

Early morning off periods in Parkinson's disease: Characterisation of non motor patterns and treatment effect. An international study.

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OBJECTIVE:

To characterise range and nature of non-motor aspects of early morning off periods (EMO) in a consecutive series of patients with Parkinson's disease (PD) across all stages.

METHODS:

In this ongoing European observational study

- PD patients on dopaminergic treatment were identified.
- EMO was identified by a structured questionnaire, including UPDRS item 35 and PDSS item 14.
- Non-motor symptoms (NMS) associated with identified EMOs were retrospectively assessed by application of NMS questionnaire.
- EMOs were classified to motor and mixed (motor+ non motor).
- NMS related to EMO were compared to pattern of general NMS in all patients.
- Patterns of dopaminergic treatments and presence of EMO was noted and compared, specifically use of prolonged release dopamine agonists (PR DA, incl. RTG patch) vs. Levodopa

BACKGROUND:

Non-motor Fluctuations

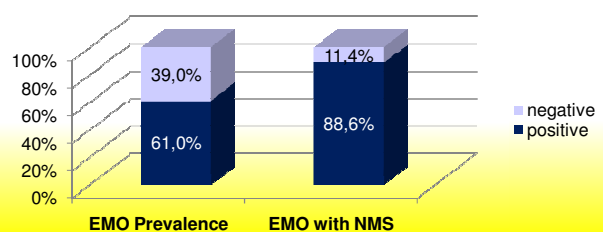
- are common and disabling.
- can be assessed by Wearing-off Questionnaire (WOQ).^{1,2}
- frequently described symptoms are anxiety (66%), drenching sweats (64%), slowness of thinking (58%), fatigue (56%) and akathisia (54%).³

Early morning off periods (EMO)

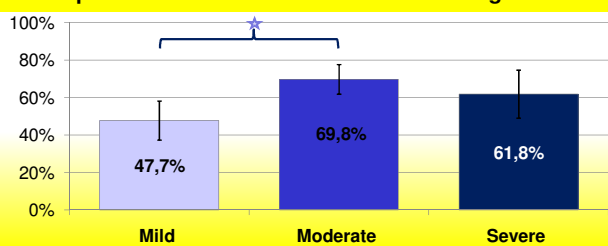
- are thought to be common in Parkinson's disease (PD) but the exact prevalence is unknown.
- clinical characteristics and non-motor associations or treatment effect have not been specifically studied.
- possibly motor and non-motor (sleep dysfunction related) subtypes can be identified by PD Sleep Scale PDSS.⁴

Demographics	Mean/ No	Median/ Range/ %
Patients	272	
Males	176	64.7%
Females	96	35.3%
Age (yrs)	69.4	42 – 89
H&Y stage	2.7	3.0 ± 2.0
Duration of Disease (yrs)	6.9	0 – 24

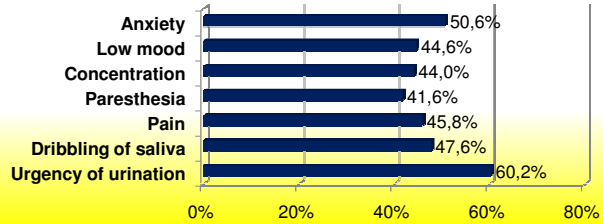
Graph 1: Prevalence of EMO with and without NMS



Graph 2: Prevalence of EMO in different stages of PD



Graph 3: Most frequent NMS during EMO



RESULTS 1:

- A consecutive series of 272 patients with treated PD (42-89 yrs) have been assessed so far (table 1).
- EMO being present in 61.0% (55.7% of males, 70.8% of females) with most (88.6%) being mixed in character (motor (M-EMO) and non-motor (NM-EMO)) while only 11.4% are pure motor in type (graph 1).
- M-EMO and NM-EMO were prevalent in mild (H&Y stages 1-2), moderate (H&Y 2.5-3) and in severe disease (H&Y 4-5) with a greater representation in moderate disease (p=0.0011 chi² test, graph 2).

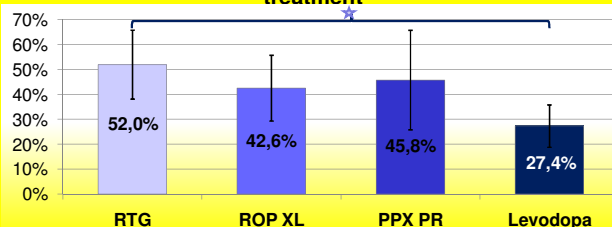
RESULTS 2:

- Most prevalent NMS in EMO were anxiety, low mood and concentration problems, pain and paresthesia, dribbling of saliva and urgency (graph 3).
- In some patients NMS like urgency, pain, anxiety, dribbling, dizziness or problems with concentration occur during EMO, but not throughout the day.
- When comparing patterns of dopaminergic therapy, addition of PR DA's appears to result in significantly less EMOs compared to levodopa therapy alone, RTG treated cohort reporting the lowest rate of EMO (p=0.0026 chi² test, graph 4).

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Graph 4: Patients without EMO under dopaminergic treatment



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CONCLUSIONS: Early morning off periods are frequent across all stages of PD and are often associated with a number of non motor symptoms. Recognition is important, as these NMS may be treatable e. g. by adding prolonged release dopamine agonists.