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Review

Systematic review on factors associated with medication non-adherence in Parkinson's disease

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ABSTRACT

Background: Medication non-adherence is prevalent in Parkinson's disease (PD) and results in substantial motor dysfunction. Although various approaches have been suggested to address non-adherence in PD, good quality evidence of associated factors is limited.
Objective: To systematically review the literature on clinical and demographic factors associated with medication non-adherence in PD.
Methods: We searched five online databases in April 2011 (updated in January 2012): MEDLINE, EMBASE, AMED, PsycINFO and CINAHL for studies reporting data on factors associated with medication non-adherence in people with idiopathic PD. Bibliographies were hand searched to acquire records not identified electronically. Two reviewers independently assessed identified articles for potential inclusion. Data extraction was undertaken using a standardised data extraction form. Methodological quality was assessed against a specially designed quality indicator tool emphasising the detection of threats to internal validity.
Results: We identified 1880 records of which six met inclusion criteria. A total of 772 PD patients were included (mean age 62 years, males 61%). We identified eleven factors (six clinical and five demographic) associated with non-adherence. We ranked each factor in order by weight of overall evidence: mood disorders, cognition, poor symptom control/QoL, younger age/longer disease duration, regimen complexity/polypharmacy, risk taking behaviours, poor knowledge of PD/education, lack of spouse/partner, low income, maintaining employment and gender.
Conclusion: Clinicians should be aware of factors associated with medication non-adherence in PD. Targeted interventions should be developed and investigated to establish if addressing factors associated with non-adherence in PD leads to greater medication adherence.

Contents

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1. Introduction

Parkinson's disease (PD) is a disabling condition which substantially reduces quality of life (QoL) [1]. Levodopa remains the most efficacious treatment by replenishing dopaminergic tone in the nigrostriatal pathway; the use of which is associated with increased QoL and life expectancy [2]. Although monotherapy represents usual early phase management, more than half of PD patients take two-to-four anti-parkinsonian medications three-to-four times daily [3]. Drugs may require differing dosage schedules or escalation/manipulation adding considerable complexity. To maintain treatment effect in advanced PD more frequent and intricate titrations are required to maximise '*On*' time [4]. Advanced PD patients may be taking up to ten daily doses to manage fluctuations [5].

To achieve symptom control adherence is imperative. However, up to half of all medications administered for long-term conditions are not taken as prescribed [6]. Therefore, not surprisingly, adherence is suboptimal in PD, especially in light of complexity and strict timing of doses. As few as 10% of people with PD fully adhere to drug regimens as intended [7]. A longitudinal study showed poor adherence to range between 60 and 70% over a 5 year period [8]. In people requiring multiple doses, complete adherence was reported as low as 3% [9]. Non-adherence is associated with wearing off of the treatment effect leading to substantial motor fluctuations and increased risk of worsening symptoms compared to medication adherent individuals [8]. Hence, medication non-adherence in PD is a serious problem. As PD treatments are mostly self-administered, the need is apparent for greater understanding and management of non-adherence.

Although pharmacological (simplifying drug regimens) and non-pharmacological (educational) approaches have been suggested to address adherence issues in PD [10], these are largely theoretical as it remains unclear which demographical and clinical factors, and to what extent, are associated with non-adherence in PD. The illumination of associated factors could allow healthcare professionals to identify potentially non-adherent individuals and facilitate the development of targeted interventions.

2. Methods

We systematically reviewed studies investigating factors associated with medication non-adherence in PD.

2.1. Search methods

1. Five online databases were systematically searched in April 2011 (updated January 2012): Medline Ovid (1948), EMBASE (1980), AMED (1985), PsycINFO (1806) and CINAHL (1982). The terms 'Parkinson's disease' and 'Parkinsonism' were combined with 'non-adherence', 'non-compliance', 'influencing factors', 'caregiver compliance', 'suboptimal', 'determinants', 'drug adherence', 'therapy adherence', 'drug compliance', 'denial psychology' and 'therapy compliance'. Key terms were mapped to database specific subject headings (MeSH) and exploded to include all sub-categories. Truncations and wild cards were used to broaden the search window. Exact search strings are available on request.
2. A supplementary hand search of bibliographies of extracted articles was conducted.

2.2. Selection criteria

Titles and abstracts were reviewed for potential inclusion. Full-articles were obtained where abstracts appeared relevant. Studies meeting specific criteria were included:

(1) English language
(2) Full-article publication
(3) Idiopathic PD population (defined by the authors).
(4) All age ranges and duration of anti-parkinsonian treatments.
(5) Presented quantitative/qualitative data on factors associated with medication non-adherence.

2.3. Data extraction

DJD and KHOD independently reviewed articles for potential inclusion using a standardised data extraction table (Appendix 1). Extracted data was checked for accuracy with a focus on study design, methodological characteristics, participants and analytical methods (Appendix 2).

2.4. Quality assessment

We systematically reviewed existing quality indicator tools. Many replicated reporting guidelines such as STROBE [11] and MOOSE [12] which were not developed for assessing methodological rigour. We therefore designed a novel '*generic use*' quality tool to facilitate the systematic detection of threats to internal validity in non-interventional studies (Table 1). Quality was assessed independently by DJD and KHOD using our customised quality indicator to minimise bias. With this we created a '*Threats to Validity*' table highlighting the methodological performance of each study (Table 2).

3. Results

Database searches yielded 1880 records. Six additional records were identified through hand searching. Fig. 1 shows the PRISMA diagram depicting each stage of study identification. After reviewing