Introduction

Parkinson’s disease (PD) is a condition where patients develop motor symptoms such as rigidity, bradykinesia, postural instability and tremor. Non motor symptoms include cognitive decline, dementia, autonomic dysfunction, fluctuation, REM sleep behavior disorder, constipation and decreased olfaction.1. 

Motor symptoms are caused by levodopa, which has a short half-life of about 1.5-2 hours. As levodopa levels decrease, “off” phenomena are experienced and the patient becomes rigid and slow (bradykinesia). If levodopa levels are too high, dyskinesias may develop, dyskinetic patients are restless may show signs of dystonia and may experience weight loss and exhaustion. “Off” periods and dyskinesia’s are called response fluctuations. In early PD response fluctuations are predictable and as levodopa levels increase, advanced PD response fluctuations may become unpredictable.1,2. If taken with protein rich foods, response to levodopa may decrease because of competition of transport of levodopa with neutral amino acids.3.

Therapy with levodopa demands frequent dosing (because of the short half life), avoiding intake with meals and strict dose timing because of response fluctuations.4 In this pilot trial we investigated whether (1) Medication Event Monitoring Systems (MEMS) used could be helpful to increase adherence and to improve the clinical situation of patients with PD. (2) MEMS could be implemented in daily pharmacy practice.

Methods

All registered ambulant levodopa users with PD were invited to have their levodopa use monitored by MEMS. If the patient agreed to monitoring, MEMS readings were performed at 1, 3 and 6 months after inclusion. More frequent readings were allowed if considered necessary by the participating pharmacist. Patients already using dosing aids were excluded from participation. During MEMS reading the pharmacist discussed the data with the patient and asked about response fluctuations, intake during meals and adherence. In this poster three different problems with adherence and clinical situations with PD are discussed.

Results

Sixty two patients were eligible for inclusion, 41 of them used some form of dosing aid or were not ambulant, five refused to participate and 14 were included in the study. During follow up two patients refused the MEMS bottles, because they were too big to carry around (Figure 1). Three different cases will be elaborated on to illustrate the possibilities of MEMS in daily pharmacy practice.

Evaluation after one month reveals the MEMS reading in Figure 2.1. The bottle had been unopened for seventeen days, there were five days with only one opening. Fifteen days of two openings, two days of three and no days of the prescribed four openings. It appeared that an external supply of levodopa was present and after transferring the "secret" supply to the MEMS bottle another reading was done after two months (Figure 2.2). The patient was asked how she thought she had taken her levodopa. She said that she never skipped a dose and also that she was unaware of any effect of the levodopa. After confronting her with the MEMS reading she claimed that the reading must be false.

After asking if the reading could be explained out of pocket dosing she denied doing so. The next question was if the patient could explain the reading in any other way. The patient finally concluded that she must have forgotten although she said she was very consequent in taking her medication. To prevent forgetfulness, the mobile phone of the patient was programmed to give a sound signal at the moment it was time to take her levodopa. After three months, another MEMS reading was done as depicted in Figure 2.3.

The levedopa dose was changes to 3 times a day 125 mg levodopa / carbidopa, which was easier for the patient to fit into her daily schedule. And the reading after another month shows the following (Figure 2.4). Adherence has increased another 15% to 82%.

Patient 2, a seventy year old man, with a high education and advanced PD presented himself with irregular movements and a dystonic thumb during the invitation at the pharmacy. He had difficulties sitting still on his chair and made choreiform movements. His levodopa / carbidopa schedule consisted of levodopa/carbidopa 100/25 mg four times a day and one additional dose if needed, when he used to conduct a choir (once a week) and levodopa/carbidopa/entacapone 75/18.5/200 mg four times a day. The MEMS reading after one month is shown in Figure 3. An additional levodopa/ carbidopa 100/25 mg was taken on at least 31 occasions. The period without intake corresponds to four days in which the patient forgot the MEMS bottle at his brother’s place and left it there.

The additional levodopa intake could explain why the patient was dyskinetic. Further evaluation of the patient revealed weight loss of a few kilograms in the last few months for which he needed high caloric special food (Fresubin, Kabi, the Netherlands). The MEMS reading was sent to his neurologist and the levodopa/ carbidopa/entacapone was discontinued and the patient was referred to a specialized clinic for PD for a second opinion. Amantadin 100 mg, 2-3 times a day was added and the dyskinetic status dramatically improved.

Patient 3, a 89 year old male patient used to take levodopa/carbidopa 200/50 mg four times a day, because to sleepiness his dosage was reduced to 3 times a day 200/50 mg levodopa/carbidopa. His MEMS reading is shown in Figure 4. A perfect adherence is shown, but the clinical situation is far from perfect. The patient takes his levodopa at 8:00, 12:00 and 19:00 hour, mostly during meals. Further investigation into his nocturnal whereabouts reveals that he has to go to the bathroom at 5:00 am to urinate, but has terrible problems reaching the bathroom, due to stiffness and bradykinesia.

The patient is instructed to take levodopa/carbidopa tablets at least half an hour before meals, to avoid lack of effect because of competition with neutral amino acid for the transporter protein in the intestine and blood brain barrier. To prevent night time problems due to wearing off of the levodopa we advised the neurologist to add slow release levodopa/carbidopa 250/50 at 11:00 pm. Slow release of levodopa would prevent any peak dosing and this would prevent sudden onset of sleepiness. The patient reported that his clinical situation improved very much.

Discussion and Conclusion

We observed different forms of adherence when introducing MEMS in patients with PD in daily pharmacy practice. We were able to improve medication adherence in patient 1, we detected “too much” adherence in patient 2 and we observed perfect adherence in patient 3. In all situations however the clinical situation was not satisfactory for the patient. With the help of MEMS we were able to identify causes that could explain the clinical situation of the patient and improve it. In this pilot study we observed many patients with PD were already using dosing aids, which excluded about 75% of the eligible patients, however, we were able to improve the clinical situation in those patients that were included in the study. Improvement of symptoms in patients with PD when using MEMS is an easy and straightforward method which needs further investigation in a larger setting.

References


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