A Multicenter, Open-Label, Sequential Study Comparing Preferences for Carbidopa-Levodopa Orally Disintegrating Tablets and Conventional Tablets in Subjects with Parkinson's Disease

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ABSTRACT

Background: Patients with Parkinson's disease (PD) may have difficulty taking their medications for various reasons. In these patients, orally disintegrating tablets (ODTs) can be given without water and may provide greater convenience and ease of use than conventional tablets.

Objective: This study compared preferences for ODTs with those of the conventional tablet formulation of the antiparkinsonism combination drug carbidopa-levodopa (C-L) in subjects with PD.

Methods: Subjects aged ≥18 years with PD controlled using a stable dosage of C-L were enrolled in this multicenter, open-label, sequential study. Subjects received their stable dose of conventional C-L for 7 ± 3 days. They were then switched to the same dose of C-L in the ODT formulation for 14 ± 3 days. During the last 3 days of each treatment period, subjects were to record in a diary their "on" and "off" times (asymptomatic and symptomatic parkinsonism, respectively) and medication use. On the final day of each treatment period, the Unified Parkinson's Disease Rating Scale (UPDRS) was administered to subjects before the first morning dose and then after dosing when they mentioned they were experiencing the "on" state. A Global Preference Questionnaire (GPQ) was completed by subjects at the end of the study. The primary variable was response to all GPQ items. Secondary variables were changes in UPDRS score and mean amount of "off" time per 24 hours. Adverse effects (AEs) also were monitored.

Results: Sixty-one subjects (31 men, 30 women; mean [SD] age, 71.8 [8.3] years; mean body weight, 76.2 kg) participated in the study and were included in the AE assessment; 60 completed the study and were included in the efficacy assessment. Twenty-seven subjects (45%) preferred ODTs compared with 12 (20%) who preferred the conventional tablets ($P < 0.017$). The remaining 21 subjects (35%) had no preference. The attributes of the ODTs that influenced subjects' preference for that formulation included accessibility to medication to treat "off" times (30 [50%]); ease of activities of daily living (28 [47%]); reduced concern about swallowing the medication (27 [45%]); and use for nighttime dosing, ease of compliance with dosing schedule, and feeling less self-conscious about others noticing medication use (each, 25 [42%]) (all, $P < 0.001$). No statistically significant differences in UPDRS scores in the "on" and "off" states were found between the 2 formulations. The incidence of AEs was statistically similar between the 2 formulations.

Conclusions: In this small study of ODT C-L versus conventional C-L tablets in these adult subjects with PD, the results suggest that the ODTs may be of value in certain patients with PD, depending on their personal preferences, disease status, and willingness to alter an aspect of their medication use. For selected patients with PD, the ODT C-L formulation may provide increased convenience, ease of use, and rapid access to medication. (*Clin Ther.* 2005;27:58–63)

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INTRODUCTION

Patients with Parkinson's disease (PD) rely on pharmacologic therapy to maintain or maximize functionality in their activities of daily living (ADLs). Long considered the "gold standard" of therapy, the antiparkinsonism combination drug carbidopa-levodopa (C-L) is the cornerstone of the pharmacologic management of PD. The characteristics of PD and its treatment necessitate that C-L be taken regularly (several times daily in most patients). Nonetheless, Leopold et al[1] reported that nonadherence to the medication schedule in persons with PD may be similar to that in other chronic diseases. Only 10% of subjects in that study had complete adherence (defined by the investigators as no missed, extra, or mistimed doses) to the dosage schedule of one antiparkinsonism drug over a 28-day observation period; 51% missed at least 1 dose per week. In that study, the 2 most common reasons for lack of adherence were forgetting or being too busy to dose (49%) and leaving home without the drug (26%). Nonadherence may lead to inadequate symptom control or the emergence of adverse effects (AEs) that may mistakenly be attributed to an inadequate dosing regimen. Results from other studies have suggested that in addition to efficacy and tolerability, patient preferences and medication convenience (eg, route of administration, dosing schedule, and restrictions such as taking with or without food or specific fluids) contribute to patients' satisfaction with their medication and may influence treatment adherence and thus its success.[2,3]

Patients with PD may benefit from new drug formulations that have been designed to help them overcome some of the difficulties in taking medications and to facilitate medication use. Orally disintegrating tablets* (ODTs) begin to disintegrate within seconds when placed on the tongue, without the need for water. This technology† has the potential to provide patients with greater convenience and faster access to their medications because the need to find water or another fluid is eliminated. Studies of other drugs in the ODT formulation have shown that participants prefer tablets that are convenient, easy to take, and do not interrupt their ADLs.[4–6] ODT and conventional C-L have been shown to be bioequivalent. Thus, ODT C-L offers a therapeutic alternative to the conventional formulation.[7]

The objective of the present study was to identify subject preferences for ODT and conventional C-L tablets.

*Trademark: Parcopa™ (Schwarz Pharma, Inc., Milwaukee, Wisconsin).

†Trademark: RapiTab™ (CIMA Labs., Inc., Eden Prairie, Minnesota).

SUBJECTS AND METHODS

Study Design

This multicenter (7 sites across the United States), open-label trial comprised 2 sequential treatment periods. In the first, baseline treatment with conventional C-L was given; in the second, ODT C-L was given. A sequential design was selected because subjects had to have had PD for at least 1 year and thus been recruited from among subjects already stabilized on conventional C-L tablets, as the ODT formulation had not yet become available. Institutional review board approval of the study protocol was obtained at each site before the trial was initiated.

Inclusion and Exclusion Criteria

Subjects ≥18 years of age with idiopathic PD of at least 1 year's duration were eligible. Each participant had to have been receiving a stable daily dose of ≤200 mg carbidopa and ≤2 g levodopa for at least 30 days. Eligible subjects were able to provide written informed consent and comply with all trial requirements. Eligible female subjects of childbearing potential were to use a reliable form of contraception throughout the trial.

Subjects with a history of chronic substance abuse were ineligible, as were those with a score >50 (severe motor disability) on the Unified Parkinson's Disease Rating Scale (UPDRS) Part III (motor examination).[8] Subjects with a score <22 on the Mini-Mental State Examination[9] (indicating mild to severe cognitive impairment) were excluded, as were those with an abnormal laboratory test result. Subjects who had undergone pallidotomy, deep brain stimulation, and/or fetal tissue transplantation were also ineligible.

Study Protocol

The sequential treatment periods were the baseline conventional treatment phase (7 ± 3 days) and the ODT treatment phase (14 ± 3 days) (**Figure**). After screening at visit 1, eligible subjects were instructed to