LEVODOPA/CARBIDOPA INTESTINAL GEL, SUBTHALAMIC DEEP BRAIN STIMULATION, BEST MEDICAL TREATMENT: A DIFFERENT LONG-TERM OUTCOME?

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OBJECTIVES

To retrospectively analyze the 5-years follow-up clinical, neuropsychological and safety data of three groups of subjects (36 patients), who opted for a treatment with STN-DBS, Levodopa/Carbidopa intestinal gel infusion (LCIG) or oral medical treatment (OMT) after a former CAPSIT-PD surgical selection.

BACKGROUND

LCIG and STN-DBS are two of the most effective therapies for advanced Parkinson's disease (PD) [1, 2]. Although based on different mechanisms of action, both therapeutic options demonstrated a significant improvement of motor complications compared to oral medical therapy (OMT). From a clinical point of view, both STN-DBS and LCIG demonstrated a long-lasting improvement in the Activities of Daily Living (ADL). Considering the incidence of side effects, the two therapies display a different profile, with rare but serious adverse events in STN-DBS, as brain hemorrhages and central nervous system infections, and more frequent but usually less severe complications with LCIG, as accidental removal, obstruction or dislocation of the percutaneous enteral gastrostomy (PEG) tube. To date, no long-term comparative study between the two therapeutic options and OMT is currently available, and comparisons between different profiles of therapeutic efficacy and complications can only be speculative,

MATERIALS AND METHODS

Thirty-six patients (12 STN-DBS, 12 LCIG and 12 OMT) with comparable demographic, clinical and neuropsychological characteristics were evaluated at baseline and after an average follow-up period of 5 years, by means of UPDRS subscores and a standardized battery of cognitive tests. Moreover, a complete list of side effects and complications was collected.

RESULTS

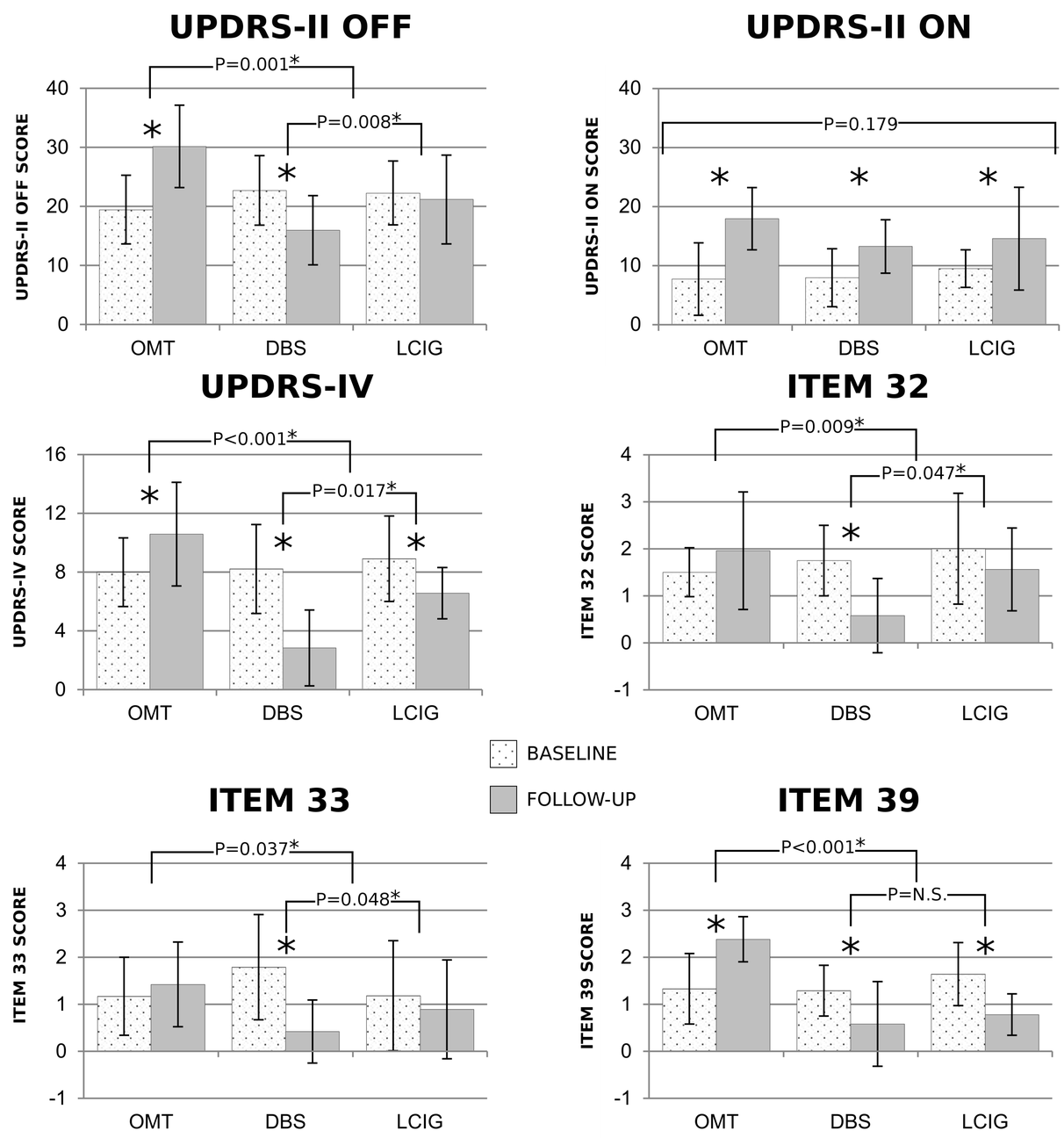
a) Motor symptoms showed a similar worsening both in "Med-OFF" and "ON" conditions in all groups (UPDRS-III score +30.5% and +28.2% for OMT, +23.0% and +21.1% for STN-DBS, +27.2% and +22.1% for LCIG; $p<0.05$).

b) Activities of daily living (Fig) (UPDRS-II) in "Med-ON" gradually worsened during follow-up in all groups. UPDRS-II in OFF condition showed a different trend among groups (p:0.001), with a significant improvement only in STN-DBS patients (-29.7%)_

c) Motor fluctuations (Fig) (UPDRS-IV) significantly improved both in STN-DBS (-65.5%) and LCIG (-26.4%), while OT patients reported a progressive worsening (+32.4%). The percentage of waking day spent in OFF (Item 39) improved both in STN-DBS (-55%) and LCIG (-52.3%), while OT patients showed a moderate worsening (+79%). On the contrary, a significant amelioration of the duration and severity of dyskinesias (Items 32 and 33) was reported only by STN-DBS subjects (-66.9% and -76.5%; $p<0.01$).

d) Neuropsychological outcomes showed similar trends in all groups, even if only STN-DBS and LCIG patients experienced a worsening of spatial span short-term memory and semantic verbal fluency; STN-DBS showed also a worsening of phonemic verbal fluency.

e) Adverse events and complications rate was higher in LCIG gruop, mainly related to PEG tube and pump disfunctions (annualized complications rates: 0.82 for LCIG, 0.23 for STN-DBS and 0.16 for OMT, without considering the scheduled "maintenance" procedures); one perioperative "procedure-related" complication was observed for both STN-DBS and LCIG.



UPDRS- II and –IV variations during follow-up

CONCLUSIONS

STN-DBS and LCIG demonstrated a long-lasting superior clinical efficacy on motor fluctuations, lessening the severity of ADL impairment associated to the advanced PD phases. Moreover, STN-DBS seems to ensure a better control of duration and severity of dyskinesias. On the contrary, no significant differences were observed in the motor symptoms control, according to a progressive increase of poorly levodopa-responsive axial and bradykinesia symptoms. Finally, LCIG was associated with a higher rate of "treatment-related" adverse events and "maintenance" procedures, even though some of them had minor clinical consequences. Taken together, these data suggest that the appropriate choice between advanced therapeutic options or optimized OMT may represent a clinical challenge in advanced PD, and that advanced surgical options should be proposed only after an accurate case-by-case clinical selection

REFERENCES

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