

Correlation between basal serum IGF-1 levels and functional autonomy in elderly women.

Correlación entre los niveles séricos de IGF-1 basal y autonomía funcional en ancianas.

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Abstract

The aim of the present study was to determine the degree of correlation between basal serum IGF-1 levels and functional autonomy in the performance of activities of daily living (ADL). The sample comprised 11 elderly individuals, disregarding their ADLs (age = 68.18 ± 5.19 years; body mass index (BMI) = 28.89 ± 3.44 kg/m²) and not enrolled in physical exercise programs for at least 3 months. The subjects were submitted to a battery of 5 functional autonomy tests from the GDLAM protocol and blood collection to assess serum IGF-1 levels. Using Pearson's correlation, we found a significant mean correlation coefficient (r) between the 10 m walking test (10mW) and IGF-1 ($r = -0.690$; $p = 0.009$) and mean correlation, but not significant between the putting on and removing a t-shirt test (PRTS) and IGF-1 ($r = -0.528$) and between the general autonomy index (AI) and IGF-1 ($r = -0.417$). The correlation was low in the remaining tests, but inverted. This suggests that the decline in IGF-1 with age may decrease ADL performance in the elderly.

Key words: Serum IGF-1; ADL; elderly.

Resumen

El objetivo del presente estudio fue comprobar el nivel de correlación entre los niveles de séricos basales de IGF-1 y la autonomía funcional para la realización de actividades de la vida diaria en personas mayores (edad = $68,18 \pm 5,19$ años; índice de la masa corporal, IMC= $28,89 \pm 3,44$ kg/m²), no participantes en programas de ejercicios físico desde hace un mínimo de 3 meses. Los sujetos fueron sometidos a una batería de 5 tareas de autonomía funcional del protocolo GDLAM y a un análisis de sangre para evaluar los niveles de séricos de IGF-1. A través de la correlación de Pearson se comprobó la existencia de un coeficiente de la correlación (r) medio y significativo entre el examen de la marcha 10m (C10m) y el IGF-1 ($r = -0,690$; $p = 0,009$) y la correlación media, pero no significativa, entre el test de vestirse y quitarse una camiseta (VTC) y el IGF-1 ($r = -0,528$), y entre el índice general de la autonomía (IG) y el IGF-1 ($r = -0,417$). En los demás test la correlación fue baja e inversa. Estos resultados sugieren que el descenso del IGF-1 con el envejecimiento puede disminuir el desempeño en las AVD (poner actividades de la vida diaria, o poner estas iniciales al principio del resumen de las personas mayores).

Palabras clave: concentración sérica de IGF-1; Actividades de la vida cotidiana; personas mayores.

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Introduction

Hormone activity seems to be strongly influenced by the passage of time, especially among growth factors (IGF) (Conceição et al., 2003). The most important of these is the Insulin-Like Growth Factor-1 (IGF-1), which has a structure similar to that of insulin, and which may influence cell growth, differentiation and metabolism (Kjaer, 2004).

IGF-1 is considered one of the most important protein anabolic agents in the body and is essential to protein synthesis throughout life (Kjaer, 2004). This hormone has a narrow relation with muscle mass, conservation of the skeletal muscle system, metabolic rate and muscle strength (Cappola et al., 2001; Manini et al., 2005; Moran et al., 2007), and can be synthesized in the same cell in which it acts (autocrine) or in neighboring cells (paracrine) (Eliakin et al., 2000; Moran et al., 2007).

IGF-1 and its carrier protein (IGFBP-3) have positive correlations related to obesity, changes in body composition and protein synthesis in the elderly (Thomas et al., 2003). Singh et al., (1999) showed that, despite the presence of atrophy and ultrastructural compromise associated to aging, the skeletal muscle fibers of elderly individuals may regenerate with increased IGF-1 and the development of myosin heavy chain as a response to strength training. This adaptation may increase with nutritional supplementation and regular physical exercise (Rubin et al., 2005).

Various situations may intervene in the IGF-1 levels of elderly individuals, given that the harmful effects of aging reduce its secretion (Eliakin et al., 2000). An unbalanced diet, low levels of physical activity, alcohol ingestion and impaired liver function are factors that may also compromise its release. Thus, this decline may be related to diminished muscle mass and strength, increased adipose mass and decreased mobility (Rubin et al., 2005; Woodhouse et al., 1999). Hence, older adults may become more susceptible to diseases and to dependence, and as a result, reduce their functional autonomy (Ruiz-Torres and Kirzner, 2002).

This being so, the aim of this study was to assess the relation between basal serum IGF-1 levels and functional autonomy in elderly individuals during the performance of activities of daily living (ADL).

Material and methods

Sample

Eleven healthy older adults took part in the study, independent of their activities of daily living (age = 68.18 ± 5.19 years; body mass index (BMI) = 28.89 ± 3.44 kg/m²). All the subjects were volunteers who had not engaged in physical activity for at least three months.

The following exclusion criteria were adopted: individuals younger than 60 years of age; those undergoing hormone replacement; those with any disease or condition that contraindicated a physical training program and the performance of autonomy tests; those considered incapable of undergoing medical assessment.

This study was approved by the Institutional Ethics Committee and met the norms for research in human beings (resolution 196/96) of the National Health Council. All the subjects signed a free and informed consent form.

Procedures

To assess body mass, height and body mass index (BMI), we used a mechanical scale with stadiometer, to the nearest 100 grams, with a 150 kilogram capacity (Filizola, Brazil).

Assessment of functional autonomy

To determine ADL performance and calculate the autonomy index (AI), we used the GDLAM protocol of functional autonomy (Dantas and Vale, 2004; Vale, 2005) as follows: a) walk 10 meters as fast as possible (Sipilä et al., 1996; b) rise from a sitting position five times (Guralnik et al., 1994); c) rise as fast as possible from a ventral decubitus position (Alexander et al., 1996); d) rise from a chair and walk five meters in a straight line, circle a cone located diagonally to the right, return and sit down, then rise and walk five meters, circle a cone diagonally to the left, and repeat the entire procedure one more time (Andreotti and Okuma, 1999); and e) put on and remove a t-shirt, with the individuals standing, arms to the side of their body and with a size G t-shirt (Hering, Brazil) in one of their hands (on the dominant side) (Dantas and Vale, 2004; Vale et al., 2006). The subjects performed the tests twice, with the better score recorded, in seconds, with a chronometer (Casio, Brazil). The reference values (Table 1) follow GDLAM standards (Vale, 2005).

Table 1: Assessment of GDLAM functional autonomy

Tests Classif.	10mW (sec)	RSP (sec)	RVDP (sec)	PRTS (sec)	RCMH (sec)	AI (scores)
Weak	+ 7.09	+ 11.19	+ 4.40	+ 13.14	+ 43.00	+ 27.42
Fair	7.09-6.34	11.19-9.55	4.40-3.30	13.14-11.62	43.00-38.69	27.42-24.98
Good	6.33-5.71	9.54-7.89	3.29-2.63	11.61-10.14	38.68-34.78	24.97-22.66
Very Good	- 5.71	- 7.89	- 2.63	- 10.14	- 34.78	- 22.66

10mW = walk 10 meters; RSP = rise from a sitting position; RVDP = rise from a ventral decubitus position; PRTS = put on and remove a t-shirt; RCMH = rise from a chair and move around the house; values in seconds. AI = GDLAM autonomy index; values in seconds.

Analysis of serum IGF-1 and IGFBP3 levels

Blood was collected from the subjects at 7:00 after 12 hour fast, to measure basal IGF-1 and IGFBP3 serum levels in a clinical analysis laboratory. IGF-1 and IGFBP3 were analyzed using the chemiluminescence method – IMMULITE – DPC MED LAB (closed vacuum system). The reference values followed the mean age group of the sample (66 to 70 years): IGF-1 – 69 to 200 ng/mL; IGFBP3 – 3.0 to 6.2 µ/mL (IPCHP, 2007).

Statistical Analysis

The data were analyzed by SPSS software, version 14.0 and presented as mean and standard deviation. The Shapiro-Wilk test was used to analyze normality of the data and Pearson's correlation to determine the level of association between the variables. A significance level of $p < 0.05$ was set for all the tests.

Results

Table 2 describes the results of the sample. The classification level, according to GDLAM standards (Table 1), was considered weak for the 10mW, RSP and RCMH tests, fair for RDVP and good for PRTS. However, overall functional autonomy for activities of daily living, represented by the general autonomy index (AI), was weak.

Serum IGF-1 levels were normal for the mean age. Mean IGFBP3 levels were slightly below the reference levels.

Table 2: Results of functional autonomy tests and IGF-1 levels

	Mean \pm (SD)	p-value (SW)
10mW	7.21 \pm 0.81	0.541(NS)
RSP	11.46 \pm 2.40	0.872(NS)
RVDP	3.49 \pm 0.80	0.112(NS)
PRTS	11.29 \pm 2.02	0.167(NS)
RCMH	45.32 \pm 4.27	0.309(NS)
AI	27.68 \pm 3.23	0.263(NS)
IGF-1	80.55 \pm 27.95	0.758(NS)
IGFBP3	2.85 \pm 0.59	0.473(NS)

10mW = walk 10 meters; RSP = rise from a sitting position; RVDP = rise from a ventral decubitus position; PRTS = put on and remove a t-shirt; SCMH = rise from a chair and move around the house; time in seconds. AI = GDLAM autonomy index; score values; IGF-1 = ng/mL; IGFBP3 = ng/mL; SD = standard deviation; SW = Shapiro-Wilk test; NS = not significant.

The association between the variables is described in table 3. It can be observed that IGF-1 and 10mW had a statistically significant mean Pearson's correlation coefficient (r). This suggests that the higher the IGF-1 level the less time will be needed to perform the 10mW test. The same result was not obtained with the other variables, but the coefficients found showed a non-significant inverse correlation, given that the "r" value found for IGF-1/PRTS and IGF-1/AI were within the mean range.

Table 3: Correlation analysis (IGF-1/GDLAM protocol)

		10mW	RSP	RVDP	PRTS	RCMH	AI	IGF-1
IGF-1	r	-.690(*)	-0.005	-0.021	-0.528	-0.318	-0.417	-
	p-value	0.009	0.987	0.945	0.063	0.289	0.156	-
IGFBP3	r	-0.060	0.367	0.071	-0.349	0.229	0.140	0.068
	p-value	0.860	0.268	0.835	0.293	0.498	0.680	0.851

*p<0.01

Discussion

The results of this study show a significant negative correlation between serum IGF-1 levels and functional autonomy in performing the activities of daily living (ADL).

The functional autonomy levels of the sample are lower than those found in other studies (Pereira et al., 2007; Vale, 2005), but IGF-1 and IGFBP3 levels are normal for the age group (Beld et al., 2003).

These findings are corroborated by Onder et al. (2006), who found faster walking speeds in elderly individuals with higher serum levels of this hormone. This may explain the results of the present study, since the 10mW test had the highest significant inverse correlation of all the GDLAM protocol tests. The 10mW was performed more rapidly, representing a faster walking speed, which may prolong the functional autonomy of these individuals.

Cappola et al. (2003) analyzed the association between IGF-1 and interleukin II (IL-II) and activities of daily living (ADL). They concluded that the elderly subjects who had a high level of difficulty in performing ADL also had low IGF-1 levels associated to high levels of IL-II. This might explain the findings of the current study, in which, among the battery of functional autonomy tests used, 10mW, PRTS and AI obtained similar results. RSP and RCMH and RVDP were also classified as weak and regular (Vale, 2005), respectively, but without a strong correlation.

One of the factors that may be related to functional autonomy is muscle strength. This tends to remain at optimal levels during regular physical activity and up to approximately 12 weeks after interrupted strength training (Rubio et al., 2007).

Thus, studies on strength training have obtained positive functional autonomy results (Pereira et al., 2007) and elevated serum IGF-1 concentrations (Cassilhas et al., Cress et al., 2004; Hand et al., 2007) in elderly subjects. Therefore, reduced muscle strength and mobility has been associated with decreased IGF-1 serum levels. This proved to be significant with lower extremity strength tests and walking speed (Cappola et al., 2001). This confirms the responses found in the present study. Although strength was not tested, the association between IGF-1 levels and shorter 10mW test completion times corroborated the hypothesis. Furthermore, a correlation was shown between mean correlation on the PRTS test and the general autonomy index (AI).

However, Lambert et al. (2007) investigated frail elderly individuals and found no relation between muscle strength assessed by the 1-RM test and the IGF-I/IGFBP3 ratio after 12 weeks of strength training using 80% of maximum load. On the other hand, a significant correlation was found between this ratio and both lean and muscle mass, which expresses muscle strength gains. Thus, these results suggest an association between these variables. All that remains is to adapt the instrument to assess muscle strength. The findings of the current study are reinforced when it is observed that elderly persons need this physical quality to execute ADL.

Amir et al. (2007) also corroborate these findings, since they found sharp increases in IGF-1 after anaerobic stimuli (Wingate's test) in fit elderly individuals. They concluded that this type of exercise may be important for minimizing the loss of muscle mass and of physical functions by significantly elevating circulating IGF-1 levels. This indicates that the physically active elderly may also prolong their functional autonomy, confirming the correlations found in this study.

Beld et al. (2003) tested the association between IGF-1, IGFBP-2 and IGFBP-3 and physical functions in the elderly and concluded that low serum IGF-1 concentrations allow IGFBP2 levels to increase and that they have a negative and significant influence on ADL, physical performance and muscle strength. They also found low serum concentrations of IGF-1 and IGFBP3 associated to low physical function levels. These results corroborate the present study, given that we showed a mean correlation between the serum levels of IGF-1 and 10mW, IGF-1 and PRTS, and IGF-1 and AI, suggesting that the sample should enroll in physical activity programs that develop physical strength, to stimulate greater IGF-1 and IGFBP3 secretion, and consequently improve the performance of daily tasks. This would provide elderly individuals with more independence and prolong their autonomy.

Conclusion

According to the findings of the current study, the activities of daily living are related to serum IGF-1 levels, especially in the results obtained on the 10mW test. This suggests that increased IGF-1 in the elderly may induce enhanced ADL performance. Therefore, regular hormone doses may contribute to the assessment of functional autonomy. We recommend further studies that monitor the behavior of anabolic and catabolic hormones associated to strength and stamina training interventions, to assess functional autonomy in this age group.

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References

- Alexander, N.B.; Ulbric, H.J.; Raheja, A.; Channer, D. (1997). Rising from the floors in older adults. *J Am Geriatr Soc*, 136(5),564–569.
- Amir, R.; Ben-Sira, D.; Sagiv, M. (2007). IGF-I and FGF-2 responses to Wingate anaerobic test in older men. *J S S M*, 6, 227-232.
- Andreotti, R.A.; Okuma, S.S. (1999). Validação de uma bateria de testes de atividades da vida diária para idosos fisicamente independentes. *Rev Paul Educ Fis*, 13(1),46-66.
- Beld, A.W.; Blum, W.F.; Pols, H.A.P.; Grobbee, D.E.; Lamberts, S.W.J. (2003). Serum insuline-like growth factor binding protein-2 levels as an indicator of functional ability in elderly men. *Eur J Endocrinol*, 148,627-634.
- Cappola, A.R.; Bandeen-Roche, K.; Wand, G.S.; Volpato, S. & Friedl, L.P.A. (2001). Association of IGF-1 levels with muscle strength and mobility in older women. *J Clin Endocrinol Metab*, 86, 4139-4146.
- Cappola, A.R.; Xue, Q-L.; Ferrucci, L.; Guralnik, J.M.; Volpato, S. & Friedl, L.P.A. (2003) Insuline-like growth factor I and interleukin-6 contribute synergistically to disability and mortality in Older Women. *J Clin Endocrinol Metab*,88, 2019-2025.
- Cassilhas, R.C.; Viana, V.A.R.; Grassmann, V.; Santos, R.T.; Santos, R.F.; Tufik, S.; Mello, M.T. (2007). The impact of resistance exercise on the cognitive function of the elderly. *Med Sci Sports Exerc*, 39(8),1401-1407.
- Conceição, F.L.; Boguszewski, C.L.;Meister, L.H.F.; Zaninelli, D.C.T.;Radominski, R.B.; Knoepfelmacher, M.; Vaisman, M. (2003). Deficiência de GH em adultos: resultados do estudo Multicêntrico Brasileiro. *Arq Bras Endocrinol Metab*, 47(4),312-322.
- Cress, M.E.; Buchner, D.M.; Prohaska, T.; Rimmer, J.; Brown, M.; Macera, C.; De Pietro, L.; Chodzko-Zajko, W. (2004). Physical activity programs and behavior counseling in older adult populations. *Med Sci Sports Exerc*, 36(11), 1997-2003.
- Dantas, E.H.M.; Vale, R.G.S. (2004). Protocolo GDLAM de avaliação da autonomia. *Fit Perf J*, 3(3),169-180.
- Eliakin, A.; Oh, Y.; Cooper, D.M. (2000). Effect of single wrist exercise on fibroblast growth factor-2, insulin-like growth factor, and growth hormone. *J Appl Physiol*, 279(2),R548-R553.
- Guralnik J.M.; Simonsick, E.M.; Ferrucci, L.; Glynn, R.J.; Berkman, L.F.; Blazer, D.G.; Scherr, P.A.; Wallace, R.B. (1994). A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol Med Sci*, 49(2),M85–M94.
- Hand, B.D.; Kostek, M.C.; Ferrell, R.E.;Delmonico, M.J.; Douglass, L.W.; Roth, S.M.; Hagberg, J.M.; Hurley, B.F. (2007). Influence of promoter region variants of insuline-like growth factor pathway genes on the strength-training response of muscle phenotypes in older adults. *J Appl Physiol*, 103,1678-1687.
- Instituto de Patologia Clínica Hermes Pardini (IPCHP). *Manual de exames*. Belo Horizonte, 2007/2008.
- Kjaer, M. (2004). Role of extra cellular matrix in adptation of tendon and skeletal muscle to mechanical loading. *Physio Rev*, 84,649-698.
- Lambert, C.P.; Bopp, M.M.; Johnson, L.E.; Sullivan, D.H. (2007). Resistance training and testosterone replacement induced changes in body composition, free testosterone, IGF-I, and IGFBP-3 in the frail elderly. *JEPonline*, 10(1),48-56.
- Manini,T.M. ; Druger, M. & Snyder-Ploutz, L. (2005). Misconceptions about strength exercise among older adults. *J Aging Phys Activity*, 13(4), 422-433.
- Moran, S., Chen, Y.; Ruthie, A.; Nir, Y. (2007). Alterations in IGF-1 affect elderly: role of physical activity. *Eur Rev Aging Phys Act*, 4,77-84.

- Onder, G.; Liperoti, R.; Russo, A.; Soldato, M.; Capoluongo, E.; Volpato, S.; Cesari, M.; Ameglio, F.; Bernabei, R.; Landi, F. (2006). Body mass index, free insuline-like growth factor I, and physical function among older adults: results from the iSIRENTE study. *Am J Physiol Endocrinol Metab*, 291,E829-E834.
- Pereira, F.F.; Monteiro, N.; Vale, R.G.S.; Gomes, A.L.M.; Novaes, J.S.; Faria Jr, A.G.; Dantas, E.H.M. (2007). Efecto del entrenamiento de fuerza sobre la autonomía funcional en mujeres mayores sanas. *Rev Esp Geriatr Geront*, 42(6),319-324.
- Rubin, M.R.; Kraemer, W.J.; Maresh, C.M.; Volek, J.S.; Ratamess, N.A.; Vanheest, J.L.; Silvestre, R.; French, D.N.; Sharman, M.J.; Judelson, D.A.; Gómez, A.L.; Vescovi, J.D.; Hymer, W.C. (2005). High-affinity growth hormone binding protein and acute heavy resistance exercise. *Med Sci Sports Exerc*, 37(3),395-403.
- Rubio, R.M.A.; Ureña, G.D.; Rave, J.M.G.; Santos-Garcia, D.J.; Valdivielso, F.N. (2007). Efecto sobre la mejora y retención de la fuerza de un programa de entrenamiento de fuerza con cargas concentradas en sujetos no entrenados. *Revista Internacional de Ciencias del Deporte*. 7(3), 24-33.<http://www.cafyd.com/REVISTA/00703.pdf>
- Ruiz-Torres, A.; Kirzner, M.S.M. (2002). Ageing and longevity are related to growth hormone/insulin-like growth factor-1 secretion. *Gerontology*, 48,401-407.
- Singh, M.A.F.; Ding, W.; Manfredi, T.J.; Solares, G.S.; O'Neill, E.F.; Clements, K.M.; Ryan, N.D.; Kehayias, J.J.; Fielding, R.A.; Evans, W.J. (1999). Insulin-like growth factor-I in skeletal muscle after weight-lifting exercise in frail elders. *Am J Physiol Endocrinol Metab*, 277(1),E135-E143.
- Sipilä, S.; Multanen, J.; Kallinen, M.; Era, P.; Suominen, H. (1996). Effects of strength and endurance training on isometric muscle strength and walking speed in elderly women. *Acta Physiol Scand*, 156,457-464.
- Thomas, S.G.; Esposito, J.G.; Ezzat, S. (2003). Exercise training benefits growth hormone (GH)-deficient adults in the absence or presence of GH treatment. *J Clin Endocrinol Metab*, 88(12),5734-5738.
- Vale, R.G.S. (2005). Avaliação da autonomia funcional do idoso. *Fit Perf J*, 4(1),4.
- Vale, R.G.S.; Pernambuco, C.S.; Novaes, J.S.; Dantas, E.H.M. (2006). Teste de autonomia funcional: vestir e tirar uma camiseta (VTC). *R bras Ci e Mov*, 14(3),71-78.
- Woodhouse, L.J.; Asa, S.L.; Thomas, S.G.; Ezzat, S. (1999). Measures of submaximal aerobic performance evaluate and predict functional response to growth hormone (GH) treatment in GH-deficient adults. *J Clin Endocrinol Metab*, 84(12),4570-4577.