Article de révision systématique de type qualitatif

Vitamine D, D pour dépression ?

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Par

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Plan de la présentation

- Bref survol sur la vitamine D
- Méthodologie
- Présentations des études
- Discussion
- Conclusion
- Référence
- Questions

Bref survol sur la vitamine D

- Hormone liposoluble
- Agit a/n du SNC : antioxydants, production de catécholamines
- Déficit chez 1/3 à 1/2 des personnes dans pays développés et sous-développés
- Besoins quotidiens : 600 unités Die
- Dose toxique : 60 000 unités Die

Méthodologie

· PICO : P= H et F > 18ans I= vitamine D C= placebo O=diminution des sx dépressifs

· Moteur= uptodate, pubmed, cochcrane, trip database , google scholar

· Filtres = > Mesh : '' Depressive Disorder'' OR ''Major Depression'' OR ''depression'' AND ''Vitamin D''/ therapeutic use.

> langue : anglais et français

> période 2000 à 2014

> type d'article: essaie clinique randomisé, p=<0,05

> Dépression légère à modérée

Échelle de Beck

- Questionnaire choix multiples 21 questions
- mesure sévérité de la dépression
- 0-9 dépression mineure
  10-18 : dépression légère
  19-29: dépression modérée
  30-63: dépression sévère

Article 1 : Hassan M-K et al., 2013

- Abrégé

The Effect of 2 Different Single Injections of High Dose of Vitamin D on Improving the Depression in Depressed Patients With Vitamin D Deficiency

A Randomized Clinical Trial

Hassan Mozaffari-Khosravi, PhD, Lale Nabizade, MSc,* Seyed Mojtaba Yassini-Ardakani, MD,† Hossein Hadinedoushan, PhD,‡ and Kazem Barzegar, MSc§*

Islamic Republic of Iran. A total of 120 patients who had a Beck Depression Inventory II score of 17+ and were affected with vitamin D deficiency were randomly assigned to 3 groups of 40. They included G300, G150, and NTG. G300 and G150 received an intramuscular single dose of 300,000 and 150,000 IU of vitamin D, respectively, and the NTG group received nothing. After 3 months of intervention, the depression state, serum vitamin D, calcium, phosphorus, and parathormone were measured.

The median of serum vitamin D after intervention were 60.2, 54.6, and 28.2 nmol/L ($P < 0.001$) for the G300, G150, and NTG, respectively. Percentages of vitamin D deficiency after intervention were 18, 20, and 91.2 for the groups, respectively. The serum calcium mean showed a statistically significant increase in just the 2 test groups receiving vitamin D. There was only significant difference in mean of Beck Depression Inventory II test score between G300 and NTG ($P = 0.003$).

The results of the study revealed that first, the correction of vitamin D deficiency improved the depression state, and second, a single injection dose of 300,000 IU of vitamin D was safe and more effective than a 150,000-IU dose.

Key Words: depression, vitamin D, Vitamin D deficiency

(*J Clin Psychopharmacol* 2013;33: 378–385)

Article 1 : Hassan M-K et al., 2013

- Type d'étude : essai clinique randomisé
- Conflit d'intérêt : Aucun
- Endroit : Iran
- Année de l'étude : 2011
- Nombre de participants : 120
- Population : H/F 20-60 ans sx dépressifs X2sem avec Beck >17 et taux de vitamine D <40nmol/L
- Sx dépressifs objectivés par : Beck et psychiatre

Article 1 : Hassan M-K et al., 2013

- taux de participation : 91%
- Taux max de vitD/sem : 25 000 UI
- Durée de l'étude : 3 mois
- résultats : améliore sx dépressif (per protocol) et bas taux vitamine D = pt plus dépressif
- Autre : pas plus e/s

Discussion : article 1

Hassan M-K et al., 2013

- Point Fort
  - bonne validité interne : confirmation dx par psychiatre
- Point faible
  - court suivi: 3 mois
  - validité externe: Iran, période ensoleillement vs pays nordique

Article 2 : Marie Kjaergaard et al. 2013

- Abrégé

Effect of vitamin D supplement on depression scores in people with low levels of serum 25-hydroxyvitamin D: nested case–control study and randomised clinical trial†

Marie Kjærgaard, Knut Waterloo, Catharina E. A. Wang, Bjørg Almås, Yngve Figenschau, Moira S. Hutchinson, Johan Svartberg and Rolf Jorde

Aims
To compare depressive symptoms in participants with low and high serum 25-hydroxyvitamin D (25(OH)D) levels and to examine whether supplementation with vitamin D_3 would improve symptoms in those with low serum 25(OH)D levels.

Method
Participants with low 25(OH)D levels were randomised to either placebo or 40000IU vitamin D_3 per week for 6 months. Individuals with high serum 25(OH)D levels were used as nested controls. Depressive symptoms were evaluated with the Beck Depression Inventory, Hospital Anxiety and Depression Scale, Seasonal Pattern Assessment Scale and Montgomery–Åsberg Depression Rating Scale. The study was registered at ClinicalTrials.gov (NCT00960232).

Results
Participants with low 25(OH)D levels ($n=230$) at baseline were more depressed ($P<0.05$) than participants with high 25(OH)D levels ($n=114$). In the intervention study no significant effect of high-dose vitamin D was found on depressive symptom scores when compared with placebo.

Conclusions
Low levels of serum 25(OH)D are associated with depressive symptoms, but no effect was found with vitamin D supplementation.

Declaration of interest
None.

Article 2 : Marie Kjaergaard et al. 2013

- Type d'étude : essai clinique randomisé
- Conflit d'intérêt : Aucun
- Endroit : Norvège
- Année de l'étude : 2007-2008
- Nombre de participants : 357
- Population : H/F 30-75 ans avec un taux de vitamine D <55nmol/L et >70 nmol/L
- Sx dépressifs objectivés par : DBI-II, HADS, SPAQ, MADRS

Article 2 : Marie Kjaergaard et al. 2013

- taux de participation : 95%
- Taux max de vitD/sem : 20 000 UI
- Durée de l'étude : 6 mois
- Résultats: pas d'améliore sx dépressif (per protocol) et bas taux vitamine D = pt plus dépressif
- Autre : pas plus e/s

Discussion : article 2

Marie Kjaergaard et al. 2013

- Point Fort
  - bonne validité interne: plrs échelles de mesure
  - bonne validité externe au niveau population et ITT (tient compte compliance)

- Point faible
  - suivi trop court : 6 mois

Article 3 Angela J.Dean et al., 2011

- Abrégé

Effects of Vitamin D Supplementation on Cognitive and Emotional Functioning in Young Adults – A Randomised Controlled Trial

Angela J. Dean[1]*, Mark A. Bellgrove[1], Teresa Hall[1], Wei Ming Jonathan Phan[1], Darryl W. Eyles[1,2], David Kvaskoff[1], John J. McGrath[1,2,3]

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Abstract

Background: Epidemiological research links vitamin D status to various brain-related outcomes. However, few trials examine whether supplementation can improve such outcomes and none have examined effects on cognition. This study examined whether Vitamin D supplementation led to improvements in diverse measures of cognitive and emotional functioning, and hypothesised that supplementation would lead to improvements in these outcomes compared to placebo.

Methods/Principal Findings: Healthy young adults were recruited to a parallel-arm, double-blind trial conducted at The University of Queensland. Participants were randomly allocated to receive Vitamin D (one capsule daily, containing 5000 IU cholecalciferol) or identical placebo capsule for six weeks. All participants and outcome assessors were blinded to group assignment. Primary outcome measures assessed at baseline and 6 weeks were working memory, response inhibition and cognitive flexibility. Secondary outcomes were: hallucination-proneness, psychotic-like experiences, and ratings of depression, anxiety and anger. 128 participants were recruited, randomised and included in primary analyses (vitamin D n = 63; placebo n = 65). Despite significant increases in vitamin D status in the active group, no significant changes were observed in working memory ($F = 1.09$; $p = 0.30$), response inhibition ($F = 0.82$; $p = 0.37$), cognitive flexibility ($F = 1.37$; $p = 0.24$) or secondary outcomes. No serious adverse effects were reported.

Conclusions: Our findings indicate that vitamin D supplementation does not influence cognitive or emotional functioning in healthy young adults. Future controlled trials in targeted populations of interest are required to determine whether supplementation can improve functioning in these domains. Australian and New Zealand Clinical Trials Registry; ACTRN12610000318088.

Article 3 Angela J.Dean et al., 2011

- Type d'étude : essais clinique randomisé
- Conflit d'intérêt : Aucun
- Endroit : Australie
- Année de l'étude : 2010
- Nombre de participants : 128
- Population : Hommes et Femmes âgés de plus de 18 ans
- Sx dépressifs objectivés par : Beck

Article 3 Angela J.Dean et al., 2011

- taux de participation : 100%
- Taux max de vitD/sem : 35 000 UI
- Durée de l'étude : 6 semaines
- Résultats : pas d'améliore sx dépressif (ITT)
- Autre : pas plus e/s

Discussion : article 3

Angela J.Dean et al., 2011

- Point Fort
  - Atteinte émotionnelle EN PLUS de l'atteinte des fonctions cognitives (mémoire de travail, réponse à l'inhibition, flexibilité cognitive)
- Point faible
  - court suivi: 6 semaines

Article 4: R. Jorde et al. 2008

- Abrégé

Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: randomized double blind trial

R. Jorde[1,2], M. Sneve[2], Y. Figenschau[3,4], J. Svartberg[1,2] & K. Waterloo[5,6]

From the [1]Institute of Clinical Medicine, University of Tromsø; Departments of [2]Internal Medicine and [3]Medical Biochemistry, University Hospital of North Norway; [4]Institute of Medical Biology, University of Tromsø; [5]Department of Neurology, University Hospital of North Norway; and [6]Department of Psychology, University of Tromsø, Tromsø, Norway

Abstract. Jorde R, Sneve M, Figenschau Y, Svartberg J, Waterloo K (University of Tromsø and University Hospital of North Norway, Tromsø, Norway). Effects of vitamin D supplementation on symptoms of depression in overweight and obese subjects: randomized double blind trial. *J Intern Med 2008*; **264**: 599–609.

Objectives. The objective of the present study was to examine the cross-sectional relation between serum 25-hydoxyvitamin D [25-(OH) D] levels and depression in overweight and obese subjects and to assess the effect of vitamin D supplementation on depressive symptoms.

Design. Cross-sectional study and randomized double blind controlled trial of 20.000 or 40.000 IU vitamin D per week versus placebo for 1 year.

Setting. A total of 441 subjects (body mass index 28–47 kg m^{-2}, 159 men and 282 women, aged 21–70 years) recruited by advertisements or from the out-patient clinic at the University Hospital of North Norway.

Main outcome measures. Beck Depression Inventory (BDI) score with subscales 1–13 and 14–21.

Results. Subjects with serum 25(OH)D levels <40 nmol L^{-1} scored significantly higher (more depressive traits) than those with serum 25(OH)D levels ≥40 nmol L^{-1} on the BDI total [6.0 (0–23) versus 4.5 (0–28) (median and range)] and the BDI subscale 1–13 [2.0 (0–15) versus 1.0 (0–29.5)] ($P < 0.05$). In the two groups given vitamin D, but not in the placebo group, there was a significant improvement in BDI scores after 1 year. There was a significant decrease in serum parathyroid hormone in the two vitamin D groups without a concomitant increase in serum calcium.

Conclusions. It appears to be a relation between serum levels of 25(OH)D and symptoms of depression. Supplementation with high doses of vitamin D seems to ameliorate these symptoms indicating a possible causal relationship.

Keywords: depression, obesity, vitamins.

Article 4: R. Jorde et al. 2008

- Type d'étude : essai clinique randomisé
- Conflit d'intérêt : Aucun
- Endroit : Norvège
- Année de l'étude : 2005-2006
- Nombre de participants : 441
- Population : Hommes et Femmes âgés de plus de 21-70 ans avec IMC 28,0-47
- Sx dépressifs objectivés par : Beck

Article 4: R. Jorde et al. 2008

- taux de participation : 76%
- Taux max de vitD/sem : 40 000 UI
- Durée de l'étude : 1 an
- Résultats : amélioration des sx dépressifs (perprotocol pas en ITT). Les pt avec faibles taux de vit D sont plus dépressifs
- Autre : pas plus e/s , pas d'influence avec IMC, possiblement valeur seuil à <40nmol/L

Discussion : article 4

R. Jorde et al. 2008

- Point Fort
  - suivi 1 an
  - introduit notion de treshold à <40nmol/L
- Point faible
  - validité externe obèse
  - haut taux d'abandon (24%)
  - haut taux d'abandon explique différence en ITT (-) vs per protocol (+)

Article 5: Kerrie M Sanders et al. 2011

- Abrégé

Annual high-dose vitamin D_3 and mental well-being: randomised controlled trial

Kerrie M. Sanders, Amanda L. Stuart, Elizabeth J. Williamson, Felice N. Jacka, Seetal Dodd, Geoff Nicholson and Michael Berk

Background
Epidemiological evidence supports a relationship between vitamin D and mental well-being, although evidence from large-scale placebo-controlled intervention trials is lacking.

Aims
To examine if vitamin D supplementation has a beneficial effect on mood in community-dwelling older women; if a single annual large dose of vitamin D has a role in the prevention of depressive symptoms; and if there is an association between serum 25-hydroxyvitamin D levels and mental health.

Method
A double-blind, randomised, placebo-controlled trial of women aged 70 or older (the Vital D Study: ISRCTN83409867 and ACTR12605000658617). Participants were randomly assigned to receive 500 000 IU vitamin D_3 (cholecalciferol) orally or placebo every autumn/winter for 3–5 consecutive years. The tools utilised at various time points were the General Health Questionnaire, the 12-item Short Form Health Survey, the Patient Global Impression–Improvement scale and the WHO Well-Being Index. Serum 25-hydroxyvitamin D levels were measured in a subset of 102 participants.

Results
In this non-clinical population, no significant differences between the vitamin D and placebo groups were detected in any of the measured outcomes of mental health. Serum 25-hydroxyvitamin D levels in the vitamin D group were 41% higher than the placebo group 12 months following their annual dose. Despite this difference, scores from the questionnaires did not differ. Furthermore, there was no interaction between those on antidepressant/anxiety medication at baseline and the treatment groups.

Conclusions
The lack of improvement in indices of mental well-being in the vitamin D group does not support the hypothesis that an annual high dose of vitamin D_3 is a practical intervention to prevent depressive symptoms in older community-dwelling women.

Declaration of interest
M.B. and S.D. have relationships with Stanley Medical Research Foundation, NHMRC, Beyond Blue, Eli Lilly, GlaxoSmithKline, Organon, Mayne Pharma and Servia. M.B. has relationships with MBF, Geelong Medical Research Foundation, Bristol-Myers Squibb, Novatis, AstraZeneca, Janssen-Cilag, Lundbeck, Pfizer, Sanofi Synthelabo, Solvay and Wyeth. S.D. has a relationship with Rotary that might have an interest in the submitted work in the previous 3 years.

Article 5: Kerrie M Sanders et al. 2011

• Type d'étude :	essai clinique randomisé
•Conflit d'intérêt	Aucun
• Endroit :	Australie
• Année de l'étude :	2005-2010
• Nombre de participants :	2258
• Population :	Femmes >=70 ans avec facteur de risque de fracture
• Sx dépressifs objectivés par :	GHQ, SF-12,WHO et PGI-1

Article 5: Kerrie M Sanders et al. 2011

- taux de participation : 100%
- Taux max de vitD/sem : 9 615 UI
- Durée de l'étude : 3-5 ans
- Résultats: pas d'amélioration des sx dépressifs (en ITT). Les pt avec faibles taux de vit D ne sont pas plus dépressifs
- Autre : pas plus e/s , plus de fractures et de chutes dans le groupe vitamine D

Discussion : article 5

Kerrie M Sanders et al. 2011

- Point Fort
  - plusieurs outils pour mesurer le bien-être psychologique, grande cohorte (2258) , long suivi (5ans)

- Point faible

  - Facteur confondant : le groupe ayant reçu de la vitamine D ont eu plus de chute et de fracture

  - Faible validité externe

**Plus de fractures chez les ptes avec vit D ?!

Discussion

- Points forts en commun :
  - Essais cliniques randomisés
  - échelles qui ont déjà fait leurs preuves
  - limiter facteurs confondants en excluant les patients avec des maladies pouvant avoir un impact sur le métabolisme de la vitamine D
  - Ils ont aussi exclu, sauf pour l'étude de Kerrie M Sanders et al , les patients prenant des antidépresseurs
  - Dose >> 600 unités DIE

Conclusion

- Pas de bénéfices clairs à supplémenter en vitamine D pour améliorer sx dépressifs
- Pour l'instant, je ne recommande pas de donner des suppléments en vit D
- Néanmoins tendance entre faible taux de vitamine D et sx dépressifs
- Objectivé par une autre méta-analyse :

- Bénéfique dans le TDAH :

  le British Journal of Psychiatry en janvier 2014

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Questions ?!