High prevalence of vitamin D deficiency and insufficiency in patients with manifest Huntington disease
An explorative study

Victor GM Chel1,2,*, Marcel E Ooms2, Jessie van der Bent3, Fleur Veldkamp1, Raymund AC Roos4, Wilco P Achterberg3,4, and Paul Lips5

1Huntington Centre Topaz; Overduin; Katwijk, the Netherlands; 2EMGO-institute; VU University Medical Center; Amsterdam, The Netherlands; 3Leiden University Medical Centre; Department of Neurology; Leiden, The Netherlands; 4Leiden University Medical Centre; Department of Public Health and Primary Care; Leiden, The Netherlands; 5VU University Medical Center; Department of Internal Medicine/Endocrinology; Amsterdam, The Netherlands

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Introduction

Severe vitamin D deficiency (25(OH)D < 12.5 nmol/L), moderate vitamin D deficiency (12.5–25 nmol/l) and mild vitamin D deficiency or vitamin D insufficiency (25–50 nmol/L) are common in older institutionalized people and known to be associated with muscle weakness, impaired balance and increased fall risk. Falls and balance problems are common in people with Huntington disease (HD). Despite this, the prevalence of vitamin D deficiency in patients with manifest HD has never been investigated.

Serum 25(OH)D levels were measured in routinely drawn blood samples from 28 Dutch institutionalized patients with manifest Huntington disease.

Mean serum 25(OH)D level was 33 nmol/l (SD 15). Twenty-five subjects (89%) were vitamin D deficient or insufficient (25(OH)D < 50 nmol/L). A positive association was found between serum 25(OH)D levels and Functional Ambulation Classification (FAC) scores (p = 0.023).

Huntington disease is a rare, inherited, progressive, neurodegenerative disorder of the central nervous system, characterized by motor impairments, psychiatric problems and dementia. It is autosomal-dominant inherited and caused by an elongated trinucleotide (CAG) repeat (36 repeats or more) on the short arm of chromosome 4p16.3 in the huntingtin gene. The mean age at onset is between 30 and 50 y (range 2–85 y). Mean duration of HD is 17–20 y. The pathophysiology of HD is not fully understood, although it is thought to be related to toxicity of the mutant huntingtin protein. The motor pattern is characterized by hyperkinesia (chorea, dystonia) and hypokinesia (bradykinesia), both leading to an increased risk of falls. Falls and balance problems in patients with HD are common and multifactorial in origin. Falls, injury, impaired activities of daily living (ADL) with loss of independent ambulation eventually often leads to nursing home admission. Despite the potential harmful effects of vitamin D deficiency in patients with HD, little is known about the vitamin D status in this population. The aim of the study therefore was to explore the vitamin D status in our residential HD population, as a high degree of deficiency was suspected.

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Results

Over a period of approximately one year, blood samples were drawn from 28 subjects. Basic characteristics of the participants are listed in Table 1. Routine care testing was the reason for blood sampling in 17 cases (61%). Other reasons were: fatigue (2 subjects); agitation (2 subjects); gastro-intestinal complaints (4 subjects); anemia (1 subject); weight loss (1 subject); change of behavior (1 subject). All participants but three had the lowest possible Total Functional Capacity (TFC). The mean age of the subjects was 59 (range 42–76). Twenty subjects (71%) went outside in the sun at least once a week. Being an exclusion criterion, none of the subjects were using meal replacement products containing extra vitamin D3. The extra daily vitamin D intake by using these products, calculated by a dietician, was between 88 IU (2.2 μg) and 352 IU (8.8 μg). One subject was bed ridden; 7 subjects (25%) were wheelchair bound; 7 subjects (25%) needed continuous help while walking and 13 subjects (46%) were able to walk without physical support, 15 subjects (54%) were considered to be “recurrent fallers.”

Mean serum 25(OH)D level was 33 nmol/L (SD 15 range 6.5–58.2), 8 subjects (29%) were vitamin D deficient (25(OH)D < 25 nmol/L); 25 subjects (89%) vitamin D insufficient (25(OH)D < 50 nmol/L); 3 subjects (10%) were vitamin D sufficient (25(OH)D ≥ 50 nmol/L). No patient had a serum 25(OH)D level > 75 nmol/L.

A positive association was found between serum 25(OH)D levels and Functional Ambulation Classification (FAC) scores (P = 0.023).

Discussion

This study is the first to demonstrate the high prevalence of vitamin D deficiency and insufficiency in institutionalized patients with manifest HD.

Huntington Centre Topaz Overduin houses 61 (long stay) patients with HD. Serum 25(OH)D levels were determined in a group of 28 subjects (46%). As the subjects were included only when blood sampling was necessary for any clinical indication, some bias may be present. The participants included in this study however did not differ substantially from the other institutionalized patients with manifest HD.14 Another limitation is the size of this study although it was performed in one of the world’s largest Huntington centers. Whether this study is generalizable to other countries is uncertain. While mass spectrometry is the current gold standard for measuring 25(OH)D, the used radioimmunoassay in this study is accurate and not influenced by vitamin D binding protein concentration.15

The common vitamin D deficiency in older nursing home residents is mainly explained by the facts that older persons do not often go outside in the sunshine, the production of vitamin D in the skin decreases considerably with aging and dietary vitamin D intake is low. In an earlier study including 338 older nursing home residents with a mean age of 84 (± 6) years, mean serum 25(OH)D was 25.0 nmol/L (SD 10.9) at baseline, and in 98%, it was lower than 50 nmol/L. In that study participants did not go outside more than once a week. The total dietary vitamin D intake was estimated at about 100 IU/day and the calcium intake at 1000 mg/day.16 Nursing home residents with HD are much younger than the average nursing home population and they come outside more often.

Most subjects (71%) went outside in the sun at least once a week and the FAC demonstrates that this population was certainly not completely dependent. In addition 10 subjects (36%) used meal replacement products containing extra vitamin D3. However, the mean serum 25(OH)D in institutionalized patients with manifest HD (33 nmol/L, SD 15, range 6.5–58.2) in this study was much lower than observed in another study (64.5 nmol/L, SD 39.3 range 19.5–99.5) in patients with pre-manifest HD.17 Vitamin D deficiency is known to be associated with fracture risk and risk of falling. Although fracture is not a high risk in HD, recurrent falls are: in another Dutch study, in 45 early to mid-stage HD patients, no less than 60% of the participants reported two or more falls in the previous year.12 In the present study, 15 subjects (54%) were considered to be “recurrent fallers.”

General policy in Dutch long stay facilities for people with HD is to preserve the autonomy of these patients as much as possible in order to maximize the quality of life. One of the consequences of this policy is that physical restraints are not used in any form, thereby accepting the fact that HD-patients fall frequently. A multidisciplinary team of physicians, physiotherapists, dietitians, occupational therapists, psychologists and nurses are employed with the aim of minimizing the number and consequences of falls by periodic evaluation and, if possible, treatment of known multifactorial causes.

Table 1. Basic characteristics of study population

| subjects (female / male) n | 28 (15/13) |
|--------------------------|----------|
| mean age (range) years n | 59 (42–76) |
| serum 25(OH)D, nmol/L mean (SD) n | 33 (15) |
| serum 25(OH)D in participants n(%) | 28 (100) |
| < 50 nmol/L n | 25 (89) |
| < 25 nmol/L n | 8 (29) |
| (UHDRS)-TFC score: 0 n(%) | 25 (89) |
| (UHDRS)-TFC score: 1 n(%) | 3 (11) |
| FAC score: n(%) | 0 (29) |
| 1 n(%) | 2 (7) |
| 2 n(%) | 5 (18) |
| 3 n(%) | 3 (11) |
| 4 n(%) | 6 (21) |
| 5 n(%) | 4 (14) |
| recurrent fallers (≥ 2x/year) n(%) | 15 (54) |
| subjects having sun exposure > 1x/week n(%) | 20 (71) |
| use of meal replacement products containing 25(OH)D, n(%) | 10 (36) |
It is not known whether vitamin D deficiency is also associated with fall risk in HD. Given the high prevalence of vitamin D deficiency in nursing home residents with HD, it would be valuable to further investigate such a possible association, since vitamin D deficiency in nursing home residents is easy to treat with oral supplementation or UV irradiation.16,18

Furthermore, it would also be useful to examine a possible association of vitamin D deficiency in patients with manifest HD and neuropsychiatric problems often seen in HD. Such an association has not been investigated, but could well exist since vitamin D is known to have neurotrophic, neuroprotective, and neurotransmissive properties and vitamin D deficiency is associated with several neuropsychiatric disorders including schizophrenia, psychosis, depression, anxiety, irritability, behavior disorders and cognitive impairment.2 The same neuropsychiatric symptoms are frequently seen in HD and known to have a profound impact on the perceived quality of life.11,19

Patients and Methods

Subjects were residents of Huntington Centre Topaz Overduin in The Netherlands with manifest, advanced HD. Physicians were asked to also determine serum 25(OH)D levels when they had the intention of drawing blood samples from their HD patients for any clinical indication. Therefore informed consent from subjects or their proxies was not obtained. Use of vitamin supplements was the only exclusion criterion. The best parameter for vitamin D status, 25-hydroxy-vitamin D (25(OH)D), was measured by a radioimmunoassay (25-OH-vitamin DRIA, Diasorin). The assay has 100% cross reactivity with 25(OH)D2 and 25(OH)D3. Total imprecision (Interassay coefficient of variation) is 9.4% at 22 nmol/L. SCAL Medical Diagnostics (foundation central primary care laboratory) is certified by RvA (Board of Accreditation) and participates in external quality assessment schemes organized by SKML (Foundation Quality Control Medical Laboratory Diagnostics).

In Huntington Centre Topaz Overduin, the standard of care contains regular assessments of Total Functional Capacity (Unified Huntington’s Disease Rating Scale; UHDRS-TFC), Functional Ambulation Classification (FAC) and systematic administration of falls. Residents having had 2 falls or more over the past 12 mo are called “recurrent fallers.”

The UHDRS-TFC consists of five items that assess occupation, financial affairs, domestic chores, activities of daily living, and care level. Scores range from 0 to 13 (score 13 is normal; 0 is completely dependent).20

The Functional Ambulation Classification consists of five items. Scores range from 0 to 5 (score 0 is Nonfunctional ambulation; 1: Ambulator, Dependent for Physical Assistance level II; 2: Ambulator, Dependent for Physical Assistance, level I; 3: Ambulator, Dependent for Supervision; 4: Ambulator, Independent Level Surfaces only; 5: Ambulator independent.21

IBM SPSS statistics 20 was used to compute the descriptive parameters.

The association between vitamin D levels and FAC was determined by anova for ordinal scales.

Conclusion

The prevalence of vitamin D deficiency and insufficiency is high in institutionalized patients with manifest Huntington disease. As it is not known yet whether in HD vitamin D deficiency is associated with fall risk and neuropsychiatric problems, further study is needed.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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