Sodium Oxybatefor Narcolepsy with Cataplexy–A Cost-Effective Analysis

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Methods

Economic Evaluation

We estimate the cost-effectiveness of sodium oxybate comparing to the current treatment by following two cohorts of patients, one receiving standard treatment plus sodium oxybate and one continuing to receive standard treatment alone for a period of time. The economic evaluation estimates the average total cost for cohort of patients treated with sodium oxybate and the other cohort of patients with standard treatment, based on published data sources.Average quality-adjusted life years (QALYs) gained for the cohort treated with sodium oxybate and the cohort receiving standard treatment alone were based on the clinical trial data assessing QoL using scores obtained from the SF-36 instrument. We calculate the incremental cost-effectiveness ratio (ICER) to estimate the additional costs associated with the use of sodium oxybate to obtain a gain of one additional QALY when compared with standard treatment alone.

This ICER is given by the following formula:

$$ICER = \frac{Cost_{\text{Sodium Oxybate}} - Cost_{\text{Standard treatment}}}{QALY_{\text{Sodium Oxybate}} - QALY_{\text{Standard treatment}}}.$$

We estimated the cost-effectiveness of sodium oxybate compared to standard treatment by assessing whether the ICER exceeded or remained below a willingness-to-pay threshold. If the ICER is no higher than a chosen threshold then sodium oxybate could be considered to be cost-effective when compared to standard treatment alone. In the UK, National Institute of Clinical Excellence (NICE) generally considers interventions with an ICER below the willingness-to-pay threshold of £20,000 per QALY gained to be cost-effective. Where the ICER is above £30,000 per QALY gained it is unlikely the intervention will be considered cost-effective, without additional exceptional factors supporting use (e.g. end-of-life care) [10].

Overview

In this economic evaluation, we developed a Markov model to follow patients from commencement of treatment with sodium oxybate to the end of a five-year time horizon. The state transition diagram of the Markov model is illustrated in Supplementary Figure1. To capture the differences in costs and utilities due to short-term events, such as non-response and patient withdrawal within the first three months, we used time-dependent parameters. The model takes an NHS perspective and incorporates utilities and costs associated with time spent on different treatments, time spent with significant side effects with sodium oxybate and death. We applied an annual discount rate of 3.5% to costs and benefits [10].

The population we considered consists of adults who suffer from narcolepsy with cataplexy and have derived inadequate benefit from treatment with antidepressants (as anti-cataleptic) and stimulants (for daytime sleepiness symptoms). Standard treatment used in clinical practice included using antidepressants such as clomipramine, fluoxetine and Venlafaxine for cataplexy symptoms, and stimulants including modafinil, dexamfetamine and methylphenidate for sleepiness symptoms. Sodium oxybate is assessed here as an add-on treatment i.e. used alongside stimulants and antidepressants. There were limitations in the data required for cost-effectiveness modelling reported in the published papers of sodium oxybate trials and so we have had to make a number of assumptions to permit comparison. These are detailed below.

Structure of the Markov model

We simulated two cohorts of patients, one receiving standard treatment plus sodium oxybate and one continuing to receive standard treatment alone, from the point of entry to the end of a five-year horizon using a Markov model (Supplementary Figure1). Three health states are defined in the model and we assume all patients, regardless of treatment, can only be in one state at any time-point. The three disease states defined are: (i) On Treatment: with maintained response (or in receipt of standard treatment alone and with ongoing inadequate response), (ii) Withdrawn from Treatment: patient withdrawal due to unsatisfactory response to sodium oxybate (for the group of patients with standard treatment, we assume the rate of withdrawal from standard treatment is zero throughout the comparison) and (iii) Dead: both cohorts of patients may die from other causes regardless of their treatment options and we have assumed likelihood of death is equal in each treatment arm. We have

is no predictable difference in the pattern of clinic visits for patients receiving either treatment.

The values of the parameters used in the model are shown in Table 2.

Parameter	Value		Source/Comments
	Base Case	Distribution	
Utilities			
Inadequate response to current treatment alone	0.763	Beta (23,7)	Use the SF-36 scores reported in Teixeira et al. [15] and apply mapping algorithm from Ara and Brazier [16] to obtain the EQ-5D utilities; Beta (Ŭ,ƀ)
No response to sodium oxybate	0.763	Beta (23,7)	The same as the utility of inadequate response to current treatment alone
In response to sodium oxybate	0.8059	-	Use the baseline utility for patients in inadequate response to current treatment alone and add the utility increase corresponding to ESS change
Difference in utilities between in response and no response to sodium oxybate	0.0429	Beta (96,2134)	Use the change in utility for 1 unit change in ESS estimated in a York economic model of CPAP in OSAH [17], assuming 4 units of ESS change [7] in the base case and adjust for age
Increase in EQ-5D utility for 1 unit decrease in ESS	0.0097	-	York economic model of CPAP in OSAH [15]
Change in ESS scores	4	-	The mean change in ESS scores for patients receiving a mean daily dose of 6 g of sodium oxybate [7]
Costs for clinic visits			
Costs per specialist visit	Ã131	Normal (131,3.24)	Consultant led follow-up attendance non-admitted face to face (neurology) [18]; Normal (ε,ů)
Costs for drugs			
Sodium oxybate	Φ		

Patients with Sodium Oxybate	From in response to withdrawal	0	-		From cycle 2 onwards
	From in response or withdrawal to death	0.0001-0.0838	-	Age dependent [11]	
Patients with current treatment	From in response to withdrawal	0	-		
	From in response or withdrawal to death	0.0001-0.0838	-	Age dependent [11]	

Table 2: Values of parameters used in the decision model.

and on-treatment score was also quite small (0.025). This difference is less that the difference we obtained by applying the ESS–utility relationship regression equation. Thus, we consider that there are currently no data which would suggest that this method yields unreliable results for narcolepsy patients.

In our model we incorporated only one outcome measure from the clinical trial data, the effect of treatment on ESS. It is likely other measures reported in the trials could impact on QoL, such as number of cataplexy attacks per week or nocturnal sleep quality, but we found no information allowing us to relate such findings to impact on cataplexy (or of resolution of cataplexy or improvement in nocturnal sleep quality), which could be related to QALY changes. Our sensitivity analyses show outcomes associated with assuming the widest possible range of utilities associated with this condition, going from the most severe end of reported utilities to total resolution. It is unlikely that the inclusion of additional data on cataplexy would represent cases not already assessed in the sensitivity analyses but the absence of these data introduces additional uncertainty to our model.

Implications

On the basis of current costs, sodium oxybate is unlikely to be cost-effective as an add-on treatment for patients who respond inadequately to standard treatment with stimulants and antidepressants. Although, it is recognised that measure of improvement in utilities used in the current model may be an underestimation of the reality.

There remains substantial uncertainty about the quality of life impact of this chronic rare condition and further research is necessary to permit future analyses to consider the cost-effectiveness of sodium oxybate. Current understanding of the impact of cataplexy is particularly limited, as is available evidence on the long-term course of the condition.

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