriptan           | Oral, intranasal, subcutaneous | 5 mg, 6 consecutive | Yes          | TTO       | 9           |        |       |
| Lipton et al.    | 2005*      | American    | Cross-sectional study   | 415         |                 | Triptan                | Oral                           |              | Yes          | TTO        | 8      |       |
| Schoenen et al.  | 2005*      | American    | Case-control study      | 323         | Acute attacked  | Eletriptan or sumatriptan | Oral, subcutaneous              | 80 mg, 6 mg  | Yes          | TTO        | 8      |       |
| Lainez et al.    | 2001–2002  | Italy       | Case-control study      | 372         | Acute attacked  | Rizatriptan, eletriptan |                               |              |              |            |        |       |
| Dowson et al.    | 2007*      | Italy       | Prospective study       | 48          | 1–4 d/m         | Zolmitriptan           | Oral                           | 2.5 mg, 5 mg; 10 mg |              | TTO        | 8           |        |       |
| Diez et al.      | 2007*      | United Kingdom | Prospective study       | 436         | 2–6 d/m         | Rizatriptan, almotriptan |                               | 10 mg, 10 mg  |              | TTO        | 9      |       |
| Lanteri et al.   | 2003       | France      | Prospective study       | 1710        | 6 d/1.5 m       | Triptans, analgesics, ergot derivatives | FrovatRIPTAN, almotriptan |              |              | Ranking    | 9      |       |
| Bartolini et al. | 2011*      | Italy       | Randomized controlled   | 133         | 1–6 d/m         | FrovatRIPTAN, almotriptan |                               | 2.5 mg, 12.5 mg |              | Ranking    | 10     |       |
| Gonzalez et al.  | 2013*      | American    | Case-control study      | 510         |                 | Triptans, ergotamine, analgesics |                               |              |              | SG         | 8      |       |
| Smelt et al.     | 2014*      | Netherlands | Case-control study      | 300         |                 | Triptans, ergotamine, analgesics |                               |              |              | Ranking    | 8      |       |

TTO, time trade-off; SG, standard gamble. *The date are year of publication, because survey dates were not reported.
4.2. Regimens for Migraines. Preventive treatment for migraines should be preemptive, short term, or maintained. Antiepileptic drugs, β-blockers, antidepressants, calcium channel antagonists, botulinum neurotoxins, and serotonin antagonists are the most commonly used drugs for migraine prevention [12]. On the basis of evidence-based medical evidence, the first-line medications identified as effective include topiramate, divalproex, propranolol, metoprolol, and timolol; the second-line medications identified as effective include venlafaxine, amitriptyline, nadolol, and atenolol [38]. For migraine prevention, β-blockers are the most widely used drugs, which can reduce the frequency of attacks by more than 50%, and there are no absolute or relative contraindications [39]. Tricyclic antidepressants are also used to prevent migraines; however, only amitriptyline has proven efficacy in migraine. In addition, the high incidence of adverse events limits its use [40]. Since the efficacy of placebo-controlled trials has been confirmed, antiepileptic drugs are increasingly recommended for migraine. However, it is worth noting that most antiepileptic drugs may substantially interfere with the efficacy of oral contraceptives [41]. Furthermore, other medications such as calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, onabotulinumtoxinA, and complementary and alternative medicines cannot be recommended for migraine prevention due to the limited evidence quality [38].

For acute symptomatic treatment, the first-line medications for mild to moderate migraine are acetaminophen and nonsteroidal anti-inflammatory drugs, whereas triptans for moderate to severe migraines; for those with refractory migraine, dihydroergotamine and antiemetics are recommended for use as second- or third-line medications [42].

### Table 3: Description of the main methods used for evaluating patient preferences and values.

| Name            | Description                                                                                                                                                                                                 | Example                                                                                                                                                                                                 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ranking         | Researchers ask patients to rate a set of outcomes on an ordered “Likert-type” scale (rating) or to rank them from the most to the least important. Rating can also use visual analog scale and in this case utilities can be derived | From Ref. [17]: “patients were ranked on a seven-point scale, with 1 being “not at all likely” and 7 being “extremely likely,” their likelihood of acceptance of and adherence to the new medication in scenarios in which either monthly or quarterly dosing is available” |
| Time trade-off  | Researchers ask patients to choose between the health states as described in a clinical scenario during X years and a shorter life in normal health. The duration X is varied until the patient is unable to choose between the two options. | From Ref. [30]: “three attacks were treated on each study medication. Assessment of subjective preference was evaluated, after which patients freely choose which study medication they wished to use to treat each of the three additional migraine attacks” |
| Standard gamble | Researchers ask patients to choose between two possible outcomes: a suboptimal health state that is certain and a gamble with one better (for example, full health) and one worse (for example, death or side effects) outcome possible. The probability of the gamble is varied during the experiment and the point of indifference is used to derive the utility of the health state. | From Ref. [18]: “respondents valued a change from a 10% reduction in headache days per month to a 50% reduction more highly than avoiding the worst levels of adverse events. Nevertheless, respondents were willing to forgo some improvements in efficacy for less-severe adverse events.” |

### Table 4: Preferences and values for preventive treatment.

| Study          | Treatment process                                                                                                                                  | Treatment outcome                                                                                                                                  |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Cowan et al. [17] | Most patients preferred monthly or quarterly dosing, while a small proportion had no preference                                                   | It was more important to change the number of migraine attack days from a 10% reduction to a 50% reduction than to avoid adverse events            |
| Mansfield et al. [18] | Patients tended to inject monthly or daily rather than twice a month when treating                                                              | Patients rated efficacy as the most important aspect of preventive treatment outcome                                                               |
| Kol et al. [19] | Fifty-five percent of patients wanted to use prophylaxis; only 8% actually used this treatment                                                         | A percentage of 95.2 expected a reduction in frequency of headaches from their treatment, 95.6% a reduction in severity of pain, 79.7% to be symptom-free, 27.8% a cure, and 95.5% an improved quality of life |
| Peres et al. [20] | Therapies with higher response rates, fewer adverse events, and less frequent dosing regimens were preferred                                     | The vast majority of patients wanted to use over-the-counter drugs to effectively prevent migraine                                                  |
| Kelman [21]    | If greater efficacy could be achieved, patients did not mind using more than 1 prophylactic agent                                             |                                                                                                                                                     |
| Rozen [22]     |                                                                                                                                                  |                                                                                                                                                     |
| Wenzel et al. [23] |                                                                                                                                                  |                                                                                                                                                     |

the most commonly used drugs for acute symptomatic treatment, and the order of priority for dosage form of triptans was tablets, nasal spray, and subcutaneous injection.

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The use of acetaminophen and nonsteroidal anti-inflammatory drugs for mild to moderate migraine attacks is supported by strong evidence [42]. Moreover, nonsteroidal anti-inflammatory drugs have better efficacy than acetaminophen, but can cause gastric irritation or antiplatelet effects [43]. Triptans share a common mechanism of action and have strong evidence of effectiveness for moderate to severe migraine attacks [43]. However, different types of triptans have different routes of administration and kinetics, and they may be expensive [44]. Hence, appropriate individualized use is essential. Furthermore, other medications such as dihydroergotamine, opioids, and antiemetics have good evidence of effectiveness for migraine. However, they are reserved as second-line drugs due to adverse effects, abuse potential, route of administration, or cost [42].

4.3. Limitations. To the best of our knowledge, this is the first study to summarize the evidence on the preferences and values of migraine patients. However, limitations should be acknowledged. First, the definition and eligibility criteria for preferences and values are broad; the lack of standardized methods for reporting and identifying the evidence of patient preferences places additional limitations on our research. Second, it is tentative and empirical to use a systematic literature review method to summarize evidence; there might be nonrigorous and inconsistent phenomena.

5. Conclusions

In summary, evidence from these included studies suggests that the efficacy is the primary consideration in the treatment of migraine. Specifically, the most important embodiment of patient preferences and values is the reduced frequency of attacks with preventive treatment as well as prompt analgesia with acute symptomatic treatment.

Abbreviations

ODT: Orally disintegrating tablet
TTO: Time trade-off
SG: Standard gamble.

Data Availability

All data generated or analyzed during this study are included in this published article.
Conflicts of Interest
The authors declare no potential conflicts of interest.

Authors’ Contributions
Xianpeng Xu, Qingjie Ji, and Min Shen participated in the design of the study and drafted the manuscript. All authors read and approved the final manuscript.

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