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Cost-Effectiveness Analysis of Rizatriptan and Sumatriptan versus Cafergot® in the Acute Treatment of Migraine

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Abstract

Background: Both ergotamine and selective serotonin 5-$HT_{1B/1D}$ receptor agonists ('triptans') are currently used in the treatment of moderate to severe migraine. Ergotamine is a traditional therapy with a lower drug acquisition cost compared with triptans. It has been shown that triptans are more efficacious than ergotamine, but the higher acquisition costs and shorter duration of action are disadvantages of triptans compared with ergotamine.

Objective: The purpose of this study was to provide a comparison of the cost-effectiveness of rizatriptan 10mg and sumatriptan 50mg tablets with that of a fixed-dose combination of ergotamine tartrate plus caffeine (Cafergot®) in the treatment of an acute migraine attack. The cost-effectiveness of rizatriptan in comparison with sumatriptan was also assessed.

Methods: Three separate decision tree models were developed (model 1: rizatriptan vs Cafergot®; model 2: sumatriptan vs Cafergot®; model 3: rizatriptan vs sumatriptan). The time horizon was 1 year. Cost-effectiveness analysis was conducted from the societal perspective using cost and effectiveness estimates from the literature. All costs were converted to US dollars (2003). The cost-effectiveness ratio was expressed as incremental cost per quality-adjusted life-year (QALY) gained.

Results: Base case evaluation showed that both rizatriptan and sumatriptan dominated Cafergot®. The net annual saving associated with use of rizatriptan was $US622.98 per patient, with an incremental QALY of 0.001. Use of sumatriptan resulted in a saving of $US620.90 and an increase in QALY. The cost-effective ratios were not sensitive to changes in key variables such as efficacy, utility, drug costs, hospitalisation cost and patient preference over alternative therapies. The study further showed that rizatriptan is more cost effective than sumatriptan, as evidenced by its lower cost and greater effectiveness. Sensitivity analysis showed that the cost-effectiveness ratios were sensitive to moderate changes in drug efficacy.

Conclusion: Rizatriptan and sumatriptan were less costly and more effective than Cafergot® in the treatment of an acute migraine attack. Rizatriptan was somewhat less costly and more effective than sumatriptan. Additional quality-of-life studies

are needed to confirm the benefits of using triptans in the management of migraine.

Background

Migraine is a common illness characterised by periodic headache that may be accompanied by visual and auditory disturbances. It affects approximately 18% of women and 6% of men in the US.[1] Migraine occurs most commonly between the ages of 25 and 55 years in both men and women.[1] From an economic viewpoint, these years of an individual's life are potentially the most productive.

Migraine has a huge social economic impact. The annual cost of migraine totals about $14 billion in the US alone.[2] Indirect costs as a result of lost productivity are substantial and comprise up to 75–90% of total costs. This is largely attributable to modest rates of medical consultation by migraineurs.[3] A population-based study showed that 19–44% of migraineurs never consult a doctor.[4] In terms of the type of medical resources utilised by migraine patients, general practitioners figure most frequently. Emergency room (ER) visits and specialist care services also play important roles in the treatment of migraine.[5,6]

Migraine can have a substantial impact on an individual's quality of life (QOL). It has been shown that migraineurs' QOL scores are even lower than those for other patients with chronic conditions such as arthritis, diabetes mellitus, back pain and depression.[7]As migraine is episodic, patients experience not only pain during acute attacks but also anxiety associated with the prospect of future attacks. In addition, migraineurs are at increased risk of developing depression and other co-morbid conditions that would further contribute to their reduced health status.[8]

Over the last decade, there have been considerable advances in the understanding and treatment of migraine. The advent of effective new treatments makes the prospect of adequately treating patients quite promising, which in turn will lead to a significant reduction in the overall economic and healthcare burden of migraine.

Among all the achievements in migraine management, the development of the selective serotonin 5-$HT_{1B/1D}$ receptor agonists ('triptans') has resulted in the greatest breakthrough in the treatment of acute migraine headache. The development of sumatriptan, the first drug in this group, dramatically changed acute migraine treatment. To date, seven triptans have become available in the US: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan. Generally, triptans are highly effective in relieving the pain and nausea of a migraine attack and thus reducing work productivity loss. Other available treatments for migraine headache include ergotamine, NSAIDs and combination analgesics. Both ergotamine and the triptans are recommended by current medical standards for the acute treatment of moderate to severe migraine. Analgesics, NSAIDs, and an anti-nausea agent are recommended for the treatment of mild to moderate migraine attacks.[9]

Because of the associated economic impact of migraine and its negative impact on the health-related QOL of patients, the cost-effectiveness analysis of migraine management is of great interest. However, while several cost-effectiveness studies of triptans in migraine are available,[10-18] most of these did not address QOL in migraine patients and comparisons were generally limited to two treatment alternatives. Comparisons of the cost-effectiveness of different triptans are rare. In these studies,[10,12-18] the denominators of the cost-effectiveness ratios were usually expressed in traditional clinical outcomes related to headache relief instead of quality-adjusted life-years (QALYs).

Purpose of the Study

With so many drugs available for the treatment of acute migraine and only a limited number of cost-effectiveness studies in this field, an economic evaluation of drugs used in the management of acute migraine is timely and necessary.

Although triptans have demonstrated efficacy in the treatment of migraine, high acquisition cost and a short duration of action[11,19] remain the major disadvantages of these drugs. The latter property results in a substantial probability of headache recurrence during a single migraine attack. Among triptans, sumatriptan was the first to be developed and tested. It has been shown to be well tolerated and effective in treating acute migraine headache.[20] Rizatriptan is a relatively new drug in this group and has proved to be more efficacious than sumatriptan.[21,22] Furthermore, current research shows that rizatriptan, which is available as an oral disintegrating tablet formula, is preferred over sumatriptan by migraine patients.[21] Eletriptan has demonstrated similar efficacy to rizatriptan, but is less well tolerated. Other triptans such as naratriptan and frovatriptan demonstrated inferior response rates when compared with sumatriptan.[22] For these reasons we chose to compare sumatriptan, the original triptan product with the most extensive supporting research and patient experience, and rizatriptan, which is slightly preferable among the newer triptans on the basis of its tolerability and efficacy. However, for any individual patient, therapy outcomes are variable, so that some triptans (e.g. eletriptan or almotriptan) may be preferred to rizatriptan by some patients.

Ergotamine is a traditional therapy for migraine and is widely available. Despite the introduction of the triptans, Cafergot® [1] (combination of ergotamine and caffeine) is still a frequently prescribed migraine treatment throughout much of the world because of its low cost (compared with triptans).

Therefore, in our study, we compared the cost-effectiveness of rizatriptan 10mg orally disintegrating tablets and sumatriptan 50mg tablets with Cafergot® (ergotamine 1mg/caffeine 100mg) tablets in the treatment of an acute migraine attack. A comparison of rizatriptan with sumatriptan was also performed. Since QOL is an important dimension in the assessment of treatment response, this study evaluated QALYs explicitly in the cost-effectiveness analysis.

Methods

This cost-effectiveness analysis was conducted from a societal perspective for the US migraine patient cohort. The time horizon was 1 year, obviating the need for discounting of costs and treatment effects. Extension of the data to other countries would be straightforward to calculate, taking into account primarily differences in treatment costs and drug prices.

Model and Probability

A decision tree was constructed to simulate potential outcomes once a patient suffers from an acute migraine attack (figure 1). Upon the initial migraine headache attack, a patient could decide to take rizatriptan 10mg, sumatriptan 50mg or Cafergot® 2mg/

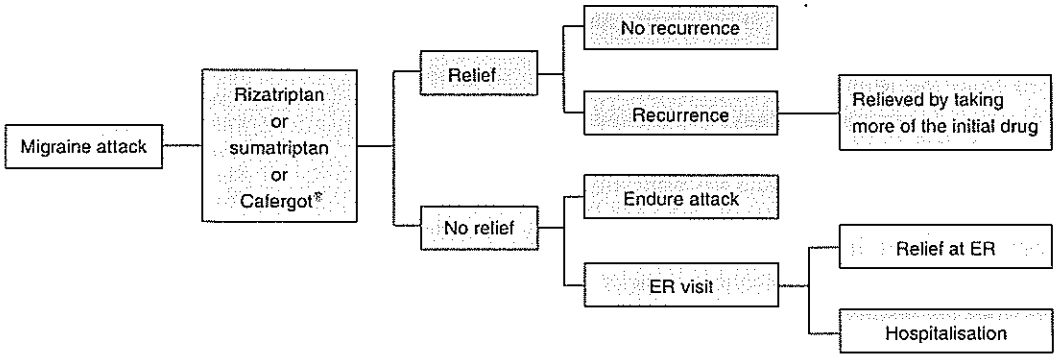

Fig. 1. Decision tree for the acute treatment of a first migraine attack. ER = emergency room.

1 The use of trade names is for product identification purposes only and does not imply endorsement.

Table I. Description of outcomes and utilities associated with acute therapies for a migraine attack[11]

Outcome	Utility	Description
A	1	Headache relieved by first administration of first medication, no recurrence
B	0.9	Headache relieved by first administration of first medication, with recurrence
C	0	Headache not relieved by first administration of first medication, patient chooses to endure attack
D	0.1	Headache not relieved by first administration of first medication, headache relieved at ER
E	0	Headache not relieved at ER, patient needs hospitalisation

ER = emergency room.

200mg for acute migraine headache relief, leading to different outcomes as described in table I. Each migraine drug is given once to abort an attack. A second dose can be given if headache recurs. A patient who does not experience relief from the first dose of each drug will either choose to endure the headache or go to the ER. When a patient chooses to endure the attack, no other treatments are taken. If the headache is not relieved at the ER, hospitalisation is required. Upon the second and following attacks, the patient can either stay with the same medication used for the first attack or switch to another medication.

Three models were developed based on the decision tree shown in figure 1. These were: model 1 – rizatriptan vs Cafergot®; model 2 – sumatriptan vs Cafergot®; model 3 – rizatriptan vs sumatriptan. For rizatriptan and sumatriptan, the probabilities of acute relief (i.e. headache response at 2 hours) after medication and of headache recurrence within 24 hours were obtained from the meta-analysis of 53 trials of triptans by Ferrari et al.[22] Headache response and recurrence rates for Cafergot® were obtained from the Multinational Oral Sumatriptan and Cafergot® Comparative Study.[23] Probabilities of going to the ER and hospitalisation were deduced from statistics showing the annual ER utilisation of migraine patients,[24] annual attack frequency[14,25] and triptan efficacy data.[22] The probability of switching therapy during subsequent attacks was derived from the results of patient preference studies.[21,26] Since there is no preference study comparing sumatriptan with Cafergot®, we assumed the preference rate for sumatriptan compared with Cafergot® would be the same as that of rizatriptan compared with Cafergot®. The probabilities of these events are shown in table II and table III.

Utility Measure

Because of the temporary nature of a migraine attack, it is difficult to capture patients' utility change during the short period of an attack. Some instruments (e.g. 24-hour Migraine Quality of Life Questionnaire[27]) have been specifically devised to measure the QOL of migraine patients during the 24-hour period after the onset of headache attacks.

Table II. Probabilities of events at a first migraine attack

Event	Drug	Probability (%)
Headache relief after first administration[22,23]	Rizatriptan	68.6
	Sumatriptan	62.7
	Cafergot®	37.9
Headache recurrence[22,23]	Rizatriptan	36.9
	Sumatriptan	27.8
	Cafergot®	15.3
Probability of enduring headache if headache not relieved by first administration[14,22,24,25]		90
Adverse events[21,26]		
Dizziness	Rizatriptan	6.7
	Sumatriptan	5.8
	Cafergot®	5.3
Nausea	Rizatriptan	4.2
	Sumatriptan	6.9
	Cafergot®	8.5
Somnolence	Rizatriptan	5.5
	Sumatriptan	6.7
	Cafergot®	2.3
Chest pain	Rizatriptan	0.7
	Sumatriptan	2.4
	Cafergot®	0.8
Probability of headache relief in ER[14,22,24,25]		94

ER = emergency room.

Table III. Probability of switching therapy during second and subsequent migraine attacks[21,26]

Treatment comparison	Treatment options	Probability (%)
Rizatriptan vs Cafergot®		
Rizatriptan	Keep taking rizatriptan	69.9
	Switch to Cafergot®	30.1
Cafergot®	Keep taking Cafergot®	30.1
	Switch to rizatriptan	69.9
Rizatriptan vs sumatriptan		
Rizatriptan	Keep taking rizatriptan	64.3
	Switch to sumatriptan	35.7
Sumatriptan	Keep taking sumatriptan	35.7
	Switch to rizatriptan	64.3
Sumatriptan vs Cafergot® [a]		
Sumatriptan	Keep taking sumatriptan	69.9
	Switch to Cafergot®	30.1
Cafergot®	Keep taking Cafergot®	30.1
	Switch to sumatriptan	69.9

a In the absence of specific data, preference rates for sumatriptan versus Cafergot® were assumed to be the same as for rizatriptan versus Cafergot®.[26]

However, there is only modest correlation between measurements on these instruments and those of other scales, such as disability measures.[28] Without a transformation algorithm, it is also impossible to convert QOL measures to health utility to be used for QALY calculations. Therefore, in this analysis, we adopted the utility values from the study by Evans et al.[1] In that study, the investigators derived utility values associated with each outcome using the Quality of Well-Being measure.[29] Utilities of different outcomes associated with each treatment arms are showed in table I. However, we assigned the utility of hospitalisation as zero instead of adopting the negative utility number used in the study by Evans et al.[1] This is because health economics researchers are generally opposed to negative utilities (implying that certain disease states are even worse than death). For the purposes of resource allocation it makes little sense to spend money to improve someone's health from a state worse than death to that of death, given that there are substantial unmet needs among patients with positive levels of health utility.

Although there might have been additional QALY loss during the non-migraine time (because of anxiety and distress between migraine attacks), this was not factored into calculations of incremental QALY in this study because of the lack of published data measuring patients' utilities over a long period of time (e.g. 1 year) for different treatment options. Since most migraine headaches are relieved during hospitalisation, if not in the ER, the probability of a patient experiencing anxiety or distress during non-migraine time would be the same for different treatment arms. Therefore, it was assumed that the additional difference in QALYs occurring between migraine attacks for different treatment arms would be cancelled out unless treatment options exerted large differential effects on patients' utility between migraine attacks.

Costs

Reflecting a societal perspective, costs were evaluated for relief from migraine attack after the first dose of medication, for subsequent doses of medication if headache recurred, and for subsequent ER visit and hospitalisation. All costs were expressed in US dollars (2003). Direct costs included: (i) physician visit cost; (ii) drug acquisition cost; and (iii) cost of hospital drugs and medical supplies. Indirect costs included patient travel and waiting time.

The cost of visiting a physician was obtained from the Resource-Based Relative Value Scale (RBRVS).[30] We assumed that patients needed to visit a physician during subsequent attacks only if they wanted to switch to an alternative therapy. Drug acquisition costs were from the 2003 Red Book (Average Wholesale Price [AWP]).[31] We discounted the AWP by 20% since most people belong to health plans that receive substantial discounts from AWP. The cost to treat migraine in the ER, based on physician and facility fees for 3 hours, was obtained from the study of Linbo et al.[32] This ER cost did not include medication and potential EEG costs. Therefore, we added the costs of EEG and medications, which include intravenous (IV) dihydroergotamine, metoclopramide and IV fluids,

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