Prolonged release dopamine agonists in clinical practice: a comparative European multicentre survey of tolerability rates and impulse control behaviour trends in young and old PD.

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OBJECTIVES:
- To address comparative tolerability/retention rates (minimum 6 months use) of oral prolonged release (PR) dopamine agonists (DAs) and rotigotine skin patch (RTG) in an European real life population base in young (<75 yrs) and old (≥75 yrs) PD.
- To compare impulse control disease/behaviour (ICD) rates in cases with active DA intake, to dissociate ICD leading to discontinuation and managed by optimising DA therapy.

BACKGROUND:
- Comparative tolerability/retention rate of prolonged release DAs are unknown in patients over 75 years of age.
- Tolerability can be classified as suggested by Shulman et al.2
- ICDs are thought to be related to the use of immediate release DAs in PD (17.1% in DOMINION2).

METHODS:
- Retrospective/prospective clinic interview and case note survey (audit based questionnaire as per Appiah-Kubi et al.1).
- 373 cases initiated on DA were included: RTG used in 152 (mean dose 8.6 mg), ROP X L in 120 (12.6 mg), PPX PR in 64 (2.8 mg).

RESULTS TOLERABILITY:
- 110 of 134 assessable patients (82.1%) on RTG tolerated the drug, 119/130 (91.5%) tolerated ROP XL and 53/57 tolerated PPX PR (93.0%).
- No significant differences of tolerability rates were observed between the age groups or the different PR DAs (p>0.09, chi² test, graph 1).
- 37 of the 373 evaluated cases (9.9%) report treatment with dual agonists (mostly oral with patch).
- 38/1148 assessed patients (33.7%) suffered from swallowing difficulties, 81.0% of which tolerated transdermal patch therapy.

Table 1: DEMOGRAPHICS

<table>
<thead>
<tr>
<th>All cases</th>
<th>ICD cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Mean/±% (Distr./ Range)</td>
</tr>
<tr>
<td>No</td>
<td>Mean/±% (Distr./ Range)</td>
</tr>
<tr>
<td>Patients (Male: Female)</td>
<td>373 (225M: 148F)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>68.4</td>
</tr>
<tr>
<td>Age of PD onset (yrs)</td>
<td>60.6</td>
</tr>
<tr>
<td>Age of PD onset &lt;50 Patients (Male: Female)</td>
<td>61/ 16.4% (48M: 15F)</td>
</tr>
<tr>
<td>Duration of Disease (yrs)</td>
<td>7.7</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr Stage</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Graph 1: Primary tolerability in young and old patients

Results ICD:
- 52 cases (13.9%) reported impulse control disorders (ICD), of which 48 were exposed to oral DA.
- 22 of 52 ICD with RTG, as well as with PPX PR was significantly lower (<0.001, binomial probability test) than ICD rate with ROP XL, or with pooled ROP data (long acting -short acting) or pooled PPX (graph 2). No significant difference between RTG and PPX PR was observed.
- Discontinuation due to ICD was reported in 44.2% (23/52) of all ICD cases. This reflects 2.0% (3/152) of all cases treated with RTG, 5.3% (8/150) of ROP XL and 3.1% (2/64) of PPX PR.
- 6 cases with ICD on PPX /ROP reported attenuation of ICD when started on RTG patch.

Graph 2: ICD rates on different DAs

REFERENCEs:
3 Weintraub et al., Arch Neurul 2010; 67(5): 589-595

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Academic grant from PDNMG and support by EPDA, Parkinson’s UK and all members of EUROPAR

CONCLUSIONS: This ongoing survey reveals
- Prolonged release DAs are well tolerated in younger (<75yrs) and older (≥75yrs).
- ICD rates are variable and RTG patch as well as PPX PR appears to have a significantly lower rate compared to other short acting or long acting DAs. The reason for this is unclear.
- In some, reversal of ICD is reported after switching to RTG.
- Our survey shows rates of swallowing difficulties similar to other published studies and in this group use of RTG patch is particularly useful.
- Contrary to common belief, somnolence and hallucinations rates are low with all observed PR DA.