

# EVALUATION OF THE CORRELATIONS BETWEEN MAGNESIUM CONCENTRATION AND SELECTED SERUM LIPID COMPONENTS IN WOMEN AND MEN OF DIFFERENT AGE WITH CHRONIC KIDNEY FAILURE

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## Abstract

In literature of the recent years, more and more attention has been paid to the correlations between magnesium and blood lipids. Lipid balance disorders induced by hypomagnesaemia bring about changes in the liquidity of cellular membranes. Increased migration of lipids, in particular of VLDL and LDL, across arterial walls has been observed in hypomagnesaemia, with their consequential deposition in the internal membrane. Kidneys, apart from urine production and elimination, fulfil many other important functions in organism. They determine normal functioning of the whole organism, while disorders in their function lead to serious changes in homeostasis. Lipid balance disorders are a serious risk factor in the development of atherosclerotic lesions in patients with chronic kidney failure.

The aim of this study was to examine the correlations between magnesium concentration and total cholesterol and HDL- and LDL-cholesterol contents in women and men with chronic kidney failure under and over 50 years of age. Subjects were divided into four groups:  $K_1$  – 14 women 34-50 years old,  $K_2$  – 14 women over 50 years old,  $M_1$  – 17 men 30-50 years old, and  $M_2$  – 13 men over 50 years old. Tests were made using a COBAS INTEGRA analyser. High concentration of Mg, exceeding the upper limit of reference values, was observed both in two women and men groups ( $K_1$  – 1.26 mmol(+)  $kg^{-1}$ ;  $K_2$  – 1.25 mmol(+)  $kg^{-1}$ ;  $M_1$  – 1.13 mmol(+)  $kg^{-1}$ ;  $M_2$  – 1.16 mmol(+)  $kg^{-1}$ ). Also the levels of total and HDL-cholesterol in all subjects were within physiological limits (respectively:  $K_1$  – 4.61 and 1.23 mmol(+)  $kg^{-1}$ ;  $K_2$  – 4.69 and 1.29 mmol(+)  $kg^{-1}$ ;  $M_1$  – 3.94 and 1.20 mmol(+)  $kg^{-1}$ ;  $M_2$  – 3.98 and 1.16 mmol(+)  $kg^{-1}$ ). Only the LDL-cholesterol concentration in the group of younger men was below normal limit (1.93 mmol(+)  $kg^{-1}$ ). Small positive correlations were obtained between Mg content and that of total and LDL-cholesterol in older

women and younger men groups as well as between Mg and HDL-cholesterol contents in both men groups. At the same time, a small negative correlation was obtained between Mg and LDL-cholesterol concentrations in the older men group. These correlations were statistically non-significant.

Key words: chronic kidney failure, magnesium, lipids.

## OCENA ZALEŻNOŚCI MIĘDZY STĘŻENIEM MAGNEZU A LIPIDAMI W SUROWICY KRWI U KOBIEŃ I MĘŻCZYŹN W RÓŻNYM WIEKU Z PRZEWLEKŁĄ CHOROBAŃ NEREK

### Abstrakt

W literaturze z ostatnich lat coraz więcej uwagi poświęca się zależności między magnezem a lipidami krwi. Zaburzenia gospodarki lipidowej wywołane hipomagnezemią powodują zmiany płynności błon komórkowych. W hipomagnezemi zauważono zwiększone przechodzenie lipidów, zwłaszcza lipoprotein VLDL i LDL, przez ścianę tętnic z następstwem odkładania się ich w błonie wewnętrznej. Nerki, oprócz tworzenia i wydalania moczu, spełniają jeszcze wiele innych ważnych zadań w organizmie. Warunkują prawidłowe funkcjonowanie ustroju jako całości, a zaburzenia ich funkcji prowadzą do poważnych zmian równowagi homeostatycznej. Zaburzenia gospodarki lipidowej stanowią poważny czynnik ryzyka rozwoju zmian miażdżycowych u osób z przewlekłą niewydolnością nerek.

Celem pracy było zbadanie zależności między stężeniem magnezu a zawartością cholesterolu całkowitego, HDL- i LDL-cholesterolu u kobiet i mężczyzn z przewlekłą niewydolnością nerek, w wieku do 50. roku życia oraz powyżej 50. roku życia. Chorych podzielono na grupy:  $K_1$  – 14 kobiet w wieku 34-50 lat,  $K_2$  – 14 kobiet w wieku powyżej 50 lat,  $M_1$  – 17. mężczyzn w wieku 30-50 lat,  $M_2$  – 13. mężczyzn w wieku powyżej 50 lat. Badania wykonano analizatorem COBAS INTEGRA. Zarówno w obydwu grupach kobiet, jak i mężczyzn stwierdzono wysokie stężenie magnezu, przekraczające górną granicę wartości referencyjnych (grupa  $K_1$  – 1,26 mmol(+)  $kg^{-1}$ ;  $K_2$  – 1,25 mmol(+)  $kg^{-1}$ ;  $M_1$  – 1,13 mmol(+)  $kg^{-1}$ ;  $M_2$  – 1,16 mmol(+)  $kg^{-1}$ ). Poziomy cholesterolu całkowitego i HDL-cholesterolu u wszystkich badanych utrzymywały się w zakresie normy fizjologicznej i wynosiły odpowiednio: u kobiet młodszych 4,61 i 1,23 mmol(+)  $kg^{-1}$ , u kobiet starszych 4,69 i 1,29 mmol(+)  $kg^{-1}$ , u mężczyzn młodszych 3,94 i 1,20 mmol(+)  $kg^{-1}$  oraz u mężczyzn starszych 3,98 i 1,16 mmol(+)  $kg^{-1}$ . Jedynie stężenie LDL-cholesterolu nie osiągało dolnej granicy normy u mężczyzn przed 50. rokiem życia i wynosiło 1,93 mmol(+)  $kg^{-1}$ . Uzyskano niewielkie dodatnie korelacje między zawartością Mg a cholesterolu całkowitego i LDL-cholesterolu u kobiet starszych i mężczyzn młodszych oraz między zawartością Mg a HDL-cholesterolu u mężczyzn z obydwu grup. Jednocześnie uzyskano niewielką ujemną korelację między Mg a LDL-cholesterolem u mężczyzn starszych. Korelacje nie były istotne statystycznie.

Słowa kluczowe: przewlekła niewydolność nerek, magnez, lipidy.

## INTRODUCTION

Chronic kidney failure (CKF) has been newly included into civilisation diseases of the 21st century, apart from cardiovascular diseases, arterial hypertension, obesity and diabetes. CKF can be a consequence or complication of all other civilisation diseases. Due to initially latent course of the dis-

ease, it is being diagnosed too rarely. The progressing disease can be a basis for development of chronic kidney failure and for the necessity of renal replacement therapy connected with that. Moreover, the mortality due to cardiovascular complications among patients with chronic renal diseases is three times higher than that resulting from direct consequences of the underlying disease itself. Therefore, early diagnostics – allowing suppression of growing kidney function failure and prevention from further complications – is very important (Go et al. 2004, KRÓL, RUTKOWSKI 2008).

The classification of chronic renal disease depends on the degree of renal function measured by glomerular filtration rate (GFR). There are 5 stages of that disease: stage 1 – kidney damage with normal or increased GFR, stage 2 – kidney damage with mild reduction in GFR, stage 3 – kidney damage with moderate reduction in GFR, stage 4 – kidney damage with severe reduction in GFR, and stage 5 – established kidney disease (CZEKALSKI 2007, MYŚLIWIEC, HRYSZKO 2008). Other definitions used for chronic renal disease in successive stages (according to the authors mentioned above) are as follows: stage 1 – kidney damage in the form of albuminuria, proteinuria, haematuria; stage 2 – latent (chronic) renal insufficiency, stage 3 – compensated (chronic) renal insufficiency, stage 4 – manifest uncompensated, advanced chronic renal insufficiency, and stage 5 – terminal (extreme) renal insufficiency.

In Poland, there are probably 4.24 million patients with CKF (about 11% of population), including 1.27 M in the first stage; 1.16 M in the second one; 1.66 M in the third one, and 77 thousand in the fourth stage of disease. On the other hand, the number of sick persons with the end-stage kidney failure (ESKF), requiring dialysis therapy or renal transplantation, is about 50 thousand (RUTKOWSKI 2007, STECIWKO et al. 2006).

Lipid balance disorders are one of the elements of clinical manifestation of the advanced chronic kidney failure. They is a serious risk factor for the development of atherosclerotic lesions and increase together with the degree of kidney failure intensification (ZWOLIŃSKA et al. 1997). It was found that the concentration of total cholesterol and triglycerides increased with hypomagnesaemia (ALTURA et al. 1990, D'ERIL, TROTTI 1991, LICHODZIEJEWSKA, KŁOŚ 1993), while that of HDL-cholesterol decreased (LICHODZIEJEWSKA, KŁOŚ 1993).

The aim of this study was to evaluate the correlations between magnesium content and the concentration of total cholesterol and its HDL and LDL fractions in women and men with chronic kidney failure.

## MATERIAL AND METHODS

Research material was the blood collected prior to dialysis from subjects with CKF who, in 2008, were patients of the Dialysis Ward of the Independent Public United Hospital in Szczecin. They were patients with the end-stage kidney failure (stage 5 CKF). The patients, due to their age and sex, were divided into four groups:  $K_1$  – 14 women 34-50 years old,  $K_2$  – 14 women over 50 years old,  $M_1$  – 17 men 30-50 years old, and  $M_2$  – 13 men over 50 years old.

In the blood serum of the examined subjects, magnesium (Mg) concentration was determined, using COBAS INTEGRA Magnesium cassette. Total cholesterol (TCh) concentration was determined by means of COBAS INTEGRA Cholesterol cassette. To determine the concentration of HDL-cholesterol (HDL-Ch) fraction, COBAS INTEGRA HDL-cholesterol plus 2 generation cassette was used. In order to determine quantitatively the concentration of LDL-cholesterol (LDL-Ch), COBAS INTEGRA LDL-cholesterol plus 2 generation cassette was used. The cassettes mentioned above were used in the COBAS INTEGRA analyser. The findings were analysed statistically, applying Statistica 8.0 computer software package.

## RESULTS AND DISCUSSION

The progressing character of chronic kidney failure leads to the necessity of implementing renal replacement therapy at the last disease stage. The method of treatment for the examined subjects was long-term ambulatory haemodialysis, three times a week. In subjects with extreme renal insufficiency, different laboratory tests are required to monitor the organism state, including examination of magnesium concentration and the content of some lipid compounds.

In all groups of the examined subjects, high serum Mg concentration was observed, exceeding the upper limit of reference values (Table 1). Higher content of that chemical element was characteristic of women, both older and younger ones, when compared to men of similar age, but these differences were not significant statistically. It results from the research works carried out by many authors that both hyper- and hypomagnesaemia may occur in subjects with ESKF, but also with normal magnesium balance. Fairly high concentration of Mg ( $1.06 \pm 0.18 \text{ mmol dm}^{-3}$  and  $1.08 \pm 0.13 \text{ mmol dm}^{-3}$ ) was found by ŚWITALSKI et al. (2000). The results obtained by NASRI and KHEIRI (2008) and ROBLES et al. (1998) in patients with ESKF were within physiological limits. Low concentration of Mg in subjects aged  $47.5 \pm 16.6$  years (on average  $0.6 \pm 0.3 \text{ mmol dm}^{-3}$ ) was found by NASRI and BARADARAN

Table 1

Concentrations of magnesium (Mg), total cholesterol (TCh), HDL-cholesterol (HDL-Ch) and LDL-cholesterol (LDL-Ch) in the blood serum of examined subjects (mmol(+) kg<sup>-1</sup>)

Parameter examined	Group								Reference values
	K <sub>1</sub>		K <sub>2</sub>		M <sub>1</sub>		M <sub>2</sub>		
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	
Mg	1.26	0.20	1.25	0.26	1.13	0.21	1.16	0.24	0.70-1.05
TCh	4.61	1.49	4.69	1.16	3.94	1.25	3.98	0.71	3.90-6.22
HDL-Ch	1.23	0.85	1.29	0.22	1.20	0.58	1.16	0.36	0.9-2.0
LDL-Ch	2.69*	0.99	2.73*	1.07	1.93*	0.71	2.35	0.58	2.2-4.0
Significance of differences	K <sub>1</sub> – M <sub>1</sub> * K <sub>2</sub> – M <sub>1</sub> *								

Explanations:  $\bar{x}$  – mean value, SD – standard deviation, \* – significance of differences at  $p \leq 0.05$ , K<sub>1</sub> – women 34-50 years old, K<sub>2</sub> – women over 50 years, M<sub>1</sub> – men 30-50 years old, M<sub>2</sub> – men over 50 years. Reference values for magnesium in blood serum are given after HEIL et al. (1999), whereas for lipids after KOKOT and KOKOT (2005)

(2004). Significantly higher mean concentration of that chemical element in a group of patients with chronic kidney failure (women aged  $62 \pm 16$  years and men aged  $58 \pm 14$  years), when compared to the control group of healthy subjects, was observed by WALASEK et al. (2005).

Hypermagnesaemia occurrence in patients with ESKF is mostly caused by a decrease in glomerular filtration in kidneys, which leads to the impairment of urinary magnesium excretion. The increase of total Mg concentration in blood serum induces reduction of its absorption, probably through reduction of the expression of magnesium protein transporter (TRAM 6) in small intestine epithelium (GROENESTEGER et al. 2006). Nevertheless, Mg absorption from the gastrointestinal tract in haemodialysed patients exceeds frequently the possibility of its elimination and leads to retention of that chemical element in organism.

Mean total cholesterol (TCh) concentration in the blood serum in all groups of examined patients was within physiological limits. However, it was higher in younger women (group K<sub>1</sub>) as well as older ones (group K<sub>2</sub>) when compared to men of both age groups, in whom it was at the lower limit. The HDL-cholesterol fraction also remained at the normal level in all examined subjects, being however observed at its lowest concentration in older men (group M<sub>2</sub>). The level of LDL-cholesterol did not reach the lower limit in younger men (group M<sub>1</sub>). In other patients, the content of that lipid was within reference values (Table 1). Similar mean concentration of TCh and HDL-Ch was obtained by Penar et al. (2005), who examined a group of 65 haemodialysed patients with an average age of  $55.6 \pm 13.4$  years. The results presented by WIELICZKO et al. (2006) obtained in long-term dialysed

subjects were also similar to those reported for the examined patients. Nasri and BARADARAN (2004), when examining 16 women and 20 men with extreme kidney insufficiency, also obtained similar values for TCh and LDL-Ch, whereas the level of HDL-Ch was below lower physiological limit. The comparison of 71 long-term dialysed subjects (with an average age of 45 years) with a group of healthy persons made by JENDRYCZKA-MACĀKIEWICZ et al. (1999) showed significantly lower concentration of total cholesterol and HDL and LDL fractions. The analysis of lipid profile results in subjects with extreme kidney insufficiency revealed a higher mean concentration of TCh and HDL- and LDL-cholesterol in women when compared to men, which was confirmed in the authors' study.

Low LDL-Ch concentration which was obtained in younger men (group M<sub>1</sub>) does not necessarily have to be connected with a decrease in the number of LDL molecules. This may also be connected with a reduction in the content of cholesterol carried by molecules and be the same as a result of LDL enrichment with apoprotein B and triglycerides. The apoB-richer molecules are smaller, denser, they easily penetrate into vascular walls and are subject to oxidation, which leads to considerable atherogenicity (WYBRAŃSKA, KWAŚNIAK 2008). Development of small, dense LDL may be the result of the abnormal function of hepatic receptors for lipoproteins affecting LDL metabolism as well as the abnormal activity of cholesterol ester transporting protein (BARTUŚ et al. 1999, BOGUCKI 2009).

Dyslipidaemia, occurring in patients with CKF, contributes to accelerated development of atherosclerosis, which occurs 30 times more frequently in those patients, while mortality due to its complications is several dozen times higher than in general population (STECIWKO, MASTALERZ-MIGAS 2006). In the opinion of BOGUCKI (2009), unfavourable changes in blood vessels may rather be a result of disorders in the lipid composition than the increase of their concentrations in blood serum.

No statistically significant effect of magnesium concentration on the content of lipids analysed in blood serum was found. Meaningful positive corre-

Table 2

Correlation coefficients (*r*) between magnesium concentration (Mg) and total cholesterol (TCh) and HDL-cholesterol (HDL-Ch) and LDL-cholesterol (LDL-Ch) levels in the blood serum of examined groups

Blood serum indicator	Group			
	K <sub>1</sub>	K <sub>2</sub>	M <sub>1</sub>	M <sub>2</sub>
Mg / TCh	-0.057	0.397	0.307	-0.080
Mg / HDL-Ch	-0.151	-0.042	0.418	0.253
Mg / LDL-Ch	-0.028	0.447	0.225	-0.311

Explanations as in Table 1

lation (but statistically non-significant) was obtained between Mg and total cholesterol in older women and younger men. Positive correlations between magnesium and total cholesterol in patients with chronic kidney failure were also obtained by other authors (NASRI, BARADARAN 2004, ROBLES et al. 1998). Magnesium content in blood serum was also positively correlated with HDL-cholesterol in men of both groups. A positive effect on LDL-cholesterol was observed in the group of older women and that of younger men (Table 2). However, also small negative correlation between Mg and LDL-cholesterol contents was obtained in older men.

## CONCLUSIONS

1. In all examined groups of patients with extreme kidney insufficiency, abnormally high mean magnesium concentration was found (above the upper limit of reference values). A probable cause of hypermagnesaemia in those people was a decrease in glomerular filtration, which led to the impairment of urinary magnesium excretion mechanisms.

2. Mean total cholesterol concentration in women was at a higher level when compared to men, in whom it oscillated around the lower limit of reference values. HDL-cholesterol showed mean values within physiological limits, which was a result of large individual variability in the groups of examined patients. The evaluation of HDL-cholesterol content in respective subjects was difficult due to no information referring to intake of diuretic drugs. The LDL-cholesterol concentration in younger men was below the reference range, while remaining within physiological limits in other women and men groups.

3. No statistically significant correlations were found between magnesium concentration and lipid content in the examined patients except only irregular relationships between these indicators.

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