Evaluating the DICE method to improve early recognition and treatment of neuropsychiatric symptoms in early Alzheimer’s disease

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Abstract

Background: While neuropsychiatric symptoms (NPS) are common in early Alzheimer’s disease (AD), they are currently underdiagnosed and undertreated in the memory clinic. Therefore, we evaluated the effectiveness of the Describe, Investigate, Create, Evaluate (DICE™) approach to structure and standardize the care for NPS in AD in the memory clinic.

Method: A total of 60 community-dwelling patients with MCI, AD dementia, or AD/VaD dementia were enrolled with their caregivers in two waves (Table-1). The first wave (n = 36) received care as usual and served as a control group, while the second wave of patients (n = 24, of which n = 20 have currently completed the study) underwent the DICE method. We applied the DICE method during two visits in which NPS were assessed, underlying causes were examined, and patients and caregivers were instructed on management strategies to deal with NPS, which were evaluated after one month. Outcomes were assessed after three and six months. Primary outcomes were quality of life of patients (QoL-AD) and caregivers (Carerqol-7D). Secondary outcomes included caregiver burden (Perseverance time), NPS prevalence and severity (NPI-Q & BEHAVE-AD), NPS-related distress (NPI-Q), competence managing NPS (additional NPI-Q item), and psychotropic drug use. We used linear mixed models to examine differences in outcomes at group-level and reliable change index to examine which participants in the intervention group showed reliable improvement in the primary outcomes.

Result: We found no significant differences between the two groups in change in quality of life or any of the secondary outcomes (all p>0.05, Table-2). A proportion of the intervention group showed reliable improvement in quality of life of patients (n = 6/20) and caregivers (n = 7/20). At baseline, these patients tended to show higher NPS...
burden and their caregivers reported more NPS-related distress and lower feelings of competence while managing NPS compared to participants that did no show reliable improvement.

**Conclusion:** This Stage 2 efficacy study shows no benefits of the DICE method on in early AD at group-level, but suggest that particular participants might benefit from this approach. Data will be re-analyzed when all intervention group participants have completed the study and will be extended with qualitative data investigating NPS-related knowledge and management styles of participants.
Table 1. Clinical and demographic characteristics at baseline according to group.

<table>
<thead>
<tr>
<th>Characteristics patients</th>
<th>Control group (n=36)</th>
<th>Intervention group (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>73.1 (7.7)</td>
<td>72.5 (6.9)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>16 (44.4%)</td>
<td>12 (50.0%)</td>
</tr>
<tr>
<td>Education, median (IQR)</td>
<td>4.5 (1.0)</td>
<td>5.0 (1.0)</td>
</tr>
<tr>
<td>Clinical diagnosis, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCI</td>
<td>9 (25.0%)</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td>AD dementia</td>
<td>24 (66.7%)</td>
<td>22 (91.7%)</td>
</tr>
<tr>
<td>Mixed AD dementia/VaD</td>
<td>3 (8.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Months after diagnosis, mean (SD)</td>
<td>3.7 (5.4)</td>
<td>2.5 (3.5)</td>
</tr>
<tr>
<td>CDR score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 (very mild)</td>
<td>17 (47.2%)</td>
<td>7 (29.2%)</td>
</tr>
<tr>
<td>1 (mild)</td>
<td>16 (44.4%)</td>
<td>15 (62.5%)</td>
</tr>
<tr>
<td>≥2 (moderate to severe)</td>
<td>3 (8.3%)</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td>AD-biomarker signature, N (%)</td>
<td>8 (22.2%)</td>
<td>9 (37.5%)</td>
</tr>
<tr>
<td>MMSE score, mean (SD)</td>
<td>23.8 (3.8)</td>
<td>23.5 (3.9)</td>
</tr>
<tr>
<td>NPI-Q total score, mean (SD)</td>
<td>16.6 (12.7)</td>
<td>18.0 (17.6)</td>
</tr>
<tr>
<td>No. NPS on NPI-Q, mean (SD)</td>
<td>4.5 (2.2)</td>
<td>4.0 (2.9)</td>
</tr>
<tr>
<td>AD drugs, N (%)</td>
<td>19 (47.8%)</td>
<td>11 (45.8%)</td>
</tr>
<tr>
<td>Psychotropic drugs, N (%)</td>
<td>6 (16.7%)</td>
<td>5 (20.8%)</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>5 (13.9%)</td>
<td>5 (20.8%)</td>
</tr>
<tr>
<td>Sedative-hypnotic</td>
<td>1 (2.8%)</td>
<td>1 (4.2%)</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Mood stabilizer</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

| Characteristics caregivers                |                      |                           |
| Age, mean (SD)                            | 65.9 (11.0)          | 64.9 (13.0)               |
| Female, N (%)                             | 26 (72.2%)           | 14 (58.3%)                |
| Education, median (IQR)                   | 5.0 (1.0)            | 5.0 (1.0)                 |
| Relationship to patient, N (%)            |                      |                           |
| Spouse or partner                         | 28 (77.8%)           | 19 (79.2%)                |
| Child                                     | 8 (22.2%)            | 5 (20.8%)                 |
| Lives together with patient, N (%)        | 27 (75.0%)           | 19 (79.2%)                |

Notes.
* Dutch education system categorized into levels ranging from 1 = less than six years of primary education to 7 = academic degree.
* established based on either CSF analysis (Aβ42 < 550pf/mL or tau/Aβ42 ratio > 0.52) or PiB-PET.
AD = Alzheimer’s disease, CDR = Clinical Dementia Rating scale, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, NPI-Q = Neuropsychiatric Inventory Questionnaire, NPS = neuropsychiatric symptoms, VaD = vascular dementia.
* p < 0.05 difference between control group and intervention group.
Table 2: Effects of DICE method compared to care as usual on longitudinal outcomes.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Outcome</th>
<th>Standardized β [95% CI]</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QoL-AD self-report</td>
<td>QoL patient</td>
<td>0.12 [-0.06, 0.30]</td>
<td>0.30</td>
</tr>
<tr>
<td>QoL-AD proxy</td>
<td>QoL patient</td>
<td>0.01 [-0.14, 0.16]</td>
<td>0.89</td>
</tr>
<tr>
<td>Careqol TDI total score</td>
<td>QoL caregiver</td>
<td>-0.01 [-0.17, 0.15]</td>
<td>0.92</td>
</tr>
<tr>
<td>Careqol TDI VAS scale</td>
<td>QoL caregiver</td>
<td>0.14 [-0.03, 0.32]</td>
<td>0.11</td>
</tr>
<tr>
<td>Pervasive anxiety</td>
<td>Caregiver burden</td>
<td>-0.20 [-1.23, 0.83]</td>
<td>0.69</td>
</tr>
<tr>
<td>BEHAVE-AD total score</td>
<td>NPS general interview</td>
<td>0.00 [-0.15, 0.15]</td>
<td>0.99</td>
</tr>
<tr>
<td>NPI-Q total score</td>
<td>NPS general questionnaire</td>
<td>0.08 [-0.11, 0.27]</td>
<td>0.42</td>
</tr>
<tr>
<td>NPI-Q average distress</td>
<td>NPS-related distress</td>
<td>-0.04 [-0.28, 0.21]</td>
<td>0.78</td>
</tr>
<tr>
<td>NPI-Q average competence</td>
<td>Competence while managing NPS</td>
<td>0.13 [-0.16, 0.41]</td>
<td>0.34</td>
</tr>
<tr>
<td>Psychotropic drug use</td>
<td>Use of any psychotropic drugs</td>
<td>-0.03 [-0.35, 0.29]</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Note: Data presented are standardized β for interaction between Group (1 = intervention group, 0 = control group) and Time (baseline, 3 months follow-up, 6 months follow-up) derived from uncorrected linear mixed models including random intercepts.

BEHAVE-AD = behavioral pathology in Alzheimer’s disease, NPI-Q = Neuropsychiatric Inventory Questionnaire, NPS = neuropsychiatric symptoms, QoL = quality of life, QoL-AD = quality of life in Alzheimer’s disease.