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Chapter 8

Summary, conclusions and recommendations

Vitamin D deficiency and insufficiency is common in older people, especially in nursing home residents. Vitamin D deficiency is defined as a serum 25-hydroxyvitamin D (25(OH)D) level lower than 25 nmol/l. Vitamin D insufficiency is defined as a serum 25(OH)D between 25 and 50 nmol/l. Persons with a serum 25(OH)D of 50 nmol/l or higher are considered vitamin D sufficient. Vitamin D-supplementation is likely to improve the Quality of Life (QOL) in this population. This thesis focuses on comparing different vitamin D treatment modalities in nursing home residents.

In *Chapter 1* an overview of the history and physiology of vitamin D is given. Also the vitamin D status in older people is discussed as well as the different possible ways to prevent and treat vitamin D deficiency in older people. Finally in this chapter nursing homes and nursing home care in The Netherlands are described as well as the fact that the emphasis in Dutch nursing home care is especially on improving the quality of life (QOL) as experienced by the residents.

Chapter 2 describes a randomised clinical trial in 45 female nursing home residents on the effect of ultraviolet irradiation, compared with oral vitamin D, on the vitamin D status and parathyroid hormone concentration. Participants in this study were randomised to receive either ultraviolet B (UV-B) irradiation (at half the minimal erythemal dose on 1000 cm2 of the lower back, three times a week during twelve weeks), or oral vitamin D 400 IU/day, or no treatment. Main outcome measures were change in fasting serum levels of vitamin D metabolites, at 0, 2, 4, 8, and 12 weeks, in the treatment groups, compared with the control group. PTH(1-84) was measured at 0 and 12 weeks. Baseline serum 25-hydroxyvitamin D (25(OH)D) was lower than 30 nmol/l in 95% of the participants. It increased to a median value of around 60 nmol/l after 12 weeks both in the UV-B and vitamin D groups, whereas there was no change in the control group. Serum 1,25-dihydroxyvitamin-D increased significantly in the UV-B group. Serum calcium increased significantly in both treatment groups. Serum PTH decreased more than 30% in both treatment groups (p < 0.001), whereas there was no significant change in the control group. It was concluded that irradiation with UV-B in older nursing home residents for a few minutes per day, 3x/week, leads to adequate improvement of the vitamin D status. It is as effective as oral vitamin D3 in increasing serum 25(OH)D and suppressing secondary hyperparathyroidism.

In *Chapter 3* the results are presented of a pilot study on the feasibility and effectiveness of weekly sunbed use (half body, full frontal UV irradiation at half the minimal erythemal dose, during eight weeks) in obtaining vitamin D sufficiency in 8 nursing home residents. Main outcome measures were change in fasting serum levels of 25(OH)D and PTH at 0, 2, 4 and 8 weeks. At baseline, mean serum 25(OH)D was 28.5 nmol/L. Mean serum 25(OH)D levels increased to 46.5 nmol/L. Median serum PTH levels decreased by 20% after 8 weeks of treatment. It was concluded that UV irradiation leads to a significant increase in 25(OH)D serum levels. A period of eight weeks with the irradiation frequency of once per week however was too short to reach vitamin D-sufficiency.

In *Chapter 4* the outcomes of a randomised controlled trial on the effect of different doses and time intervals of oral vitamin D supplementation in 338 nursing home residents, spread over ten nursing homes in the Netherlands, are presented and discussed. In this study the effect of equivalent oral doses of cholecalciferol 600 IU/day; 4200 IE/week and 18,000 IU/month on vitamin D status was compared. After 4 months, calcium was added during 2 weeks, 800 mg calcium carbonate (320 mg Ca²⁺)/day or 1600 mg calcium carbonate (640 mg Ca²⁺)/day or placebo. The treatment period of four months was completed by 276 participants (82%). The treatment period of four and a half months was completed by 269 participants (80%). At baseline, mean serum 25(OH)D was 25.0 nmol/L (SD 10.9). In 77% of the participants, baseline serum 25(OH)D was lower than 30 nmol/L, in 98% lower than 50 nmol/L. The median daily calcium intake with dairy products was 750 mg (interquartile range 560-1030). The mean serum 25(OH)D levels increased to 62.5 nmol/L (after daily vitamin D3 69.9nmol/L, weekly 67.2 nmol/L and monthly 53.1 nmol/L, p<0.001 between groups) and the median serum PTH levels decreased by 23% (p<0.001). At 4 months, the percentage of patients with serum 25(OH)D < 50 nmol/L was 10.9, 10.6 and 36.4% in the daily, weekly and monthly groups of vitamin D supplementation respectively. After 4 months in the vitamin D supplemented groups, there was no decrease of bone turnover markers (CTX and alkaline phosphatase). No additional effect was found of the subsequent calcium supplementation. It was concluded that daily vitamin D supplementation was slightly but significantly more effective in raising serum levels of 25-hydroxyvitamin D (25(OH)D) than weekly supplementation. Monthly administration was the least effective. Calcium supplementation had no effect on serum PTH and bone turnover. A survey among

the nursing staffs of the participating nursing homes showed a distinct preference (72%) for daily administration compared to weekly and monthly. 39 % Of the nursing staffs reported the impression that fewer mistakes were made using daily administration.

In **Chapter 5** the results from a survey study, among elderly care physicians and general practitioners, to adherence to the guidelines of the Health Council of the Netherlands, concerning vitamin D supplementation in older people, are presented and discussed. Short surveys were sent to all 1300 elderly care physicians in the Netherlands. At a meeting of the Academic Network of GP practices of the VU University medical center in Amsterdam (51 GPs), a short questionnaire was given to the 42 general practitioners present. 50% Of the elderly care physicians returned the questionnaire. It was shown that, although more than 2/3 of the respondents are familiar with vitamin D supplementation in older people, approximately 50% of the elderly care physician and general practitioners do not prescribe vitamin D when the guideline advises to do so. If supplementation is prescribed, 50% of the elderly care physicians and 20% of the general practitioners uses an insufficient supplementation dose. In a meeting with different occupational groups, organised by the Netherlands Nutrition Centre, as well as in a meeting of the Academic Network of GP practices of the VU University medical center in Amsterdam, the following possible explanations for not supplementing vitamin D in older people were reported: lack of sense of urgency; doubts about the health benefits; the conviction that implementation of primary prevention in large groups of the population is not appropriate and not feasible in GP practices; the complexity of the applied age limits in earlier guidelines, the large range of different vitamin D prescriptions and the lack of clear, appealing information material for consumers. It is concluded in this chapter that in the Netherlands elderly care physicians and probably also general practitioners do not sufficiently follow the advice of the Dutch Health Council regarding vitamin D supplementation in older people. Familiarity with, and support for the Health Council advice could be improved. It is likely that both the new Health Council report "Evaluation of the nutritional standards for vitamin D" published in September 2012 and the digital platform www.voedingscentrum.nl/vitamin D from the Netherlands Nutrition Centre, can contribute to this improvement.

In *Chapter 6* the high prevalence of vitamin D deficiency and insufficiency is described in a special sub group of (relatively young) nursing home residents: patients with Huntington's

disease. Huntington's disease is a rare, inherited, progressive, neurodegenerative disorder of the central nervous system, characterized by motor impairments, psychiatric problems and dementia. The mean age at onset is between 30 and 50 years (range 2-85 years). Mean duration of HD is 17-20 years. Serum 25(OH)D levels were measured in routinely drawn blood samples from 28 out of 61 (long stay) Dutch nursing home residents with Huntington's disease (46%). 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 was using vitamin supplements, however, 10 subjects (36%) were using meal replacement products containing vitamin D, mainly because of poor food intake. Mean serum 25(OH)D level was 33 nmol/l (SD 15). Eight subjects (29%) were vitamin D deficient (25(OH)D < 25 nmol/L). In 25 (89%) participants, serum 25(OH)D was lower than 50 nmol/L. Three subjects (10%) were vitamin D sufficient (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). The study presented in this chapter is the first to describe the high prevalence of vitamin D deficiency and insufficiency in institutionalised HD patients and its possible health consequences in this younger than average population of nursing home residents.

In the general discussion, *chapter 7*, methodological considerations and main findings of the studies included in this thesis are discussed as well as possible implications of the findings for clinical practice and future research.

Main conclusions are:

- Most nursing home residents are vitamin D deficient or insufficient
- Although the aged skin is known to have a decreased capacity to produce vitamin D,
 even the very aged skin is still capable of producing adequate amounts of vitamin D,
 following ultraviolet irradiation (UV-B).
- Vitamin D treatment in nursing home residents by ultraviolet irradiation (UV-B) is equally effective as oral vitamin D supplementation in increasing serum 25(OH)D and suppressing secondary hyperparathyroidism.
- Vitamin D treatment by using sunbeds (UV-B exposure) is feasible and easy to perform in daily nursing home care practice and therefore a realistic alternative (with

possible adjusted health benefits) for oral vitamin D supplementation in this population.

- Several vitamin D supplementation regimens exist. Daily and weekly vitamin Dsupplementation are more effective in reaching vitamin D sufficiency than monthly administrations
- Vitamin D supplementation in Dutch nursing homes is open to improvement: approximately 75% of the nursing home residents is undertreated.
- The prevalence of vitamin D deficiency and –insufficiency is high in a specific subgroup of, younger than average, nursing home residents: patients with Huntington's disease
 (HD). Vitamin D supplementation in this group is not common practice.
 It has to be further investigated whether also in this population vitamin D- deficiency is associated with increased fall risk and neuropsychiatric symptoms often seen in HD.

A follow up survey after for instance five years is suggested, in order to investigate whether the recently launched information platform on vitamin D by the Netherlands Nutrition Centre (Voedingscentrum) and the renewed advice of the Health Council regarding vitamin D supplementation will have contributed to a higher awareness of, and support for the vitamin D supplementation guidelines among health care providers resulting in a better prevention of vitamin D deficiency in older people.

Moreover, further research is recommended on the topics of:

- the possible association of vitamin D deficiency in nursing home residents with HD and fall risk and neuropsychiatric problems often seen in HD (A research protocol has already been designed).
- the added value of rapid correction of vitamin D deficiency by using cholecalciferol loading dosages in nursing home residents.
- the assumed added value on quality of life in nursing home residents when using UV irradiation in vitamin D supplementation (a research protocol has already been designed)

recommendations:

- Several vitamin D supplementation regimens exist. Since vitamin D probably is more effective and safer when administered more frequently in a not too high dosage, a daily

or weekly dose is recommended for routine oral vitamin D supplementation in institutionalised older people

- Since vitamin D deficiency is also very prevalent in institutionalised HD patients, all nursing home residents with HD should be advised to take 800 IU cholecalciferol daily, irrespective of their age.
- In order to achieve adequate vitamin D supplementation in nursing home residents, it is desirable that vitamin D supplementation as a basic element in all care plans, is considered as an indicator and standard for responsible care in nursing homes by the Health Care Inspectorate of the Netherlands (IGZ).