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COST-EFFECTIVENESS ANALYSIS OF 5% LIDOCAINE MEDICATED PLASTER MONOTHERAPY VERSUS PREGABALIN OR GABAPENTIN IN THE TREATMENT OF POST HERPETIC NEURALGIA AND DIABETIC POLYNEUROPATHY UNDER THE PERSPECTIVE OF BRAZILIAN PUBLIC HEALTHCARE SYSTEM

PSY68

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INTRODUCTION

- Neuropathic pain can occur after damage to the nerve pathways at any point caused by different etiologies. Symptoms can be spontaneous or provoked and can have different presentations (1);
- Post-herpetic neuralgia (PHN) is a type of neuropathic pain, whose occurrence is a complication of herpes zoster infection (2, 3);
- Diabetic polyneuropathy (DPN) is a form of neuropathic pain, originated as a complication of diabetes (2, 4);
- In the current clinical practice, tricyclics antidepressants, anticonvulsants (e.g., pregabalin and gabapentin), topical treatments (e.g., lidocaine, capsaicin) and invasive techniques (e.g., blocking of the sympathetic ganglia) are widely used for neuropathic pain management (5, 6);
- A 5% lidocaine medicated plaster (LMP) was developed to treat PHN and localized neuropathic pain (7);

OBJECTIVE

- The objective of this analysis was based on the results of a systematic literature review of randomized controlled trials, performed specifically for this study, comparing LMP and placebo or active comparators in the treatment of neuropathic pain, which showed that LMP brings benefits in the treatment of these patients.
- Thus, our objective was to assess these benefits combined with costs, performing a cost-effectiveness analysis of LMP versus pregabalin and gabapentin monotherapy for the treatment of PHN and DPN under the perspective of the Brazilian public healthcare system.

METHODS

Systematic Review

- A systematic review was performed to assess efficacy and safety of LMP compared with placebo or active comparators in the treatment of neuropathic pain;
- Randomized controlled trials (RCT) were retrieved, analyzed and selected from the databases MEDLINE, LILACS and CENTRAL;
- Search strategy was: ((“lidocaine”[MeSH Terms] OR “lidocaine”[All Fields]) AND (“neuralgia”[MeSH Terms] OR “neuralgia”[All Fields] OR (“neuropathic”[All Fields] AND “pain”[All Fields]) OR “neuropathic pain”[All Fields])) AND Randomized Controlled Trial [ptyp].

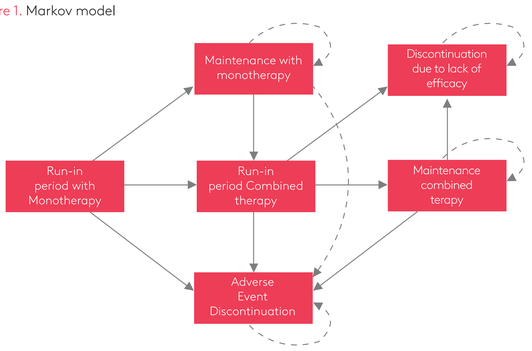
Cost-Effectiveness Analysis

- Due to the highest number of studies available regarding PHN detected by the systematic review, a cost-effectiveness analysis (CEA) was built based on the management of this disease and adapted for DPN;
- Perspective was the Brazilian public healthcare system;
- Intervention was LMP;
- Comparators was antiepileptic drugs (pregabalin and gabapentin), since they are the main treatment for PHN patients in Brazil (8);
- Time horizon was 6 months to cover the duration of treatment with LMP (9);
- No discount rate was used due to the short time horizon;
- Results were reported as incremental cost-effectiveness ratios (ICER).

Markov Model

- The structure of the Markov Model was based on published CEAs of LMP in PHN (10-13);
- Patients entered in the “run-in monotherapy” state receiving LMP, pregabalin or gabapentin, and moved from one state to another every 30 days according to their response to treatment (Figure 1);
- Transition probabilities were extracted from head-to-head trial and, when necessary, from placebo-controlled trials (10, 14-17);
- The same structure was used for PHN and DPN.

Figure 1. Markov model



Parameters

- Adverse events were retrieved from head-to-head trial for LMP and pregabalin, and from safety profile studies for gabapentin (14, 18);
- Utilities were extracted from previous studies performed by United Kingdom primary care setting (Table 1) to calculate quality adjusted life-years (QALY) (19);
- Resources used were retrieved from the literature and validated by a specialist with experience in the Brazilian public healthcare system.
- Costs were calculated for the Brazilian perspective using public tables and databases, as SIGTAP and BPS.

Table 1. Utilities

LMP	Utility	Gabapentin or pregabalin	Utility
First 1.5 days treatment	0.55	First 15 days treatment	0.55
Maintenance (after first 15 days)	0.95	Maintenance (after first 15 days)	0.85
Maintenance combined therapy (after first 15 days)	0.95	Maintenance combined therapy (after first 15 days)	0.85
Dropout (AE or lack of efficacy)	0.55	Dropout (AE or lack of efficacy)	0.55

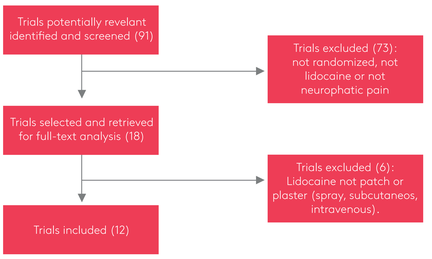
Sensitivity Analysis

- A one-way sensitivity analysis was performed in order to evaluate the robustness of the model;
- The six parameters considered to have greater uncertainty were varied: time horizon, number of plasters, pregabalin dosage, gabapentin dosage dropout medications due to adverse events, and dropout medications due to lack of efficacy.

RESULTS

Systematic Review

Figure 2. Flow Diagram



- Nine double-blind studies compared LMP with placebo and PHN was the most studied pathology;
- One RCT evaluated the use of LMP and placebo for PHN treatment. LMP was associated with improvements in pain, allodynia, quality of life and sleep measures. The incidence of adverse events was not statistically different (20);
- Four RCTs compared LMP and vehicle plaster use in PHN patients. LMP was superior in terms of pain relief (21-24);
- A pivotal study, with 300 patients with PHN, compared LMP with pregabalin. The per protocol analysis demonstrated improvement in pain control and reduction of adverse events with LMP (14);
- The other RCTs included evaluated chronic back pain (25), myofascial pain syndrome of the upper trapezius (26, 27), and postsurgical incisional pain (28)

Cost-Effectiveness Analysis

- The Cost-Effectiveness Analysis was developed for PHN and PND patients because these were the most frequent pathologies with trials were found by the systematic review.

Post-Herpetic Neuropathy

- Estimated total treatment costs for LMP, pregabalin and gabapentin were $ 2,088.48 BRL, $ 1,212.36 BRL, and $ 604.42 BRL, respectively;
- QALYs were 0,422 for LMP, 0,359 for pregabalin, and 0,344 for gabapentin;
- Compared with pregabalin, ICER for LMP was $ 19,256.33 BRL/QALY. Compared with gabapentin, it was reduced to $ 19,102.47 BRL/QALY;
- Considering the cost-effectiveness threshold consensus established by the World Health Organization (WHO) based on the per capita GDP ($ 27,229.00 BRL), LMP was highly cost-effective compared with pregabalin and gabapentin for the treatment of PHN in the Brazilian public healthcare system;
- All the results obtained by the sensitivity analysis maintained LMP highly cost-effective compared with pregabalin and gabapentin.

Diabetic Polyneuropathy

- Estimated total costs for LMP, pregabalin and gabapentin were $ 2,092.88 BRL, $ 880.29 BRL, and $ 568.27 BRL, respectively;
- QALYs were 0,422 for LMP, 0,359 for pregabalin, and 0,356 for gabapentin;
- Compared with pregabalin, ICER for LMP was $ 19,244.16 BRL/QALY. Compared with gabapentin, it was $ 23,208.75 BRL/QALY;
- Considering the cost-effectiveness threshold consensus established by WHO based on the per capita GDP ($ 27,229.00 BRL), LMP was highly cost-effective compared with pregabalin and gabapentin for the treatment of DPN in the Brazilian public healthcare system;
- All the results obtained by the sensitivity analysis maintained the LMP highly cost-effective compared with pregabalin and gabapentin.

Table 2. Results

Treatment	Cost per petient	QALY	ICER (cost/QALY)
Post-Herpetic Neuropathy			
LMP	$ 2,088.48 BRL	0,422	
Pregabalin monotherapy	$ 1,212.36 BRL	0,359	$ 19,256.33/QALY
Gabapentin monotherapy	$ 604.42 BRL	0,344	$ 19,102.47/QALY
Diabetic Polyneuropathy			
LMP	$ 2,092.88 BRL	0,422	
Pregabalin monotherapy	$ 880.29 BRL	0,359	$ 19,244.16/QALY
Gabapentin monotherapy	$ 568.27 BRL	0,356	$ 23,208.75/QALY

CONCLUSIONS

- Use of LMP for the treatment of patients with PHN and DPN was considered highly cost-effective, compared with pregabalin and gabapentin, under the perspective of the Brazilian public healthcare system.

Disclaimer

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