Study on Metabolic Parameters in Obese Patients Compared to Normal Weight Subjects Before and After Joint Replacement Surgery

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Surgical interventions represent an important stress for the organism. Metabolic parameters can exhibit important changes in a short period of time related to surgery. Differences might occur between normal weight and obese patients. Weight excess represents a risk factor for osteoarthritis.The aim of the study was to assess metabolic parameters before and after total hip and knee replacement in patients with osteoarthritis. The study was performed during 2016-2017 at the Clinic of Orthopedics and Traumatology of the Emergency County Hospital in Tirgu Mures. The study group was divided, based on body mass index values, in normal weight (43 patients) and obese individuals (52 patients). Plasma uric acid level, glycemia and lipid profile (triglycerides, total cholesterol) were determined for each patient before surgery and one day after the intervention, the values being compared. Differences between the metabolic parameters of the two subgroups were also determined. In case of obese individuals, all followed metabolic parameters were significantly different one day after the intervention compared to the values obtained before the surgery: plasma uric acid, cholesterol and triglyceride values decreased, glycemia increased. In the group of normal weight subjects the level of plasma lipids and uric acid differed significantly between the first and second sample, mean values being decreased in the second one. Comparing the two subgroups, significant difference occured regarding plasma glucose levels one day after the intervention, the mean value being higher in case of obese patients, also a higher percentage of hyperuricemia has been found in the group of obese patients. Dynamics of the followed metabolic parameters shows important changes on short term following surgical intervention. Hyperglycemia and hyperuricemia was most common in obese patients, plasma glucose showing increasing tendency after surgery.

Keywords: metabolic parameters, obesity, surgical intervention

Last decades witnessed a rapid change in lifestyle and nutritional habits in modern society, which fundamentally transformed the way obesity and its direct complications, such as diabetes and heart disease, were perceived, from a peripheric metabolic condition to a real, undisputed pandemic [1]. This major health problem of obesity, as a complex disease caused by a result of genetics, diet, metabolism and physical activity, has numerous consequences on lipid, glucose and protein metabolism with hyperglycemia and insulin resistance, hyperlipidemia and hyperuricemia [2,3]. Diabetes mellitus in Romania has one of the highest incidence in Europe, over 10% of the population being affected [4]. Indisputable that obesity, as a first rank component of the metabolic syndrome, leads to many imbalances of the cardiac function, respectively neurohormonal activation with hypervolemia, apoptosis, fibrosis and hypertrophy, triggered by the pro-inflammatory adipocytokines, associated with the lypotoxic effect of the fats of myocardial cells [5]. The most significant impact of obesity on the musculoskeletal system is associated with osteoarthritis, a disabling degenerative joint disorder characterized by pain, decreased mobility and negative impact on quality of life. Osteoarthritis pathogenesis relates to both excessive joint loading and altered biomechanical patterns together with hormonal and cytokine dysregulation [6]. In the conservative therapy of osteoarthritis it's a high demand for medication combining good potential of symptomatic relief with prevention of cartilage degradation [7]. In severe cases total hip or knee arthroplasty is necessary. Although surgical care is an integral part of health care throughout the world, with an estimated 234 million operations performed annually, every intervention represents an important supplemental stress for human organism [8].

Adipose tissue triglycerides reflect the energy storage level of the body [9]. Metabolic parameters can exhibit important changes in a short period of time related to surgery. Based on the long-term experience and strong scientific evidence, hyperuricemia and dyslipidemia (elevated plasma concentration of lipid (triglyceride), total cholesterol and their blood transporting lipoproteins, as well) are considered some of the most obvious risk factors for chronic cardiovascular diseases [10]. According to genetic studies, IL-6 (proinflammatory cytokine) and several coagulation factors are also causal for cardiovascular diseases, unlike to C reactive protein and fibrinogen, whose causal role was not supported [11]. But the dynamics of these metabolic parameters may change rapidly in acute situations. A pilot study has proved that uric acid is pro-inflammatory and amplifies the inflammatory response to other stimuli [12].

The aim of the study was to determine metabolic parameters (glycemia, plasma cholesterol, triglyceride, uric acid level) in patients suffering from knee or hip osteoarthritis before and one day after undergoing joint replacement intervention.

Experimental part

The subjects for the study were selected from the patients admitted to the Clinic of Orthopedics and Traumatology of the Emergency County Hospital in Tîrgu Mures between 2016-2017 suffering from severe knee or

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hip osteoarthritis, joint prosthesis being necessary for all subjects. Patients enrolled to the study were divided in subgroups based on their body mass index values (BMI) expressed in kg/m^2, calculated from height and weight data. Obese and normal weight individuals were followed separately. Patients who agreed to be enrolled to the study and signed the informed consent document were included in the followed group. Exclusion criteria were autoimmune diseases and systemic corticotherapy. The study was approved by the ethics committee of the Emergency County Clinical Hospital in Tirgu Mures. All patients underwent orthopedic surgery for knee or hip joint replacement. Demographic data were recorded for these subjects. Blood samples were taken from all enrolled patients in the morning before the intervention and one day after surgery for assessment of metabolic parameters. EDTA-blood samples underwent centrifugation, plasma being separated and stored frozen till the day of the measurement at -80ºC. Glucose, cholesterol, triglyceride and uric acid concentration were determined from both samples, while HDL-cholesterol measurement has been performed only once, before the surgery. LDL-cholesterol values were calculated using the formula: total cholesterol - HDL - triglycerides/5. Measurements were performed by spectrophotometric method at the Advanced Research Centre of the University of Medicine and Pharmacy in Tirgu Mures on Cobas Integra 400 Plus analyzer, using appropriate commercial kits from Roche Diagnostics. Dynamics of the measured metabolic parameters was followed in all patients, and also the difference between the values obtained in case of normal weight and obese individuals. Statistics included paired Student t test, chi square and multiple comparison tests (Anova, Bonferroni). The threshold of significance was set at p under 0.05.

Results and discussions

The mean age of normal weight patients was 60.42 years ± 12.00 (SD), that of obese individuals being 64.92 years ± 9.94 (SD). 53.5% of the normal weight subjects and 36.5% of the obese patients were from rural areas.

Significant difference could be observed between the BMI averages of the two subgroups ($p<0.0001$), the mean value being 24.07 kg/m^2 ± 1.13 (SD) in the subgroup of normal weight subjects, while obese individuals had an average BMI of 31.59 kg/m^2 ± 1.97 (SD).

The gender distribution showed significantly ($p=0.049$) higher percentage of male patients in the group of normal weight subjects (53.5%) compared to the group of obese individuals, where the percentage of women was higher, and only 28.8% were male patients.

Comparing the results of metabolic parameters obtained from the first and second sample, in the group of normal weight subjects significant difference ($p<0.0001$) could be observed regarding plasma cholesterol and triglyceride concentration, and also in the level of uric acid, the values being higher in the first sample for all these parameters. Plasma glucose level didn't present significant change in this patient group ($p=0.329$) (table 1, fig. 1).

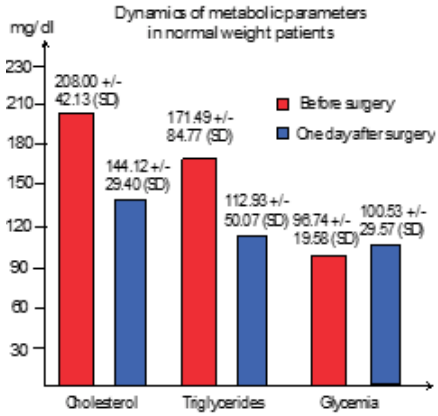

Fig. 1. Dynamics of metabolic parameters in normal weight patients before and after surgery

In the group of obese subjects significantly lower ($p<0.0001$) values occured in the concentration of plasma cholesterol, triglyceride and uric acid concentration in the second sample compared to the values obtained before the intervention, while plasma glucose values showed significant increase in the second sample compared to the first one ($p<0.0001$) (table 2, fig. 2).

Parameters measured in plasma samples	Unit	Mean value ± standard deviation before surgery	Mean value ± standard deviation one day after surgery	p value
Uric acid	mg/dl	5.97 ± 1.52	5.05 ± 1.53	<0.0001
Cholesterol	mg/dl	208.01 ± 42.23	144.12 ± 29.40	<0.0001
Triglycerides	mg/dl	171.49 ± 84.77	112.93 ± 50.07	<0.0001
Glucose	mg/dl	96.74 ± 19.58	100.53 ± 29.57	0.329
HDL-cholesterol	mg/dl	44.08 ± 15.16	-	
LDL-cholesterol	mg/dl	129.64 ± 40.92	-	

Table 1
METABOLIC PARAMETERS OBTAINED IN NORMAL WEIGHT PATIENTS BEFORE AND AFTER JOINT REPLACEMENT

Parameters measured in plasma samples	Unit	Mean value ± standard deviation before surgery	Mean value ± standard deviation one day after surgery	p value
Uric acid	mg/dl	6.58 ± 1.55	5.59 ± 1.43	<0.0001
Cholesterol	mg/dl	204.97 ± 43.65	139.21 ± 32.24	<0.0001
Triglycerides	mg/dl	171.49 ± 84.77	112.93 ± 50.07	<0.0001
Glucose	mg/dl	101.44 ± 21.14	117.00 ± 36.03	<0.0001
HDL-cholesterol	mg/dl	42.68 ± 19.90	-	
LDL-cholesterol	mg/dl	126.82 ± 40.47	-	

Table 2
METABOLIC PARAMETERS IN OBESE PATIENTS BEFORE AND AFTER JOINT REPLACEMENT

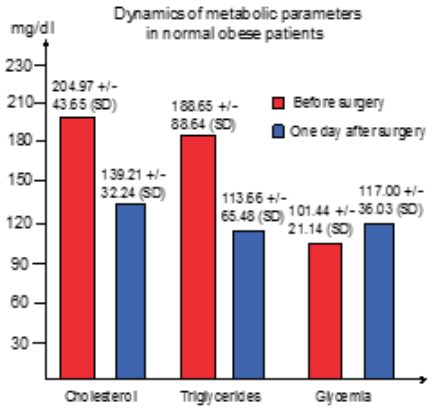

Fig. 2. Evolution of metabolic parameters in obese ents before and after the intervention

Regarding the comparison of metabolic parameter average values obtained at these two subgroups (normal weight and obese subjects), no significant difference could be observed in the lipid profile, glycemia and plasma uric acid concentration obtained before the surgery. However, a notable difference could be observed between the two patient groups in the distribution of uric acid values before surgery. 28.8% of obese individuals, and only 16.3% of normal weight subjects presented plasma uric acid values exceeding 7 mg/dL in the first sample ($p=0.2216$).

In the second sample, taken one day after the intervention, average glycemia was significantly higher ($p=0.025$) in the subgroup of obese patients compared to the mean value obtained in case of normal weight subjects.

The distribution of total, HDL- and LDL-cholesterol values revealed a high percentage of patients with dyslipidemia in both subgroups. Plasma cholesterol values exceeded 200 mg/dL in 54% of the obese patients and in 51% of normal weight subjects. Triglyceride concentration was higher than 150 mg/dL in 62% of the obese patients and in 56% of normal weight subjects. First sample results were taken into consideration in case of these parameters.

44% of the obese patients and 42% of normal weight subjects presented HDL-cholesterol levels under 40 mg/dL. LDL-cholesterol exceeded 100 mg/dL in 73% of the obese patients and in 77% of normal weight individuals. No significant difference could be observed between the distribution of normo- and dyslipidemia in these two subgroups.

In patients undergoing total hip arthroplasty several studies showed smaller improvement during postoperative period and more wound healing complications in obese patients compared to normal weight subjects [13, 14]. Other sources indicate no significant difference in the occurrence of complications (such as dislocation) between normal weight and obese patients after hip and knee replacement, except for those with extreme obesity [15]. Our study has a limitation related to the short follow-up period (only one day) after the surgery, but some differences could be observed between the studied patient groups even during this time range. Obesity predisposes to impaired carbohydrate metabolic balance, and insulin necessities increase when the body is exposed to stress situations. This could explain the significantly higher plasma glucose values in case of the obese patients compared to normal weight subjects.

Major surgical interventions induce insulin resistance, which can be present in up to 41% of obese non-diabetic subjects. This percentage can become higher after the surgery, increasing the risk of post-operative complications, especially considering the pro-inflammatory state induced by the intervention [16].

Overweight is considered an important risk factor for hip and knee osteoarthritis. Mechanical overload of the joints of the lower limb activates chondrocytes and enhances cartilage degeneration. Studies suggest that obesity also contributes to similar changes in the joints of the upper limb, pro-inflammatory cytokines released by the adipose tissue and some joint cells might contribute to the degeneration process. Osteoarthritis is often associated with some parameters of the metabolic syndrome, such as type 2 diabetes mellitus and hypertension [17, 18].

According to recent data in the medical literature, impaired carbohydrate metabolic balance and important weight excess can contribute to painful joints in patients suffering from osteoarthritis after hip or knee joint replacement therapy [19]. Treatment plan should be estabilished with special care, taking into consideration the possible side effects of medication, the presence of comorbidities and the potential risk for cardiovascular diseases, increased especially in obese and diabetic patients [20]. Inherited predisposition of certain individuals and the relationship between different components of metabolic syndrome (visceral obesity, dyslipidemia, hyperglycemia, hypertension) should also be taken into consideration [21].

Relationship between dyslipidemia and osteoarthritis was found in a study performed on 246 patients, suggesting that high serum cholesterol level can be associated with an increased risk for knee and generalized osteoarthritis, the association being stronger for knee joint inflammation [22]. Further studied would be necessary on larger population to study this kind of relationship.

Elevated serum uric acid concentration is often associated with weight excess. Our results are similar to data found in the literature, higher percentage of hyperuricemia being found in the group of obese patients compared to normal weight subjects. In spite of the classic antioxidant effect of uric acid, hyperuricemia can affect adipocytes by inducing oxidative stress through NADPH oxidase-dependent pathway, which enhances the inflammatory state and produces endocrine dysfunction in the adipose tissue [23].

Uric acid also increases the production of several pro-inflammatory cytokines such as interleukine-18 and IL-1β, by the activation of NLRP3 inflammasome. Data support that synovial fluid uric acid can be considered a marker of knee osteoarthritis severity. Although synovial fluid can be considered an ultrafiltrate of plasma, containing also some components added from the joints, only synovial fluid, and not serum uric acid concentration showed significant correlation with the severity of knee osteoarthritis, evaluated by X-ray (static measure of disease severity) and late-phase bone scan imaging (dynamic measure of bone turnover), the second investigation being associated with clinical symptoms of osteoarthritis [24]. Other studies suggest a positive relationship between increased serum uric acid concentration and osteoarthritis, including the formation of knee osteophytes in the female subjects [25]. On long term the stability of the implant and the life quality of the patients with arthroplasty is very important [26].

In a study having similar design to ours, performed on a group of patients undergoing hip or knee surgery, metabolic biochemical parameters were determined before the intervention and 48 h after the surgery. Serum uric acid decreased significantly after the intervention compared to the initial values, similar to our results [27].

Conclusions

High frequency of hyerglycemia, dyslipidemia and hyperuricemia could be found in the studied patients groups, especially in case of obese subjects.

Based on the data obtained in our study, metabolic parameters (plasma uric acid, cholesterol and triglyceride level) show important decrease after surgical intervention both in normal weight and obese patients compared to the initial values. Significantly increased plasma glucose level could be observed in obese subjects after arthroplasty, glycemia being significantly higher in this patient group compared to normal weight individuals.

A longer and more complex follow-up could reveal other important changes in metabolic parameters related to orthopedic surgery and the interrelation especially between the components of metabolic syndrome.

Acknowledgements: Financial support for this study was provided by SC CATTUS SRL a private research grant no.5068/26.04.2016 with involvement of UMPh Tirgu Mures. Special thanks to the staff of the Clinic of Orthopedics and Traumatology of the Emergency County Hospital Tîrgu Mures for the remarkable support given for this study and also to the staff of the Center for Advanced Medical and Pharmaceutical Research UMPh Tîrgu Mures.

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Manuscript received: 18.09.2018