Introduction

In traditional Ayurvedic Indian medicine, preparations of Mucuna pruriens seeds (Fig. 1) are used in the treatment of Parkinson’s disease (PD). It has been suggested that Mucuna preparations may possess some clinical advantages over conventional, synthetic L-DOPA/carbiparbiprole preparations, including a rapid onset of action and longer on time without consequent increase in akinesias (Katzenschlager et al. 2004, Wierup et al. 2002, Lieu et al. 2010). Alcoholic extracts of MP seeds are rich in L-DOPA, but other, as yet unknown compounds may contribute to its therapeutic effects.

Objectives

In 6-hydroxydopamine (6-OHDA) lesioned rats we determined:

1. Therapeutic effective doses of a methanol extract of Mucuna pruriens seeds and of (synthetic) L-DOPA treatments without additives.
2. Abnormal involuntary movements (AIM) during chronic treatment at therapeutically effective doses.
3. Dose-dependent effects of Mucuna extract and L-DOPA in the presence of benserazide (peripheral decarboxylase inhibitor).
4. Effects of a Mucuna preparation lacking L-DOPA.

Materials and Methods

Twenty-four 6-hydroxydopamine (6-OHDA)-lesioned rats were used (Sprague Dawley, males; 8 µg 6-OHDA free base in 2 µl saline, 0.1% ascorbic acid and 0.5% ascorbic acid in saline). All lesions were confirmed by HPLC with electrochemical detection (Lundblad et al. 2002).

Materials and Methods

Therapeutic effective doses of a methanol extract of Mucuna pruriens seeds and (synthetic) L-DOPA treatments were assessed using the pristane test, recorded on video and rated on a scale from 0 (Lundblad et al. 2002).

Mucuna extracts containing ca. 20% L-DOPA (dry weight extract) were prepared and the chemical profiles of different batches were assessed by HPLC and mass spectrometry to ensure reproducibility quality. A Mucuna extract lacking the major constituent L-DOPA was prepared by preparative HPLC.

Mucuna or L-DOPA preparations were solubilized in saline, 1% ascorbic acid and administered i.p. in a volume of 12.5 mg/kg. Mucuna was prepared at a dose of 10 mg/kg. Rats were killed and brains dissected one week after the last Mucuna or L-DOPA injection. Dopamine and 5-hydroxytryptamine (5-HT) levels in ipsilateral and contralateral striatum were determined by HPLC with electrochemical detection (Gramsbergen et al. 2003).

Results

Therapeutic effective doses of a methanol extract of Mucuna pruriens seeds without or with L-DOPA were assessed using the pristane test, recorded on video and rated on a scale from 0 (Lundblad et al. 2002).

Conclusions

- Chronic Mucuna treatments induced a sustained motor improvement that took days to build up and lasted for 3-4 days after cessation of treatment, i.e. similar to the long duration response of L-DOPA treatment. Determination of the lowest, therapeutically effective doses required therefore repeated dosing.
- Mucuna extract was more effective than (synthetic) L-DOPA at equivalent L-DOPA doses of 12.5-25 mg/kg ip.
- However, chronic treatment with these doses of Mucuna extract caused also more severe AIBs (predominantly ipsilateral, but also axial and orofacial dyskinesias) than L-DOPA alone.
- Co-treatments with benserazide in Mucuna or L-DOPA-sensitized rats, did not reveal differences in therapeutic or adverse effects of Mucuna or L-DOPA.
- Mucuna extract lacking L-DOPA did not show any therapeutic effect.

This study in 6-OHDA lesioned rats did not reveal clinical benefits of Mucuna treatment over conventional L-DOPA therapy.

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Dose- and time-dependent therapeutic and adverse effects of Mucuna pruriens extract in the 6-OHDA rat model of Parkinson’s disease

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References


