DUE NUOVE EQUAZIONI PER LA STIMA DELLA FUNZIONE RENALE IN ULTRASETTANTENNI

Fonte: Ann Intern Med. 2 October 2012; 157(7): 471-481.

Negli anziani, le equazioni attuali per stimare la velocità di filtrazione glomerulare (GFR) non sono sempre validate per la classificazione corretta in termini di stadio della malattia renale cronica in ultrasettantenni. Lo studio riguarda la equazione derivante dallo studio Berlino Initiative (BRI). Si trattava di uno studio trasversale. I dati sono stati suddivisi per l'analisi in 2 gruppi, di cui uno per lo sviluppo dell'equazione e l'altro per la verifica della validità della stessa. Hanno partecipato allo studio 610 soggetti di età superiore a 70 anni (età media 78,5 anni). Il dosaggio della clearance plasmatica come gold standard è avvenuta con il metodo Iohexol. È stata effettuata una stima del GFR misurato dalla creatinina con metodiche standardizzate e sulla base anche dei livelli di cistatina C, il sesso, l'età e la raccolta del campione, ed il confronto delle equazioni BIS (bis1: creatinina-based; BIS2: creatinina e cistatina C-based) con altre equazioni di stima e la determinazione di parzialità, la precisione e l'accuratezza nel campione di validazione. L'equazione BIS2 ha evidenziato una minore distorsione rispetto alla creatinina bis1 ed alla equazione Cockcroft-Gault. Le equazioni della BRI hanno permesso di confermare un'alta prevalenza di persone di età superiore a 70 anni con un GFR inferiore a 60 ml/min per 1,73 m 2 (bis1, 50,4%; BIS2, il 47,4%, GFR dosato, 47,9%). Il tasso di errata classificazione totale per questo criterio è stato minore per l'equazione BIS2 (11,6%), seguita dalla equazione cistatina C 2 (15,1%), proposta dal Chronic Kidney Disease Epidemiology Collaboration. Tra le equazioni per il calcolo della creatinina, bis1 avuto il tasso di errata classificazione minore(17,2%), seguito dall'equazione del Chronic Kidney Disease Epidemiology Collaboration (20,4%).

STA DAVVERO DIMINUENDO L'INCIDENZA DI DEMENZA? TRENDS DAL 1990 NEL ROTTERDAM STUDY

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Objective: To investigate whether dementia incidence has changed over the last 2 decades.
Methods: We compared dementia incidence in 2 independent subcohorts of persons aged 60–90 years from the Rotterdam Study, a population-based cohort study. The first subcohort started in 1990 (n _ 5,727), the second in 2000 (n _ 1,769). Participants were dementia-free at baseline and followed for at maximum 5 years. We calculated age-adjusted dementia incidence rates for the 2 subcohorts in total, in 10-year age strata, and for men and women separately. We also
compared mortality rates, differences in prevalence of vascular risk factors, and medication use.
Finally, we compared brain volumes and the extent of cerebral small vessel disease in participants who underwent brain imaging 5 years after the baseline examinations.
Results: In the 1990 subcohort (25,696 person-years), 286 persons developed dementia, and in the 2000 subcohort (8,384 person-years), 49 persons. Age-adjusted dementia incidence rates were consistently, yet nonsignificantly, lower in the 2000 subcohort in all strata, reaching borderline significance in the overall analysis (incidence rate ratio 0.75, 95% confidence interval [CI] 0.56–1.02). Mortality rates were also lower in the 2000 subcohort (rate ratio 0.63, 95% CI 0.52–0.77). The prevalence of hypertension and obesity significantly increased between 1990 and 2000. This was paralleled by a strong increase in use of antithrombotics and lipid-lowering drugs. Participants in 2005–2006 had larger total brain volumes (p _ 0.001) and less cerebral small vessel disease (although nonsignificant in men) than participants in 1995–1996.

Conclusions: Although the differences in dementia incidence were nonsignificant, our study suggests that dementia incidence has decreased between 1990 and 2005.

TUMORE ALLA PROSTATA: NUOVO MARCATORE PIÙ PRECISO

Un nuovo marker consente di discriminare meglio il tumore prostatico in pazienti con Psa elevato, così da evitare inutili biopsie. Si tratta del proPsa impiegato in un'equazione nota come prostate health index (Phi, indice di salute prostatica), disponibile a Roma nella Patologia clinica dell'Istituto nazionale tumori Regina Elena, diretto da Laura Conti. Il nuovo esame, con un semplice prelievo di sangue, permette di stabilire e monitorare l'aggressività del tumore. Il test non è rimborsato dal Servizio sanitario nazionale, ha una tariffa minima e il costo è comunque inferiore a quello di una biopsia.
«Il Psa totale - spiega Laura Conti - è caratterizzato da una ridotta specificità per l'identificazione precoce del tumore prostatico». Da qui la necessità di affiancare al Psa totale e al Psa libero, il nuovo marcatore [-2]pro Psa e l'algoritmo Phi per una diagnosi più accurata e specifica. «Il Phi non sostituisce il test del Psa - sottolinea Conti - bensì migliora la specificità clinica di rilevamento del carcinoma prostatico rispetto ai test attualmente in uso (Psa totale e % free Psa) identificando con maggiore accuratezza il paziente candidato ad una biopsia prostatica». Il tumore della prostata è la neoplasia più frequente tra gli uomini, nel 2012 sono attesi 36mila nuovi casi. L'incidenza stimata nel 2020 è di oltre 43mila casi e nel 2030 di oltre 50mila.

PRESSIONE DIFFERENZIALE E DEFICIT COGNITIVO: ESISTE UNA CORRELAZIONE!

Fonte: J Cardiovasc Med 2012, 13:735-740.

Dai risultati di questo studio emerge che valori elevati di pressione differenziale (PP) sono correlati con un deficit cognitivo. La Dott.ssa Sirakova ed i suoi colleghi hanno esaminato 148 pazienti , di cui 51 uomini (34.5%) e 97 donne (65.5%), età media 64.16±11.18 anni, con una media in termini di storia di ipertensione arteriosa pari a 13.1±11.05 anni. Tutti i pazienti sono stati sottoposti ad un'estensiva valutazione medica con anamnesi, esame obiettivo, esami di laboratorio, misurazione ambulatoriale della pressione arteriosa ed a test neuropsicologici quali Mini Mental State Examination (MMSE) ed il Montreal Cognitive Assessment (MoCA). Dall'analisi di regressione è emerso che esiste una correlazione tra i valori di PP diurni e notturni ed i risultati dei test neuropsicologici. In particolare, è stata riscontrata una differenza significativa ($p=0.02$ per il MMSE) nei valori medi dei test neuropsicologici tra i due gruppi con PP >50 mmHg e cpn PP≤ 50 mmHg. Questo risultato non dipendeva dall'età dei pazienti. Inoltre, vi era una differenza significativa tra i valori medi di PP diurni ($p=0.01$) e notturni ($p=0.02$) nei pazienti con deficit cognitivo e quelli senza (rispettivamente valori > e < di 55mmHg). In conclusione, elevati valori di PP, diurni e notturni, sono correlati con un impairment cognitivo.

BASSI LIVELLI SIERICI DI VITAMINA D ASSOCIATI A MALATTIA DI ALZHEIMER

Pauline Anderson

September 28, 2012 — Yet another study has linked low vitamin D levels with significant health issues — in this case, poor cognition.

In this latest systematic review of the literature, people with Alzheimer's disease (AD) had lower concentrations of vitamin D than those without AD, and better cognitive test results were linked to higher vitamin D concentrations.

Overall, the results provide sufficient evidence to warrant further investigation to determine whether a cause-and-effect relationship exists, said lead author Cynthia Balion, PhD, a clinical biochemist and associate professor, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada.

"I think we have really good data now to make it clear that people need to do the interventional studies and see whether or not giving vitamin D helps people at higher risk for developing cognitive decline," Dr. Balion told*Medscape Medical News*.

The new review was published in the September 25 issue of *Neurology*.

Included Studies

Dr. Balion and colleagues searched MEDLINE, EMBASE, AMED, PsychINFO, and the Cochrane Central database for English-language studies of adults that measured vitamin D levels and included validated tests (for example, global function, executive function, psychomotor speed, attention, memory, or intelligence) as a measure of cognitive function. They accepted all recognized diagnostic criteria.

The review encompassed 37 studies, including 21 cross-sectional, 10 case-control, 1 before-after with a comparison group, and 2 prospective cohort studies, as well as 3 randomized, controlled trials (RCTs). The study sample sizes varied from 27 to 17,099 participants.

Thirty studies included only older participants, generally age 65 years or older, whereas 9 studies included only women and 2, only men. Exclusion criteria varied across studies (and included, for example, nutritional supplements, such as calcium and vitamin D; hormonal treatment; and diseases such as kidney disease, liver disease, and osteoporosis.)

All studies measured 25-hydroxyvitamin D [25(OH)D] concentrations except for 1 that measured 1,25-dihydroxyvitamin D [1.25(OH)D]; 4 studies measured both. Various vitamin D cut points were classified as deficient or insufficient (<25 nmol/L, ≥25 to 50 nmol/L, <50 nmol/L) or sufficient (≥25 nmol/L, ≥50 nmol/L, ≥50 to <75 nmol/L, >75 nmol/L).

In 14 studies, the cognition outcome included the diagnosis of dementia, which was most commonly defined according to the *Diagnostic and Statistical Manual of Mental Disorders* or National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria. Of the 24 studies that included a test of cognitive function, the most commonly used test was the Mini-Mental State Examination (MMSE).

In most cases, the relationship between vitamin D and cognition was assessed by comparing mean vitamin D concentrations between patients diagnosed with dementia and controls or mean neuropsychological test scores between vitamin D groups.

2 Meta-Analyses

There were sufficient data to conduct 2 meta-analyses. The first compared the mean 25(OH)D concentration between AD and control groups. Six cross-sectional or case-control studies comparing data from 888 participants demonstrated a lower mean 25(OH)D concentration in patients with AD than in controls. The mean difference was −15.0 nmol/L (95% confidence interval [CI], −26.2 to −3.9 nmol/L).

The researchers found that an important determinant of the statistically significant heterogeneity was the method of 25(OH)D measurement used. The competitive protein-binding assay (CPBA) explained the heterogeneity, but this method has been withdrawn from commercial use because of accuracy issues, said Dr. Balion.

When the analysis was restricted to the 4 studies that used methods other than the CPBA, the overall difference between the AD and control groups was −6.2 nmol/L (95% CI, −10.6 to −1.8 nmol/L), with results consistent across studies. Similar results were found when studies comparing any dementia against a control group used methods other than the CPBA to measure vitamin D.

Dr. Balion stressed the need for standardization of methods of measuring 25(OH)D and noted that relevant organizations are addressing this issue. In the meantime, it's important to consider the type of analytical method being used when comparing results from different studies, she said.

Lack of true standardization is "a big problem in the field right now," commented Raj C. Shah, MD, a geriatrician and associate professor of family medicine, Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, Illinois. "It's important to realize that all measurements of vitamin D are not equal."

The second meta-analysis compared mean MMSE scores between participants with 25(OH)D concentrations less than 50 mmol/L and those with concentrations of 50 mmol/L or greater; 50 mmol/L is the most common cut-point reported in these studies and is often used to define vitamin D deficiency. Eight cross-sectional and case-control studies, which included data from 2749 participants, contributed to this analysis. Taken together, these studies showed a higher average MMSE score in participants with higher vitamin D concentrations.

The average difference in MMSE score was 1.2 (95% CI, 0.5 to 1.9), although there was statistically significant heterogeneity. None of the subgroup analyses (for example, percentage of female participants, adjustment for at least age and sex) explained this heterogeneity.

Dr. Balion noted that except for 2 studies, the average MMSE score of the groups was very similar. When 4 studies that used another type of cognitive screening tool were added, the results did not change substantially.

Of the 2 cohort studies included in the analysis, the 1 that included only men reported no significant association between vitamin D and baseline cognitive impairment; in the other, however, participants with a deficiency in vitamin D had an increased risk for substantial cognitive decline over 6 years compared with those who had sufficient concentrations of the vitamin. As for the RCTs, the only study to use a supplement of vitamin D alone found no significant between-group differences for the single cognitive measure used.

Comprehensive Analysis

According to Dr. Balion, the results of this current review differ from those of 2 earlier ones because it was more comprehensive in its search strategy and in its inclusion criteria, which resulted in more articles screened (3229 vs 99 for a previous review). It also included more studies (37 vs 5 for the previous reviews). "We decided not to be limited in what we looked at," she said.

Dr. Balion pointed out that some factors affecting vitamin D concentrations, including skin pigmentation, age, genetics, and time of sun exposure and testing, were not considered by some studies. As well, she said, reverse causation can't be ruled out because older people may have poor nutrition and spend less time exposed to sunlight, a major source of vitamin D. Despite these limitations, "I'm pretty happy saying that vitamin D plays a role in brain health," she said.

How exactly vitamin D protects the brain is not clear, but research suggests that vitamin D acts as a neurosteroid, said Dr. Balion. At the molecular level, the brain can synthesize the active form of vitamin D [1,25(OH)D] within several cell types and regions, predominantly in the hypothalamus and large neurons in the substantia nigra. Many genes are regulated by vitamin D, which contributes to neuroprotection by modulating the production of such things as nerve growth factor, and regulating neurotransmitters.

The ideal concentration of vitamin D is also not really known, said Dr. Balion. "We tried to assess that with the data that we had from all these papers, and some studies show there might be this magic cut point and other studies did not really find a cut point. Most studies aren't designed to look for that because they're not outcome studies."

However, she noted that 2 cut points are recommended worldwide: 50 and 75 nmol/L. Canada, for example, recommends the upper level for bone health.

Physicians should recommend supplements for patients not getting sufficient vitamin D, said Dr. Balion. Many jurisdictions, including Canada, recommend 600 IU of vitamin D daily for older children and adults; recommendations differ for younger children and pregnant women.

Vitamin D Testing

Ontario's universal healthcare system does not provide for vitamin D testing except for certain conditions (osteoporosis, osteopenia, rickets, malabsorption syndrome, renal disease, or taking medications that affect vitamin D metabolism) because the evidence is not yet established, said Dr. Balion.

The United States has recommendations similar to Canada's, Dr. Shah notes. Americans are becoming more aware of vitamin D's health benefits and are taking more supplements; however, although the vitamin is fat soluble, and so may be safer than some other vitamins when taken at higher doses, Dr. Shah noted that it can still lead to muscle pains and gastrointestinal tract problems.

When asked to comment on this review, Dr. Shah said, "it helps clinicians like me and researchers to understand where the state of science is in this field, and it tells us we have a lot more work to do." He noted that of the 37 papers included in the review, only a few were clinical trials.

However, that may be changing. VITAL (VITamin D and OmegA-3 TriaL), a large 5-year clinical trial sponsored by the National Institutes of Health, is randomly assigning 20,000 people across the United States. The placebo-controlled trial will investigate whether vitamin D or omega fatty acid affects various aspects of health, including cognition.

Dr. Shah raised several important issues pertaining to the analysis. For one thing, results of vitamin D studies may depend on where participants live and the time of the year that testing was done.

He also noted that most studies were probably not done in diverse populations. "I suspect that subjects were mainly Caucasian," but because the United States has an increasingly diverse population, "we need to have measures of these effects in various older adults."

Dr. Shah said that as with any meta-analysis, some publication bias probably exists, with negative studies not being published or available for review.

He also questioned whether intervening through supplementation to arrive at a target vitamin D level would affect outcomes. He used the example of high-density lipoprotein, where experts believed that raising levels would reduce risks for heart disease. Preliminary research suggests that such efforts not only might not produce the expected result but also may cause some harm in terms of adverse effects.

The study was funded by the Ontario Research Coalition of Research Institutes/Centers on Health & Aging, Ontario Ministry of Long-Term Care. Dr. Balion receives research support from the Canadian Institutes of Health Research, the Agency for Healthcare Research and Quality, the Canada Foundation for Innovation (CFI), and the Ontario Ministry of Health and Long-Term Care. For disclosures for other authors, see original paper. Dr. Shah has disclosed no relevant financial relationships.

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GLI ANTAGONISTI DELL'ALDOSTERONE MIGLIORANO LA FRAZIONE DI EIEZIONE E LA CAPACITÀ FUNZIONALE, INDIPENDENTEMENTE DALLA CLASSE FUNZIONALE INIZIALE

Fonte: Heart 2012;98:1693-1700.

Attualmente le linee guida consigliano l'uso di antagonisti dell'aldosterone (AA) in pazienti con sintomi moderato-severi o severi [classe NYHA III-IV] e insufficienza cardiaca sistolica. Questa metanalisi di studi randomizzati-controllati ha raccolto dati su 1.575 pazienti arruolati in quattordici studi evidenziando nel complesso un miglioramento medio ponderato della FE del 3,2% e della classe NYHA di 0,13 nei soggetti trattati con AA rispetto ai controlli (p<0,001). Metanalisi di regressione hanno, inoltre, evidenziato che la classe funzionale basale non é predittiva di miglioramento della frazione d'eiezione (p=0,67), né della classe NYHA attuale (p=0,18).Questa evidenza supporta il recente studio EMPHASIS-HF nel suggerire una rivisitazione delle linee guida circa l'attuale limitazione dell'uso di AA in pazienti con classe NYHA III-IV.

ATORVASTATINA ED INSORGENZA DI DIABETE: ALTRE EVIDENZE...

J Am Coll Cardiol 2012; http://dx.doi.org/10.1016/j.jacc.2012.09.042.

Lo scopo dello studio è stato paragonare l'incidenza di diabete di nuova insorgenza (NOD) con la riduzione di eventi cardiovascolari (CV). Le statine riducono il numero di eventi cardiovascolari ma sembrano aumentare il rischio di diabete di nuova diagnosi. È stata paragonata l'incidenza di NOD con la riduzione di eventi CV tra 15.056 pazienti con patologia coronarica ma senza diabete al basale negli studi **TNT (Treating to New Targets)** (n = 7.595) e **IDEAL (Incremental Decrease in Endpoints Through Aggressive Lipid Lowering)** (n=7.461). Fattori di rischio per NOD sono stati considerati: glicemia a digiuno >100 mg/dl, trigliceridi a digiuno >150 mg/dl, indice di massa corporea >30 kg/m(2), e storia di ipertensione. Gli eventi CV includevano morte per patologia coronarica, infarto, ictus, e arresto cardiaco resuscitato. Tra gli 8.825 pazienti con da 0 a 1 fattori di rischio per NOD al basale, si è sviluppato NOD in 142 dei 4.407 pazienti nel gruppo trattato con atorvastatina 80 mg e in 148 dei 4.418 soggetti trattati con atorvastatina 10 mg e simvastatina da 20 a 40 mg (3.22% vs. 3.35%; hazard ratio [HR]: 0.97; 95% intervallo di confidenza [CI]: da 0.77 a 1.22). Tra i rimanenti 6.231 pazienti con da 2 a 4 fattori di rischio per NOD, NOD si è sviluppato in 448 dei 3.128 soggetti trattati con atorvastatina 80 mg e in 368 dei 3.103 soggetti trattati con bassi dosaggi di statine (14.3% vs. 11.9%; HR: 1.24; 95% CI: 1.08 to 1.42; p=0.0027). Il numero di eventi CV è stato significativamente ridotto con atorvastatina 80 mg in entrambi i gruppi a rischio per NOD. Quindi rispetto alle statine a basso dosaggio, atorvastatina 80 mg al giorno non ha aumentato l'incidenza di NOD nei pazienti con da 0 a 1 fattore di rischio, ma lo ha aumentato del 24% nei pazienti con da 2 a 4 fattori di rischio, anche se il numero di eventi CV è stato nettamente ridotto da atorvastatina 80 mg in entrambi i gruppi.

MENO LESIONI CEREBRALI TIPO ALZHEIMER IN PAZIENTI TRATTATI CON β-BLOCCANTI

American Academy of Neurology's 65th Annual Meeting. Abstract 2171. Released January 7, 2013.

The use of beta-blockers for the treatment of hypertension was associated with fewer Alzheimer's-type brain lesions on autopsy than other antihypertensive medications, a new study shows.
The study, which is to be presented at the upcoming American Academy of Neurology meeting in March, was conducted by a team led by Lon White, MD, University of Hawaii, Honolulu.
"These results suggest that beta-blockers may have some special benefits in reducing Alzheimer-type brain lesions," Dr. White told *Medscape Medical News*.

Honolulu-Asia Aging Study

The findings come from the Honolulu-Asia Aging Study, funded by the US National Institute on Aging, which has followed a large cohort of Japanese-American men who were aged 71 to 93 years at baseline in 1991. They have been examined every 3 years, and now autopsies have started to be performed after the death of the participants.
"One of the key issues to be addressed in the study is how to prevent the development of late-life dementia, which affects about 30-40% of people, the most common form being Alzheimer's," Dr. White explained. "It is now pretty well established that the risk of Alzheimer's is related to mid-life hypertension, more so than late-life hypertension."
In this particular study, they looked at the hypertension-Alzheimer's link in more detail and extended observations to autopsy data.
"With 774 brain autopsies and information on drug use and cognition, this is the largest brain autopsy study ever done in a prospective manner," he said. "And no other study that I am aware of has looked at different treatments for hypertension in relation to Alzheimer's."
Of the 774 patients, both with and without clinical signs of dementia, for whom brain autopsies were available, 610 had been hypertensive or treated with antihypertensive drugs. Drugs used as monotherapy for the treatment of hypertension included beta-blockers (40 patients), angiotensin-converting enzyme inhibitors (n = 35), diuretics (n = 60), calcium blockers (n = 103), and vasodilators (n = 13). In addition, 43 patients were taking beta-blockers in combination with other antihypertensives and 46 were taking other combinations of antihypertensives.
The average age at death was 86 to 87 years in all groups. Education status was similar in all groups, and the incidence of diabetes varied from 17% to 30%. The *LPA4* gene was not related to drug treatment. Logistic and linear regression analyses were performed to control for potential biases.
Results showed that patients who had had hypertension and had been taking beta-blockers had fewer Alzheimer-type lesions (both neurofibrillary tangles and amyloid plaques) than those taking no drug therapy or those taking other medications. There was also a significant but less dramatic reduction in infarcts in the small arteries of the brain (a vascular marker of dementia) in patients who had been taking beta-blockers.
The lowest-level Alzheimer's lesions were seen in the patients who did not have hypertension. The group who had been taking beta-blockers had low levels of lesions similar to those of the nonhypertensive group, Dr. White reported. Those who had received beta-blockers plus other medications had intermediate or marginally fewer brain abnormalities.

'First Hint' of Effect

"This is the first hint that different kinds of antihypertensive therapy might have differential effects on Alzheimer's lesions and other brain lesions," Dr. White said. But he cautioned that the numbers are small and nothing definite can be concluded. "This is just a clue that perhaps beta-blockers may be potentially a good choice of antihypertensive for preventing Alzheimer's. But we are obviously a long way from making clinical recommendations."
Speculating on the mechanism, Dr. White noted that beta-blockers reduce pulse rate, which might have an effect on small vessel micro-infarcts in the brain. "Lifelong exposure of the pulse pressure in the brain might cause some damage," he said. "While we thought beta-blockers may reduce brain micro-infarcts, which they

did, we actually saw a larger reduction in the Alzheimer-type lesions which we had not expected. This is somewhat of a mystery at present and may be a chance finding. But if it is a real effect I would think it was something to do with autonomic function."
Dr. White suggested that a reasonable next step could be to test this hypothesis in mice genetically engineered to produce these Alzheimer's lesions. "If we treat these mice with beta-blockers and they develop fewer lesions, then we will know that it is an effect of the drugs," he commented.

LA PAPAIA INTERAGISCE CON LA DIGITALE

Questo studio ripropone la problematica delle interferenze farmacologiche tra erbe medicinali e farmaci, in particolare la digitale, senz'altro uno dei farmaci più comuni somministrati nell'anziano. In questo lavoro sperimentale sono state cimentate semplici droghe vegetali ed è stato dimostrato che la papaia, integratore comunemente utilizzato in Italia nell'anziano, sembra aumentare significativamente la biodisponibilità della digossina ponendo quindi il cardiopatico e in particolare l'anziano, che di per sé ha frequentemente una ridotta clearance dei farmaci, a rischio di alterazioni sia della farmacodinamica che farmacocinetica della digossina, una sostanza utile a dosaggi appropriati, ma pericolosamente aritmogena quando raggiunge dosaggi plasmatici superiori alla norma.

Postgrad Med. 2012 Nov;124(6):110-6. doi: 10.3810/pgm.2012.11.2589.

DONEPEZIL A DOSI ELEVATE (23 MG/DIE) PER IL TRATTAMENTO DEI PAZIENTI CON MALATTIA DI ALZHEIMER MODERATO-SEVERA.

Christensen DD.

Source

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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that primarily affects the elderly. An estimated 5.4 million people in the United States have AD, and its prevalence is expected to increase rapidly in the coming years. Few US Food and Drug Administration (FDA)-approved treatment options for AD are currently available. Donepezil is 1 of only 2 therapies approved in the United States for the treatment of moderate-to-severe AD. In 2010, the FDA approved a higher daily dose of donepezil (23 mg/day) for the treatment of AD in the moderate-to-severe stages based on positive results from a large, global, phase 3 clinical trial that compared switching to donepezil 23 mg/day with continuing treatment with donepezil 10 mg/day. In that trial, no benefit was seen in the co-primary endpoint of global functioning; however, donepezil 23 mg/day provided a small but significant improvement in the cognitive endpoint compared with donepezil 10 mg/day. A subgroup analysis subsequently showed that the cognitive benefits were significant irrespective of concomitant memantine use. Adverse events were mainly gastrointestinal related and were more prevalent in patients receiving the donepezil 23-mg/day dose during the first month of therapy, but were relatively infrequent thereafter. These data indicate that once-daily donepezil 23 mg may be an effective treatment option for patients with moderate-to-severe AD with or without concomitant memantine. This article reviews the rationale for using higher-dose donepezil, the clinical data supporting its use, and some of the practical implications that should be considered by practicing physicians when using donepezil 23 mg/day for patients with AD.

CHI È STATO BILINGUE SIN DA PICCOLO PRESENTA MIGLIORI ABILITÀ COGNITIVE

Gli anziani che fin da bambini hanno parlato due o più lingue invecchiano meglio soprattutto per quanto riguarda le abilità cognitive. A dirlo è il College of Medicine della University of Kentucky dove il professor Brian Gold ha studiato un centinaio di volontari di età compresa tra i 60 e i 68 anni, bilingui e non.
Sottoposti a test di memoria i bilingui sono risultati più veloci nel gestire contemporaneamente due compiti diversi. Nei soggetti giovani non si sono osservate differenze nelle prestazioni. Lo studio, pubblicato sul *Journal of Neuroscience*, suggerisce che a essere meno compromessa negli anziani bilingui sia la flessibilità, forse proprio per il continuo controllo cognitivo necessario per passare da una lingua all'altra. Utilizzando la risonanza magnetica funzionale, sono stati osservati diversi modelli di funzionamento neurale nei due gruppi di anziani.
Il vantaggio dei bilingui sarebbe dovuto a una minore attivazione di alcune aree prefrontali, nella corteccia anteriore del cingolo e nella corteccia prefrontale dorsolaterale e dorsoventrale sinistra, vale a dire nelle aree della working memory, dove si mantengono le informazioni in modo temporaneo e dove vengono manipolate.

LE FUNZIONI COGNITIVE INFLUENZANO LA CAPACITÀ DI TRAINING PER ESERCIZIO FISICO IN ANZIANI CON MCI

Background: Although much evidence supports the hypothesis that cognitive function and physical function are interrelated, it is unclear whether cognitive decline with mild cognitive impairment influences trainability of physical performance in exercise intervention. The purpose of this study was to examine the association between cognitive function at baseline and change in physical performance after exercise intervention in older adults with mild cognitive impairment.
Methods: Forty-four older adults diagnosed with mild cognitive impairment based on the Peterson criteria (mean age 74.8 years) consented to and completed a 6-month twice weekly exercise intervention. The Timed Up and Go (TUG) test was used as a measure of physical performance. The Mini-Mental State Examination (MMSE), Trail Making Test Part B, Geriatric Depression Scale, baseline muscle strength of knee extension, and attendance rate of intervention, were measured as factors for predicting trainability.
Results: In the correlation analysis, the change in TUG showed modest correlations with attendance rate in the exercise program ($r = -0.354$, $P = 0.027$) and MMSE at baseline ($r = -0.321$, $P = 0.034$). A multiple regression analysis revealed that change in TUG was independently associated with attendance rate ($\beta = -0.322$, $P = 0.026$) and MMSE score ($\beta = -0.295$, $P = 0.041$), controlling for age and gender.
Conclusion: General cognitive function was associated with improvements in physical performance after exercise intervention in subjects with mild cognitive impairment. Further research is needed to examine the effects of exercise programs designed to address cognitive obstacles in older adults with mild cognitive impairment.

Clinical Interventions in Aging 2013:8 97–102