Vitamin D(25-OH-cholecalciferol) in Cystic Fibrosis and the Relations with Cholesterol and Proteins

IOANA MIHAIELA CIUCA[1], LIVIU LAURENTIU POP[1], MIHAELA DEDIU[1], SONIA ANIELA TANASESCU[1]*, FLORINA ARDELEAN[2], GHEORGHE IOVANESCU[1], ESTERA BOERIU[1], CRISTINA DALIBORCA VLAD[1], MONICA STELUTA MARC[1], BOGDAN ALMAJAN GUTA[3]

[1] Victor Babes University of Medicine and Pharmacy Timisoara, Faculty of Medicine, 2 Eftimie Murgu Sq., 300041, Timisoara, Romania

[2]West University, Sport and Physical Activity Department , 4 Vasile Parvan Boulevard, Timisoara, Romania

Study aimed to assess the level of 25-OH-cholecalciferol(vitamin D) and the relation with cholesterol, proteins and glycaemia levels in patients with cystic fibrosis. 58 patients underwent for the annual evaluations and were tested for vitamin D deficiency, as the centre's protocol requires, besides dosage of cholesterol, glycaemia and proteins levels. Serum levels of 25-hydroxycholecalciferol were compared to levels of cholesterol, proteins and glycaemia, using Pearson correlation and logistic regression. The average value of 25-OH-cholecalciferol was 22,9 ng/mL, suggesting an important deficiency and different stages of 25-OH-cholecalciferol deficiency was found in the majority of patients. Nor a positive correlation neither negative relationship was found between vitamin D and cholesterol (r=0,23), glycaemia or proteins level. Vitamin D levels are not related to cholesterol or proteins in our study. Although cystic fibrosis is characterised by liposoluble vitamins deficiency and lipids impaired digestion, other factors influence the seric levels of vitamin D and lipids.

Keywords: vitamin D, cystic fibrosis, cholesterol

25-OH-cholecalciferol(known as Vitamin D) is an inactive precursor of the main active form 1,25-dihydroxyvitamin D [1] , which has anti-inflammatory action [2], antimicrobial [3] and antiviral influence [4] It was noticed that adequate vitamin D is probable to decrease the risk of severe infections [5], childhood asthma [6], asthma exacerbation [7] and infectious diseases [8] like tuberculosis [9] or other respiratory exacerbations [10] Vitamin D can be produced in the skin (5), under ultraviolet action, by exposure of 7-dehydrocholesterol present in membrane to sunlight or ultraviolet light irradiation [11] which causes the production of vitamin D3 (cholecalciferol) [12]. But the main basis is exogenous: D_3 (cholecalciferol) from animals and vitamin D_2 (ergocalciferol) from vegetables [13]. Both vitamins D2 and D3 are metabolized in the liver and the kidney into the active form 1,25-dihydroxyvitamin D [14]. 25-hydroxyvitamin D is commonly measured to assess and monitor the vitamin D status in individuals, being the most dosed form in the serum and a useful tool for deficiency estimation.

Cystic fibrosis is a genetic disease expressed by chronic obstructive pneumopathy [15], pancreatic insufficiency with chronic diarrhoea and several secondary complications [16] like liver disease [17] with complicated cirrhosis [18], osteoporosis or diabetes [19]. Because of the pancreatic exocrine deficiency, reduced capacity for vitamin D storing in adipose tissue, a deficiency in liposolubles vitamins occur [20], with complications like osteoporosis, osteopenia [21], frequently infections and modified biochemistry influenced by multiple factors like environment or smoking [22]. Absorption of lipids is diminished by the maldigestion of lipids and protein because of the pancreatic insufficiency, therefore reduced levels of lipid-dependent nutrients are associated and protein, glucides metabolism impairment. Also, the protein metabolism might be impaired by the proteins maldigestion and absorbtion secondary to insufficiency of the proteolytic enzymes absent lacking pancreatic enzymes, therefore an appraisal of protein level would be of an interest [5]. Between the biomarkers considered for their potential role in detecting the CF complications, vitamin D is a reliable and accurate parameter, its level being influenced by the lipid intake, and metabolism [20].

The aim of the paper is to evaluate the serum level of 25-OH-cholecolesterol (vitamin D) in the group of cystic fibrosis patients and the relations with cholesterol, proteins serum levels and glycaemia.

Experimental part

Methods

58 patients underwent for the biannual evaluations and were tested for vitamin D deficiency, as the centre's protocol requires, besides dosage of cholesterol, glycaemia and proteins levels. The blood serum obtained by centrifugation was utilised for dosage with different methods and the assay for quantitative measurements of the vitamin D, cholesterol, glycemia and protein , in the Clinical County Hospital Timisoara Laboratory. 25-OH-cholecalciferol was measured using quantitative tests of 25-OH-cholecalciferol by liquid chromatography–tandem mass spectrometry . The reference range of the total 25(OH)D level is 10-100 ng/mL and the deficiency was quantified as follow: severe deficiency< 10 ng/mL, deficiency (10-30 ng/mL, insufficiency (30- 50 ng/mL). For cholesterol dosage an enzymatic colorimetric assay and the acceptable range values were considered between 100 mg/dL-160 mg/dL. Glycaemia was measured by glucose colorimetric assay and fasting plasmatic glucose values were normal if between 70-99 mg/dL. Statistical analysis used the Pearson correlation test for the

* email: sonia.tanasescu@yahoo.com

comparison of 25-OH-cholecalciferol with other numeric values of cholesterol, glycaemia and proteins levels. The cut-off value for the p statistic value was <0.05 in order the results to be considered statistically reliable. SPSS was used for statistical analysis. The patients and patient's tutors agreed with the study and signed informed consensus, also the Hospitals Ethics Committee approval was obtained.

Results and discussions

The average value of 25-OH-cholecalciferol was 22.94 ng/mL, and the different stages of 25-OH-cholecalciferol found in the majority of patients ; only 24.14% had normal vitamin D range. Cholesterol average value 108.03 mg% , the median value for glycaemia 95.58mg% and total protein average was normal 7.34 g%.

25-hydroxyvitamin D and Cholesterol

Comparing the values of and cholesterol by linear regression we found the correlation coefficient of r= 0.23 (p=0.07) which did not showed a relation between the level of vitamin D , a liposoluble vitamin and cholesterol (fig. 1).

We did not find a statistic correlation, between the two parameters, probably because of the predominance of endogenous cholesterol synthesis. In the human body, about 80% of total cholesterol concentration is obtained endogenously, especially when exogenous intake and absorption is low, like in our CF patients. Considering that, we would be expecting a positive relation between the parameters, but the result infirmed it, which is a result that suggest that not only the absorption would be responsible for the deficit and further mechanism are intricate.

25-hydroxyvitamin D and proteins values

In the second analysis, we interrelate the vitamin D value with proteins levels and , relation expressed in the figure 2, where no correlation was found between vitamin D and cholesterol level.

We applied the same statistical linear regression test and obtained the Pearson correlation index that has a value of r=0.162, with a statistical value of 0.64, showing that there is no correlation between the 25-OH-cholecalciferol value and the serum protein level at patients with cystic fibrosis studied. Although the coefficient was low, the statistical power was low, because of a not significant p value which suggest that the relation was not a statistic significant one. It seems that the vitamin D deficiency associated with cystic fibrosis does not impair the protein levels.

25-hydroxyvitamin D and glycaemia

The correlation between vitamin D and Pearson's correlation coefficient r2 was -0.05, and 95% confidence interval (-1.556- 69.522), with a p value of 0.667, denies the existence of a correlation between the two compared variables. We did not find any relation between the level of the vitamin D and the glycemia values in cystic fibrosis patients, although some studies suggest the effect of the vitamin D deficiency in diabetes occurrence and impaired glucose tolerance [23].

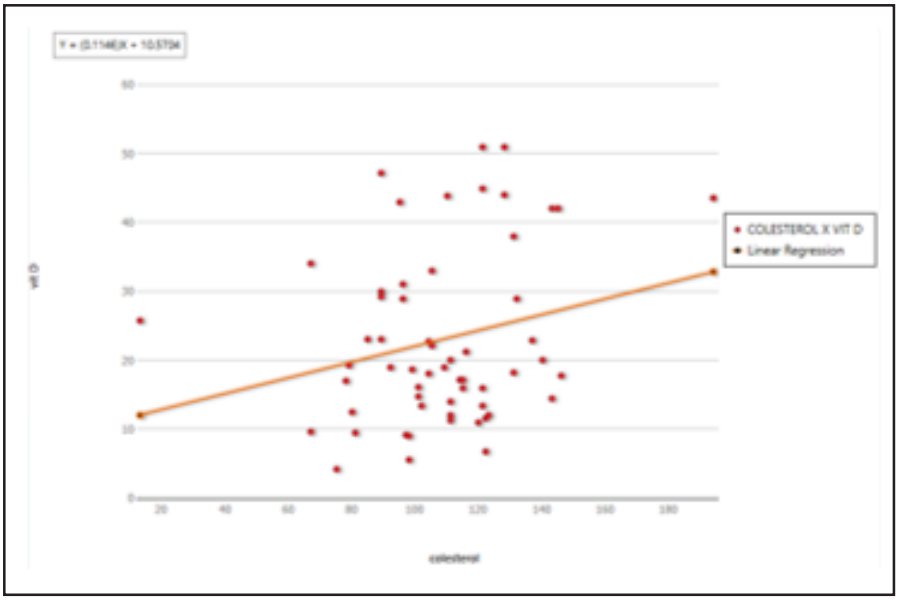

Fig. 1. 25-hydroxyvitamin D and cholesterol linear regression

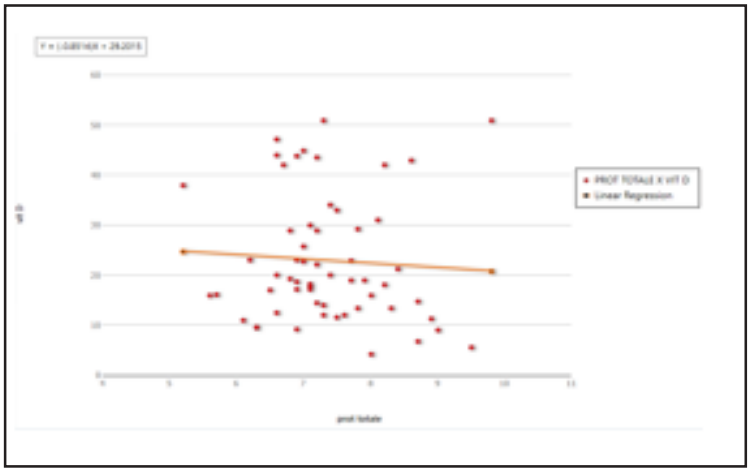

Fig. 2. 25-hydroxyvitamin D and levels of protein-regression analysis

Conclusions

The paper revealed that the level of 25-hydroxycolecalciferol did not correlate with the cholesterol levels, neither with proteins or glycaemia, among cystic fibrosis patients. Even if , in CF, there is a maldigestion and impaired absorption of the lipids and proteins , secondary to pancreatic insufficiency, this not influenced the cholesterol levels of the patients, nor the proteins levels, probably because of the use of enzymes mandatory supplementation and endogenous cholesterol synthesis. A further evaluation of the serum lipids values and the 25-hydroxycolecalciferol and other liposoluble vitamins might be evaluated for subsequent actions of disease's evolution improvement.

References

1. BIKLE DD. Chemistry and Biology. 2014. 14;21(3):319-29.
2. FINKLEA JD, GROSMANN RE, TANGPRICHA V. Adv Nutr. 2011, 2(3):244-53
3. MOUSTAKI M, LOUKU I, PRIFTIS KN, ET ALL. World J Clin Pediatr. 2017; 6(3): 132-142
4. LONGENECKER CT, HILEMAN CO, CARMAN TL, Antivir Ther. 2012; 17(4):613-21
5. BRODLIE M, ORCHARD WA, REEKS GA, P Arch Dis Child. 2012; 97(11):982-4
6. GUPTA A, BUSH A, HAWRYLOWICZ C, SAGLANI S. Paediatric Respiratory Reviews. 2012. 13(4):236-43
7. BREHM JM, SCHUEMANN B, FUHLBRIDGGE AL, ET ALL .J Allergy Clin Immunol. 2010; 12(2): 179–185.
8. LIU PT, STENGER S, Li H, et ALL. Science (80-). 2006; 311(5768) :1770-1773
9. CHOCANO-BEDOYA P, RONNENBERG AG. Nutrition Reviews. 2009, 67(5):289-93
10. SIMONEAU T, BAZZAZ O, SAWICKI GS, ET ALL. Ann Am Thorac Soc. 2014; 11(2):205-10.
11. ADAMS JS, HEWISON M. J Clin Endocrinol Metab. 2010; 95(2):471-8
12. LIPS P. Progress in Biophysics and Molecular Biology. 2006, 92(1):4-8
13. PRENTICE A, GOLDBERG GR, SCHOENMAKERS I. American Journal of Clinical Nutrition. 2008, 88(2):500S-506S
14. HOLICK M. Sol Radiat Hum Heal 2008;(1):147–66.
15. DONALDSON SH, BOUCHER RC. : Chest. 2007 Nov;132(5):1631-6.
16. DOS SANTOS ALM, DE MELO SANTOS H, NOGUEIRA MB, Pediatr Gastroenterol Hepatol Nutr. 2018; 21(4):306-314
17. CIUCA IM, POP L, RANETTI A. E, ET ALL .Farmacia. 2015; 63 (4), 543-547
18. SFARTI, C.V., CIOBICA, A.,STANCIU, C.. et. al., Rev. Chim. (Bucharest), **69**, no. 8, 2018, p. 2172-75
19. PROESMANS M, VERMEULEN F, DE BOECK K. European Journal of Pediatrics. 2008, 167(8):839-49
20. TURK D, BRAEGGER CP, COLOMBO C, ET ALL Clin Nutr. 2016; 35:557-77.
21. SERMET-GAUDELUS I, BIANCHI ML, GARABEDIAN M, ET ALL. J Cyst Fibros. 2011; 10(Suppl 2):S16-23.
22. TROFOR, A., PETRIS, O., TROFOR, L., et. al., Rev. Chim. (Bucharest). **68**, no. 5, 2017, p. 1002-1006
23. PINCIKOVA T, NILSSON , K., MOEN I.E. et al. Diabetologia (2011) 54, 3007–3015

Manuscript received: 6.06.2019