Movement Disorders
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DA Agonists - Non-Ergot derivatives: Piribedil

BASIC PHARMACOLOGY

MECHANISM OF ACTION

Piribedil is a non-ergot derivative D2/D-3 agonist[1] with alpha-2 antagonistic effects[2]. Piribedil is effective in reversing parkinsonian symptoms in the MPTP-treated primate[3]. The clinical effects of piribedil cause lower prolactin plasma levels and blood pressure, and induces nausea. There is also some evidence that piribedil has neuroprotective effects in experimental models[4].

PHARMACOKINETICS

Piribedil is administered orally, Tmax is reached within 1 hour, and it has a relatively long plasma elimination half-life (20 hours). Piribedil solubility allows it to be used intravenously for experimental purposes or acute challenge tests.

REVIEW OF CLINICAL STUDIES

PREVENTION OF DISEASE PROGRESSION

No qualified Level-I studies were identified.

SYMPTOMATIC CONTROL OF PARKINSONISM

MONOTHERAPY

No Level-I clinical trial was identified, as based on the predefined inclusion criteria. There is a large randomized placebo-controlled study presently on-going. However, at the moment, only one uncontrolled, Level-III trial was identified[5]. It will briefly be reviewed here in the absence of other available published evidence.

Rondot et al. (1992)[5]: This is an open-label, 3-month study assessing the efficacy of piribedil in 113 de novo patients with PD. The Webster scale was used to assess efficacy. Twenty-tree patients dropped-out prematurely, and analysis was performed in the 90 patients who completed the study. In these patients, piribedil, at a mean dose of 207 mg/d, improved the Webster scale by 41% ($p<0.001$). Adverse reactions were consistent with those of any D2 agonist (eg. digestive, cardiovascular, psychiatric).

ADJUNCT THERAPY

No qualified studies were identified. The publication of a recently conducted randomized placebo-controlled study in stable levodopa-treated PD patients is expected.

PREVENTION OF MOTOR COMPLICATIONS

No qualified studies were identified. There is an on-going 2-year levodopa-controlled extension of the placebo-controlled study mentioned in the section on Control of Parkinsonism as Monotherapy.

CONTROL OF MOTOR COMPLICATIONS

No qualified studies were identified.

REVIEW OF SAFETY

Based on the limited amount of available data and its long use in clinical practice in several countries, it appears that adverse reactions associated with piribedil are similar to other dopamine agonists in this class of drug including gastrointestinal cardiovascular and neuropsychiatric events. One case report of possible "sleep attacks" in a patient on piribedil has recently been reported.[6]

CONCLUSIONS

EFFICACY, SAFETY AND IMPLICATIONS FOR CLINICAL PRACTICE

According to the paucity of Level-I data and the lack of studies published that met inclusion criteria, there is INSUFFICIENT EVIDENCE to conclude about the efficacy, safety and implications for clinical practice of piribedil. Level-I studies are ongoing, and future recommendations will be based on these forthcoming reports.

IMPLICATIONS FOR CLINICAL RESEARCH

- There is a clear need to conduct modern, randomized, controlled, well-designed trials to assess the benefit/risk ratio of piribedil in the treatment of PD.
- Pharmacoeconomic studies are needed to compare the cost benefits of piribedil to other treatments in this class of drug and also to other medications used to treat PD.
- Studies that specifically assess the impact of piribedil on quality of life and the effect on mortality are also needed.

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