ORIGINAL ARTICLE

Cost-Effectiveness and Cost-Utility Analysis of Cinnarizine Compared to Valproate in Pediatric Migraine: An Iranian Perspective

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ABSTRACT

Objectives: Childhood migraine is a prevalent neurovascular disease in children with a considerable reduction in quality of life and high social cost. Anticonvulsants, such as Valproate and calcium channel blockers, including Cinnarizine are used frequently as preventive medications. This research evaluates the cost-effectiveness and cost-utility of Cinnarizine versus Valproate in managing childhood migraine, based on an Iranian societal perspective.

Materials & Methods: A randomized cohort trial was conducted, involving 150 children aged 5 to 17 years at the Imam Reza Clinic in Shiraz, Iran. Patients were administered Cinnarizine (1–2 mg/kg/day) or Valproate (10–20 mg/kg/day) for three months, evaluated by decision-tree models for cost-utility and cost-effectiveness. Effectiveness was measured by reduction in migraine attack frequency and Quality-Adjusted Life Years (QALYs). Costs were obtained from patient medical records, questionnaires, and national datasets, including direct and indirect costs. Sensitivity analysis, such as Monte Carlo simulations, was performed to validate the results.

Results: Patients receiving Cinnarizine experienced a mean QALYs of 0.213 versus 0.209 for the Valproate group and a higher rate of response at 26% (Cinnarizine) versus 14% (Valproate). Total costs during the study period favored Cinnarizine ($183 vs. $191) with an Incremental Cost Effectiveness Ratio of $-156 per additional effect and an Incremental Cost Utility Ratio of $-2069 per QALYs. Adverse effects noted were drowsiness (17.8%) for the Cinnarizine and dizziness (13.5%) for the Valproate arm. Probabilistic sensitivity analysis contained an 88.2% probability that Cinnarizine was cost-effective with a willingness-to-pay of $17,922 per QALYs.

Conclusion: Cinnarizine was a cheaper option compared to Valproate as a prophylactic agent in pediatric migraine in Iran with higher response rates, lower expenses, and similar effectiveness. Further research with long-term follow-ups and varied populations is needed to validate the results.

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Introduction

Migraine is a kind of chronic headache disorder with a hereditary ground, initiating in some time of childhood, adolescence, or early adulthood and recurs in later years [1]. A typical attack of migraine-associated unilateral headache worsened by physical

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activities, commonly presents with nausea, vomiting, photophobia, phonophobia, and cutaneous allodynia [2, 3]. Among children aged 11 to 13 years, the estimated prevalence of headache types varies between 5.9 and 88%[4]. Furthermore, some epidemiologic data suggest that 10 to 20% of school-aged children and older adolescents suffer from chronic migraine [5].

The prevalence of migraine is different in various geographical regions. Based on the findings of epidemiological studies, the incidence of migraine in European countries is 8–17.6% among adults and 5.2%–9.1% in children and adolescents. [6]. According to some other studies, the prevalence of migraine in the countries of Asia is less than in other countries [6]. According to various research, the prevalence of migraines is within the range of 5.4-41.6% in adults [7] and 4.8-28.1% in children and adolescents in Iran [8]. A 2023 meta-analysis study conducted in Iran reported a migraine prevalence of 11.2% among adolescents. In addition, the prevalence among boys and girls was 8.2% and 8.0%, respectively. Similarly, a survey-based study involving 4,571 children reported a migraine prevalence of 5.2% [9].

Children with migraine miss more days of school annually than matched controls [10], and the rate of their quality of life has been reported worse, mainly due to health-related factors. The quality of life for children with migraine is comparable to that of children suffering from arthritis or cancer. Considering the rising prevalence of pediatric migraine and its substantial associated costs, prompt and accurate diagnosis is crucial for effective management [11].

Migraine prevention is the most common indication for using β-blockers, calcium channel blockers, serotonin antagonists, monoamine oxidase inhibitors, and anticonvulsant agents [12, 13]. Topiramate is the only FDA-approved medication for prophylaxis in children, but less responsiveness, compared to placebo, was recorded as a positive agent, the opposite of what was observed in adults [14, 15]. A 2024 study by Gargar reported that pregabalin, topiramate, flunarizine, levetiracetam, riboflavin, Cinnarizine, and amitriptyline all decreased migraine frequency significantly compared to a placebo. For headache severity, as scored by participants, Cinnarizine (with and without propranolol), pregabalin, Valproate, and levetiracetam were all effective in decreasing headache severity comared to a placebo [16].

Valproate is well-established treatment for epilepsy, believed to work by mimicking the action of γ-aminobutyric acid (GABA). Several reports indicate that Valproate is effective in preventing migraine attacks, leading to its widespread use for migraine management in the United States and European countries [17]. Hering and Kuritzky reported that Valproate had a significant effect in preventing migraine or reduction of the frequency, severity, and duration of the attack in 86.2% of patients.[17, 18]

Cinnarizine is an L-type calcium channel blocker, inhibiting contractions of vascular smooth muscle cells, and directly inhibits vestibular hair cells stimulation [19]. It also has antihistaminic actions, and all these mechanisms can potentially contribute to its preventive effects on migraine [12].

A study showed that 71% of cases in the Cinnarizine group, 66% of those in the Valproate group, reported more than 50% reduction in episodes at the end of the trial [20]. Second, a meta-analysis suggests that Cinnarizine will be more effective than Valproate in reducing the headache frequency [16].

Cost-effectiveness analysis, a technique in pharmacoeconomics, examines how much money is spent per unit of effectiveness achieved from two or more treatments. The findings assist doctors in obtaining the best outcomes with the minimum resources and promote rational use of medicines. Limited evidence exists regarding the cost-effectiveness of Cinarizine and Valproate. The findings can assist doctors in obtaining the best outcomes with the minimum resources and promote rational use of medicines. Accordingly, the present study aimed to assess the cost-effectiveness of flunarizine in managing migraine headache among children and adolescents aged 5 to under 17 years.

Materials & Methods

Study design and setting

A prospective randomized open-label cohort study was conducted in Imam Reza Clinic, a tertiary care referral center affiliated to the Shiraz University of Medical Sciences, Shiraz, Iran. Data were collected from June 22 to November 19, 2024. The study evaluated the clinical efficacy, safety, and cost-effectiveness of Cinnarizine versus sodium Valproate in the prophylactic treatment of pediatric migraine. The study lasted for three months, during which time the participants were supervised and data were collected at intervals for assessment of clinical outcomes and economic implications. From this, a decision-analytic model was developed using a decision tree for simulating the cost-utility and cost-effectiveness of Cinnarizine (1-2 mg/kg/day, used as needed) against Valproate (10-20 mg/kg/day) performed from a societal perspective. The model takes into account all aspects of costs, whether direct or indirect, measuring outcomes on the basis of the number of migraine days, response to treatment, adverse effects, and Quality-Adjusted Life Years (QALYs).

Participant eligibility

Inclusion criteria

Only subjects who fulfil the following criteria could enter the study:

- Being between 5 and 17 years.
- Being diagnosed with migraine (with or without aura) using the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria and confirmed by a pediatric neurologist.
- Having had at least four attacks of migraines in a month during the last three months.
- Undergoing no preventive therapy for migraine; otherwise, a washout period of four weeks was necessary.

Exclusion criteria

Children and adolescents ineligible for participation were those with:

- Cinnarizine or Valproate.
- History of significant hepatic, renal, or cardiovascular disorders.
- Presence of comorbid neurological and psychiatric disorders, affecting the study evaluation.
- Use of concurrent migraine prophylaxis or interacting drugs.
- Pregnancy or nursing.
- Inability or unwillingness of the child or guardian to give appropriate informed consent or cooperate with any aspect of the study.

Sample size determination

Using the Cochrane sample size formula, a level of significance (α) of 0.05, and a precision (d) of 0.05 desired, it was calculated that an adequate power could be achieved with at least 150 participants. Therefore, 75 patients were assigned to each treatment arm. Stratified random sampling ensured balance in age and sex across the groups. The baseline characteristics of the patients are reported in Table1.

Outcome measures

Primary outcome

Change in migraine frequency: The principal efficacy outcome was a change in the mean number of migraine attacks per month from baseline to the end of the study period. Attack frequency was recorded using patient diaries and validated by clinical review at monthly visits.

Secondary outcomes

Treatment response: Response rates to treatment in different treatment settings are reported in Table 3. Response categories were defined as follows:

- No response (< 25% reduction in frequency)
- Partial response (25–49% reduction)
- Moderate response (50–74% reduction)
- Complete response (≥ 75% reduction)

Health-related quality of life (HRQoL): Measured using EQ-5D-Y-3L questionnaire administered at baseline and study end. Utility values were derived for QALY calculation using area under the curve methodology.

Safety and tolerability: All adverse events reported by patients and/or guardians were documented, including severity, duration, and potential causality.

Economic evaluation

The economic evaluation was conducted from the societal perspective over a 6-month horizon without discounting. Costs were estimated in Purchasing Power Parity (PPP) dollars using a conversion factor of 1 USD = 91,086 IRR. The following categories were included:

- Direct medical costs: Cost of medications, physician consultations, diagnostic imaging, and laboratory tests, retrieved from clinical billing records and government tariffs.
- Direct non-medical costs: Transportation, accommodation and out-of-pocket expenses.
- Indirect costs: Productivity losses due to school absence and caregiver time off work, calculated using the average daily wage ($26.22/day).

The costs of direct medical services were calculated from patients' medical records and medical tariffs for 2024. The prices of the medicines were also obtained from the official website of the Food and Drug Administration at https://irc.fda.gov.ir/nfi. A questionnaire was designed to calculate direct and indirect costs of treatment. After completing the study period (3 months), the costs incurred by the patients during this period were obtained based on the questionnaire. To assess the direct and indirect costs of patients in each group, a questionnaire was filled out by the patient's parents or the patient. The indirect cost, derived from per capita disposable income, pertains to any loss of income incurred due to caring for a child or attending hospital clinical appointments.

Utility data for cost-utility analysis were derived from the EQ-5D-Y-3L tool completed by participants aged ≥ 5 years or their guardians. The "3L" in the name signifies three levels of severity for each of the five dimensions measured: Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. QALYs were calculated by multiplying the utility value by the number of years lived in a particular health state. QALYs were calculated by multiplying utility scores by duration in each health state. Both Incremental Cost-Effectiveness Ratio (ICER) and Incremental Cost-Utility Ratio (ICUR) were computed. A willingness-to-pay threshold of $17,922 (2023 GDP

per capita PPP for Iran) was used [21]. The schematic diagram of the model is shown in Figure 1.

For every eight hours of daily work, based on information from the Ministry of Labor and Social Welfare, the revised wage rate was set at $26.22 in 2024. All Iranian Rials were converted into PPP US dollars, 1 US. dollar = 91086 Rial [22]. The medical costs and utility are detailed in Tables 4 and 5.

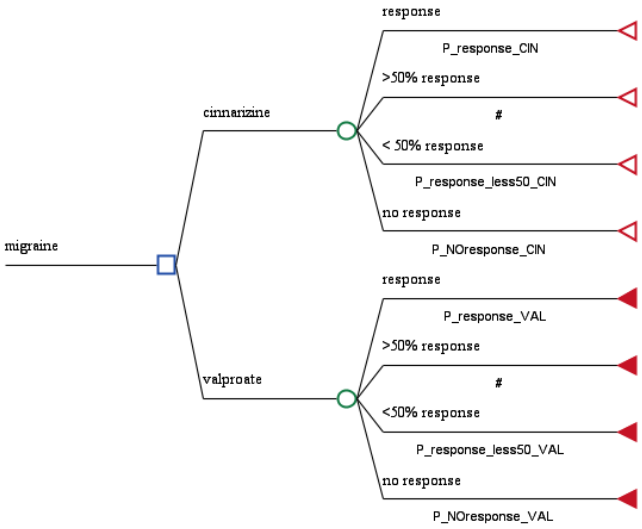

Figure 1. The schematic structure of the decision tree

Sensitivity analysis

One-way sensitivity analyses were performed on key variables, including drug price, utility values, and migraine frequency. Probabilistic sensitivity analysis (PSA) was conducted with 10,000 Monte Carlo simulations. Cost parameters followed a gamma distribution, while probabilities and utility values followed beta distributions. A willingness-to-pay threshold of $17,922 (based on Iran's GDP per capita, PPP) was used for interpretation.

Results

Patient demographics and clinical characteristics

One hundred fifity patients were enrolled from one clinical center. In the Cinnarizine and Valproate enrolled patients, 60% and 63% were maleand female (Table 1). The median age was 11.9 (4-17) years in the Cinnarizine group and 11.3 (6-17) years in the Valproate group. 65.3% and 63.7% of the family history of migraine was in the Cinnarizine and Valproate groups. Mean (SD) time since diagnosis was 1.5 (1.4) in the Cinnarizine and 1.1 (1.3) years in the Valproate group. Correspondingly, in the Cinnarizine and Valproate groups, the mean and duration of headache (hours) before medication were 11.4 (9.5) and 9.8 (7.3). The number of migraine attacks in the week before treatment was almost the same in both groups (Table 1).

Efficacy and safety

Cinnarizine showed an overall response rate of 26%, while Valproate appeared to have a somewhat poorer rate (14%). In the responder group of over 50%, Cinnarizine had a rate of 47% and Valproate a rate of 55%. In contrast, responses indicating less than 50% were recorded at 18% for Cinnarizine and 23% for Valproate. No response was indicated in 9% of the Cinnarizine and in 8% of Valproate groups.

Drowsiness was recorded in a significantly higher percentage of patients on Cinnarizine (17.8%) compared to Valproate (0%). Dizziness was more common; on the other hand, in those who were administered Valproate (13.5%) than in those on Cinnarizine (5.5%). Weight gain recorded by the two medications was apparently among the same lines, with Cinnarizine at 11% and Valproate at 9.5%.

Table 1. Baseline characteristics of the patients

Baseline characteristics	Cinnarizine	Valproate
Total number of patients	75	75
Mean age (SD), years	11.9 (1.2)	11.6 (1.4)
Sex, n (%)		
Female	45 (60)	47 (63)
Male	30 (40)	28 (37)
Mean (SD) time since diagnosis, years	1.5 (1.4)	1.1 (1.3)
Mean (SD) Duration of headache before medication, hour	11.4 (9.5)	9.8 (7.3)
Frequency of attacks before medication, per month		
Once a week	16 (21%)	15 (20%)
Twice a week	13 (17%)	12 (16%)
Three times a week	20 (27%)	20 (27%)
More than 4 times a week	26 (35%)	28 (37%)
Family history of migraine	65.3	66.7

Base case cost-effectiveness analysis

Cost-effectiveness analysis, as compared to Valproate, showed that adding Cinnarizine decreased the cost by $9 over three months, with an incremental response rate of 5.75%, resulting in an ICER of $-156 per additional effect (see Table 6).

Table 2. Transition probability among different states

Transition probability	Cinnarizine	Valproate
response	0.26	0.14
> 50% response	0.47	0.55
< 50% response	0.18	0.23
No response	0.09	0.08

Base case cost-utility analysis

The mean QALYs over the entire time horizon for the total population were 0.213 for Cinnarizine and 0.209 for Valproate. The mean costs over the entire time horizon for the total population were equel, based on case cost-effectiveness analysis. The ICUR was -2069 for migrain ptients. The total QALYs and response rate for Cinnarizine in migrain patients were higher, and the total costs were lower compared with Valproate (see Table 6).

Table 3. Adverse events during three months

Characteristics	Cinnarizine (n = 75)	Valproate (n = 75)
Weight gain	0.110	0.095
Dizziness	0.055	0.135
Drowsiness	0.178	0
Insomnia	0.110	0.054
Muscle weaknes	0.068	0
Nausea and vomiting	0.027	0.014
Severe hair loss	0	0.068
Menstrual irregularities	0	0.041
Abdominal pain	0.041	0.068
Loss of appetite	0	0.027
Urinary incontinence	0	0.027
Weight loss	0.014	0

Table 4. Medical direct cost by health state per three months

Components	Response	>50% response	<50% response	No response
Neurologist visit	26	29	37	47
Laboratory test	17	18	65	73
Psychological counseling	10	12	17	27
Radiology	22	97	179	366
Total cost	74	155	297	514

Table 5. Input in the economic evalution model

	Base case	Range (SD)	Distribution
Drug cost per 3 months ($)			
Cinnarizine	51	31	gamma
Valproate	117	84	gamma
Medical cost per 3 months ($)			
Response	75	16	gamma
>50% response	157	36	gamma
<50% response	301	52	gamma
No response	520	97	gamma
Direct non-medical cost			
Response	868	198	gamma
>50% response	893	210	gamma
<50% response	1074	233	gamma
No response	1143	275	gamma
Indirect cost			
Pesponse	574	120	gamma
>50% response	603	124	gamma
<50% response	667	153	gamma
No response	1101	263	gamma
Health utilities			
Response	0.91	0.07	beta
>50% response	0.84	0.1	beta
<50% response	0.78	0.12	beta
No response	0.69	0.16	beta

Sensitivity analysis

Figure 2 shows the results of the univariable sensitivity analysis in cost utility analysis. The ICUR of the Cinnarizine group compared to the Valproate group ranged from $-18256/QALY to $-1742/ QALY, and the utility value of the response state had the greatest effect on the ICUR. Factors, such as a utility value of response > 50 migrain, response < 50 migrain,

the indirect cost, and indirect non-medical cost also affected the ICUR, while the other factors had little effect on the ICUR.

Table 6. Base-case analysis results

Groups	Cinnarizine	Valproate
Effect	48.5	42.7
Increased effect	5.75%	-
Cost	183	191
Increased Cost	-9	-
QALY	0.213	0.209
Increased QALY	0.004	-
ICER	-156	-
ICUR	-2069	-

Figure 3 shows that the indirect and indirect non-medical costs in response state, > 50% response, and < 50% in attack of migrain and probability of response in > 50% in Valproate group had the greatest impact on ICER results. The ICER of the Cinnarizine group, compared to the Valproate group, ranged from $-189/QALY to $-120/ QALY

Results of the PSA are shown in Figure 4. The incremental outcomes showed that Cinnarizine always resulted in more QALYs (0.01 [credible interval: 0–0.03]); however, most cases revealed less costs ($-9 [−$16 to $8]), compared with Valproate. Based on the PSA results, Cinnarizine had a 88.2% chance of being cost-efective compared with Valproate if the WTP per QALY was $17,922.

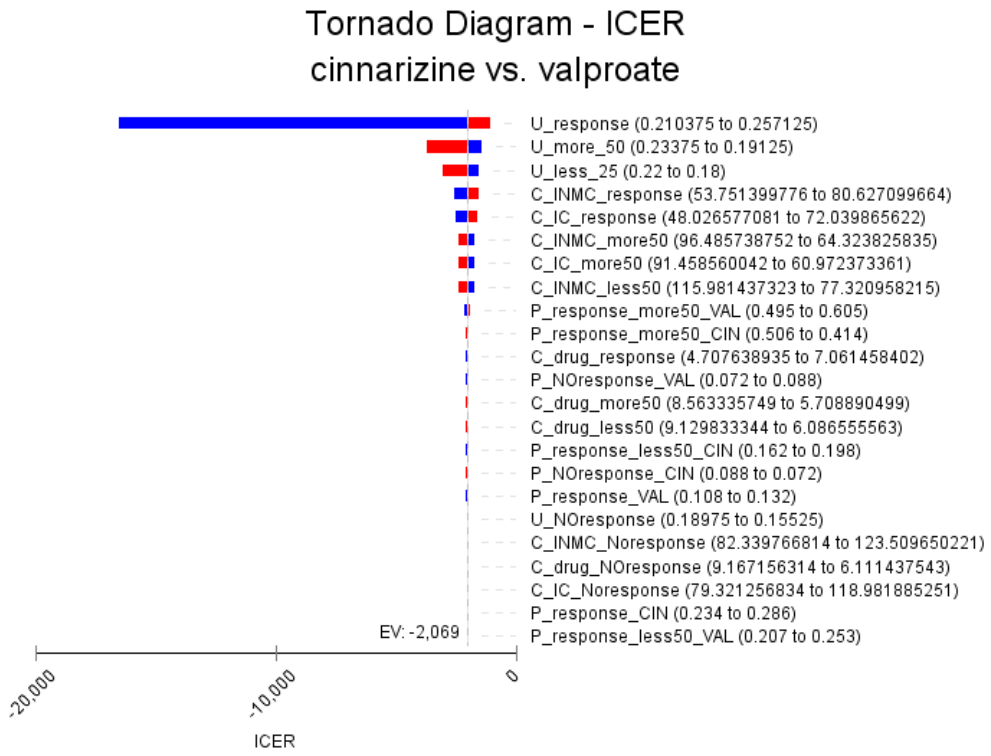

Figure 2. Tornado diagram of the deterministic sensitivity analysis in cost-utility analysis. The diagram shows the association of variables with the ICUR of Cinnarizine vs. Valproate. The vertical black line represents the base-case results of $-2069 per QALY. Red columns indicate an incremental change in that variable and its impact on ICUR, while blue columns indicate a decreasing change in that variable and its impact on ICUR.

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Figure 3. Tornado diagram of the deterministic sensitivity analysis in cost-effectiveness analysis

Figure 4. Probability sensitivity analysis in 10000 Monte Carlo simulations. This Figure displays the distributions imposed on the variables to explore the uncertainty of cost-effectiveness between Cinnarizine and Valproate at the WTP thresholds.

Discussion

The study utilized a combined sample of 150 patients with a slight male preponderance in both treatment arms (60% for the Cinnarizine and 63% for the Valproate groups). The median subject ages were

very close to one another, at 11.9 years in the Cinnarizine-treated participants and 11.3 years in the Valproate-treated subjects. Furthermore, both pharmacotherapies were thereby compared within an equally divided pediatric population. The significant proportion of patients exhibiting a familial migraine history (65.3% with Cinnarizine and 63.7% with Valproate) lends credibility to the genetic underpinnings of migraine and suggests a potential influence on treatment responsiveness. Consequently, this necessitates the development of individualized treatment approaches.The mean duration since diagnosis was slightly greater for the Cinnarizine group (1.5 years) than for the Valproate group (1.1 year), and this could imply that patients in the Cinnarizine group might have suffered from migraine for more years before treatment. This could be a sign of more disease burden, and this may affect the way they respond to treatment. There was heterogeneity in the average duration of headache when the patients initiated treatment found in the study. In the Cinnarizine group, the average headache duration was 11.4 hours (SD = 9.5), while for the Valproate group it was slightly shorter at 9.8 hours (SD = 7.3). The variation in headache duration prior to treatment can have significant implications for evaluating treatment effectiveness and the overall burden of migraines on patients.

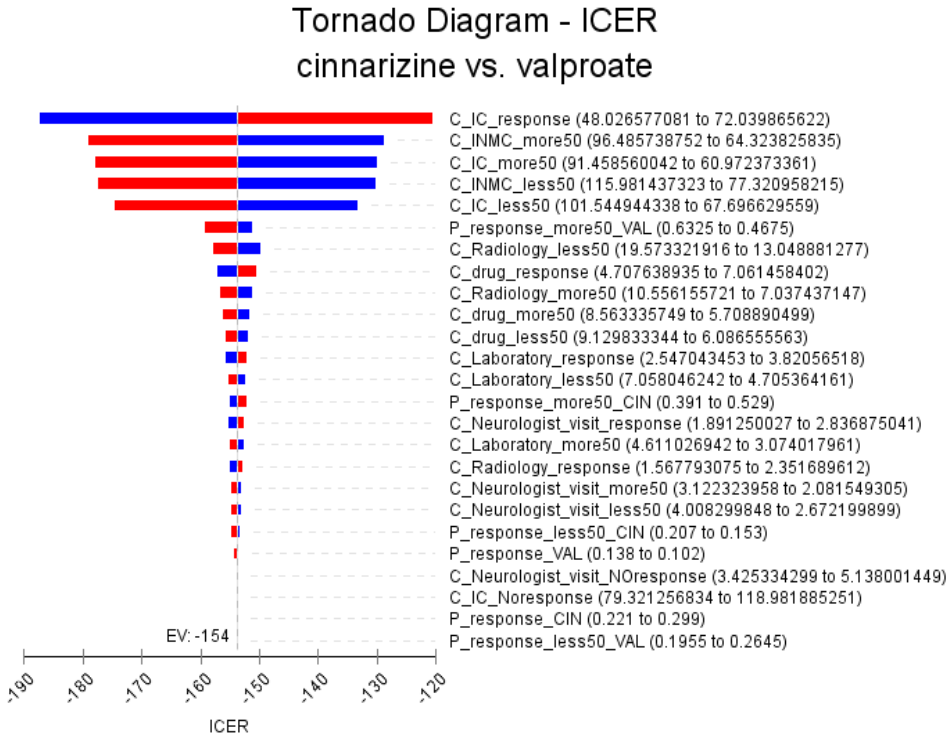

Figure 3. Tornado diagram of the deterministic sensitivity analysis in cost-effectiveness analysis

The longer average duration of headaches in the Cinnarizine group suggests that these patients may have experienced more severe or more chronic migraine episodes leading to their treatment. This difference raises essential considerations when evaluating treatment outcomes, as patients with longer headaches might respond differently to medications than those with less severe presentations. Understanding patient characteristics, such as baseline headache duration can help clinicians tailor their approach, ensuring that treatment decisions are informed by the severity and frequency of migraine attacks.

These results of an intercomparison study between Cinnarizine and Valproate contributes to understanding their relative efficacy and side effects, vital in considerations of using under medical settings. In this regard, the overall response rate of Cinnarizine was slightly higher at 26% compared to Valproate at 14%; the differences in response gave insight into the detailed performance of the two.

Valproate was more effective than Cinnarizine in a number of patients with a greater than 50% response —

55% to 47%. Thus, this would probably imply that for some patients, Valproate would be more effective in feeling way much better than before. These results reflect earlier observations regarding Valproate's stronger impact on certain migraine subsets [23]. For responses below the 50% improvement threshold, the situation was a little better in the case of Cinnarizine, where a response was noted in only 18% of cases compared to 23% for Valproate. Similarly, the lack of response rate was quite the same, standing at 9% for Cinnarizine and 8% for Valproate, which gave the impression that a reasonable number of patients were not responding to either medication. Notably, side effects with these two medications appear quite different.

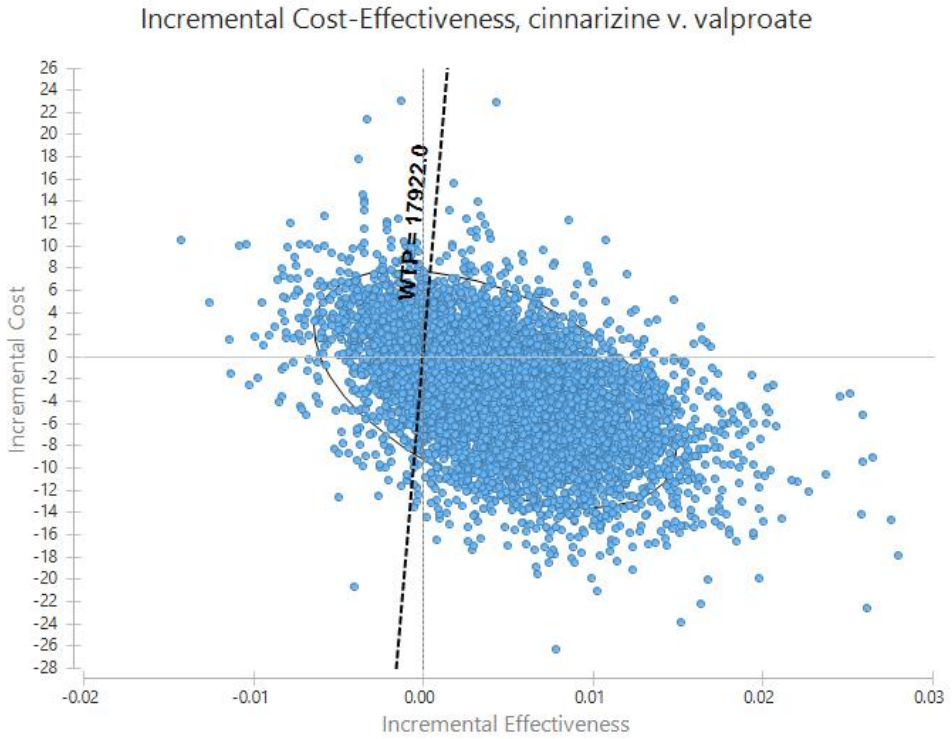

Figure 4. Probability sensitivity analysis in 10000 Monte Carlo simulations. This Figure displays the distributions imposed on the variables to explore the uncertainty of cost-effectiveness between Cinnarizine and Valproate at the WTP thresholds.

The drug most likely to cause drowsiness was Cinnarizine (17.8%) although Valproate did not cause drowsiness in either patient. Additionally, earlier trials consistently identified drowsiness as a hallmark side effect of Cinnarizine. Dizziness was reported more in the Valproate group (13.5%) compared to the Cinnarizine group (5.5%). Thus, this means that Cinnarizine could impact more on making people drowsy, while Valproate could have more balancing issues [20, 23]. Weight gain proved to be a common adverse event of the two drugs, with tightly similar rates of 11% for Cinnarizine and 9.5% for Valproate. Weight gain is a known adverse effect of both drug regimens, but with the potential of variability across patient groups. This pattern aligns with that of Bostani et al.'s study [23].

In choosing between Cinnarizine and Valproate, one must consider not only the overall success rates but also the magnitude of the side effects and the idiosyncratic reaction of each patient to them. For a patient who may be particularly sensitive to drowsiness, the better option might be Valproate. In contrast, for a patient who wants to stay away from dizziness, Cinnarizine would perhaps be better suited.

The cost-effectiveness analysis shows the advantage of using Cinnarizine for treating migraines in children over Valproate by $9 over three months. It also achieves a better response rate of 5.75%. Such results give a strong incremental ICER of $-156 per additional effect obtained, that is why Cinnarizine is a better cost-effective choice for preventing migraines in these children.

These findings confirm the results from one clinical trial, demonstrating the very effectiveness of Cinnarizine in reducing the frequency and intensity of migraine attacks in children [20]. The trial pinpointed that children tolerated Cinnarizine quite well, another important fact, as children might find it difficult to stay on their medications. The current analysis supports these findings with evidence that these cost savings

linked to Cinnarizine are not made at the expense of effectiveness, as the mean QALYs were higher at 0.213 for Cinnarizine compared to 0.209 for Valproate.

Further, the research conducted by Bostani et al. supports these results, suggesting that Cinnarizine is just as, if not more, proficient in recovery of therapeutic benefits compared to Valproate among pediatrics [23]. The study indicated that Cinnarizine possesses a good side effect profile, a notable advantage considering that Valproate is associated with adverse effects such as weight gain and teratogenicity. The observed higher response rate in the review could suggest that Cinnarizine is a more suitable first-line treatment option for patients. In addition, the data are in the same line that of Togha et al. who concluded that Cinnarizine was effective even among those with refractory migraines, indicating suitability for use even in more severe cases [12]. Total costs were lower for Cinnarizine in this study, which may be related to its applicability and overall effectiveness in diversified scenarios of migraine treatment, even where alternative drugs were ineffective.

The present analysis concludes that Cinnarizine is a competitive and cost-effective alternative to Valproate for pediatric migraine prevention. Its advantages include lower associated costs, higher success rates, and improved tolerance, making it a favorable option for clinicians and families managing migraines in children. Continued research into long-term outcomes and cost-effectiveness in varied pediatric cohorts is warranted to build upon these findings.

The sensitivity analysis confirmed the robustness of the cost-effectiveness results in the cost-effectiveness deterministic sensitivity. Cost-effectiveness through Cinnarizine was further confirmed through the probability sensitivity analysis, with a probability of 88.2% that is cost-effective compared to Valproate in the WTP threshold value of $17,922 per QALY. This high probability justifies the practice of Cinnarizine adaptation in clinical practice, specifically in settings where a budget impact should be taken into consideration.

Limitations

The obtained results are noteworthy; however, certain limitations warrant consideration. The single-center nature of this investigation restricts its applicability to a wider demographic. Differences in patient demographics, treatment modalities, or health resource allocation may exist in other clinical environments. Consequently, future studies should be designed as multi-center trials encompassing populations from diverse geographical locations to improve the potential for wider application of the findings and to ensure the reproducibility of results within routine clinical practice. Furthermore, the follow-up period was notably brief, potentially failing to fully elucidate the long-term effects and financial burdens inherent in migraine management. Migraine treatment frequently necessitates prolonged care and varied pharmacotherapy, significantly influencing both practical treatment success and cost evaluation. Future long-term follow-up studies will be instrumental in understanding the sustained efficacy of treatments, the emergence of delayed adverse effects, and the cumulative costs over time.

In Conclusion

This study highlights the cost-effectiveness of Cinnarizine compared to Valproate in treating migraines in a pediatric population. The similar sociodemographic and clinical profiles of the patients in both groups, combined with the favorable economic outcomes for Cinnarizine, suggest that it may be a preferable option for managing migraines. Further research is warranted to explore long-term effects and broader applicability of these findings.

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Ethical approval for the study was granted by the Institutional Review Board of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1403.180; Project code: 30390). Written informed consent was obtained from the guardians of all the enrolled participants.

Authors' Contributions

Z.G.: Methodology, Formal Analysis, Investigation, Writing. M.N.: Methodology, Data gathering, Writing. K.K.: Methodology, Investigation. H.N.: Conceptualization, Resources, Supervision, Funding acquisition, Writing, Review & Editing

Conflict of Interest

The authors declare no conflicts of interest.

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