Supplemental Appendix e-1.

Efficacy of THC in the treatment of pain in dementia patients with NPS.

Methods: The efficacy on pain-related behavior and pain intensity was evaluated in a subgroup of patients suffering from NPS as well as pain. This subgroup was defined as follows: 1) patients with persistent pain complaints, who could indicate their own pain intensity reliably, as judged by a research physician, or 2) patients with score of four points or more at baseline on the Pain Assessment Checklist for Seniors with Limited Ability to Communicate, Dutch version (PACSLAC-D). The PACSLAC-D[1] is an observational assessment scale for assessment of pain in non-communicative persons and was used in this study to assess pain-related behaviour at baseline and after 21 days of treatment. Pain intensity was assessed by self-report, using the Verbal Rating Scale (VRS).[2] This is a six-point scale ranging from 'no pain' to 'worst imaginable pain'. VRS assessments were done at every visit by means of an interview with the participant, and on a daily basis using a diary. Efficacy of THC on pain reduction was evaluated in a Linear Mixed Model with participants as random factor and baseline scores as fixed factor. VRS diary scores were not analyzed, as these assessments did not appear to be feasible in this patient group because of their cognitive decline, and resulted in too few available and reliable scores. Pearson correlation coefficients were calculated for change from baseline for PACSLAC-D and VRS interview scores, NPI and PACSLAC-D at day 21, NPI and VRS interview at day 21

Results: In total, 23 patients were included in the subgroup 'pain'. Within this group, more patients received placebo than THC (15 vs. 8 patients).

PACSLAC-D scores were available for 20 patients (THC, n=7; Placebo, n=13), while 13 patients completed the VRS interview assessments (THC, n=4; Placebo, n=9). No treatment differences between THC and placebo were observed on PACSLAC-D (-1.1, 95%CI -6.0 to 3.8) or VRS (-0.03, 95%CI -0.95 to 0.90) (Table e-2). Overall, there is an indication that a reduction in PACSLAC-D score is positively correlated with VRS interview score (Pearson's r 0.35, p=0.06). No correlation was found between PACSLAC-D and NPI total score (Pearson's r 0.21, p=0.21) nor between VRS interview and NPI total score (Pearson's r 0.16, p=0.36).

Discussion: Low dose of THC did not result in benefit on pain-related behavior and pain intensity, compared to placebo. Our ability to study the analgesic effects of THC was limited, due to the small number of patients included in the pain assessments, because of lower prevalence of pain related behavioural disturbances than expected and the limitations of pain assessment in this patient group. These results should therefore be interpreted with caution. While self-reporting of pain is often referred to as 'gold-standard',[3] VRS assessments are only suitable for patients with mild dementia severity as it requires the capability of understanding the task and communicating the experienced sensation. Therefore, the PACSLAC-D, an observational assessment scale, is developed for assessment of pain in non-communicative persons.[1] This scale is more appropriate for nursing home patients than for community-dwelling patients, as this first group often express pain and discomfort through changes in behaviour. Future studies on the efficacy of THC as analgesic treatment, which are still warranted, should focus on a more homogeneous patient group, in whom a single pain assessment scale is feasible.

References

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