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EXPERIMENTAL STUDY

Serum omentin levels predicts mesenteric ischemia

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Abstract: *Background:*Acute mesenteric ischemia (AMI) is an intestinal vascular disease with high mortality. Clinical diagnosis of acute mesenteric ischemia is difficult. Adipose tissue is an important mediator of metabolism and inflammation.Omentin is produced by visceral adipose tissue and decreased serum levels of omentin are associated with poor metabolic outcomes. We aimed to investigate whether serum omentin level predicts early diagnosis of AMI before development of transmural ischemia.
Methods: Twenty-four Sprague Dawley rats weighted about 200–250 gr grouped in 3 experimental groups as sham, transient ischemia and permanent ischemia. Each group consisted of 8 rats. Blood samples were evaluated to determine serum urea, creatinine, omentin and C-reactive protein (CRP) levels. A blinded histological examination performed with the same histologist for hemotoxileneosine painted ileal tissue samples.
Results: Mean serum omentin level in sham group (27.5±4.67) was significantly elevated compared to rats in Ischemia-reperfusion (IR) group (10.9±9.01).The difference reached the statistical significance (p=0.004). Serum omentin levels were not correlated to urea, creatinine or CRPlevels.
*Conclusion:*Omentin levels may be a biochemical indicator to detect AMI. However, further human studies are needed *(Tab. 3, Fig. 3, Ref. 34)*. Text in PDF *www.elis.sk.*
Key words: mesenteric ischemia, omentin, early diagnosis, inflammation, adipose tissue.

Introduction

A shortage in blood flow to any organ or tissue causes cellular dysfunction and death(1). Although reperfusion rescues the tissues affected by ischemia, it may also cause further destruction. Ischemia–reperfusion injury (IRI), may be caused by many factors such as; release of free oxygen radical products and lipid peroxidation products, apoptosis, necrosis, inflammatory cytokines and microvascular damage(1–4).Possible causes of intestinal IRI are as follows: cardiopulmonary bypass, trauma, organ transplantation, newborn necrotizing enterocolitis, andpatentductus arteriosus(5, 6). Intestinal ischemia and reperfusion is hazardous in terms of both impairing nutritional capacity and barrier integrity. Dysfunction in intestinal wall may cause bacterial translocation, peritonitis and sepsis(5). Mechanisms and treatment options of intestinal IRI have been studied recently. Acute mesenteric ischemia (AMI) is an intestinal vascular disease with a high mortality. It causes an acute abdomen. There is no specific and sensitive laboratory test for early diagnosis and treatment of AMI. Early diagnosis is important because treatment modalities such as embolectomy, patch angioplasty and endarterectomymay be available and a massive resection of the intestines may be avoided.

Adipose tissue is an important mediator of metabolism and inflammation.Proinflammatory cytokines and TNF alpha are increased in adipocytes of obese animals. Weakening of TNF alpha by soluble TNF alpha receptor reduced insulin resistance in literature(7). Adipose tissue is a source of energy in terms of energy expenditure and if energy is adequate, it becomes an energy storage. Also it acts like a pillow and insulator in human(8). Especially adipose tissue of the abdomen is considered as an endocrinetissue. After the discovery of leptin in adipose tissue, itbecome an endocrine gland. The list of adipocytokines is growing(9, 10). Omentin is an adipokine that primarily secreted by visceral adipose tissue (11).It is firstly isolated from intestinal paneth cells. Secretion of the omentin messenger ribonucleic acid (mRNA)is reduced in Crohn's disease; which is a chronic inflammatory disease of the intestine(12).Omentin has been shown to suppress nuclear factors that stimulated by CRP and TNF alpha(13). Decreased serum levels of omentinare associated with poor metabolic outcomes (12, 14).

We aimed to study whether serum omentin level is effective in predict early diagnosis of AMI before development of transmural ischemia.

Materials and methods

All procedures of this experimental study were approved by the Ethical Committee of Abant Izzet Baysal University.Twenty-four Sprague Dawley rats weighted about 200–250 g grouped in to 3 experimental groups. They have been fed with standard rat food.

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Surgical technique

All surgical interventions performed in sterile rooms and under anesthesiawith 50 mg/kg Ketamin and 5mg/kg Xylasine. Abdominal skin was shaved and sterilized with povidineiod solution. All surgical interventions performed for all rats in the same day with the same surgical staff. Surgical retrograde injection technique was used for mesenteric ischemia model. First group of rats (Sham group) (n=8), undergone laparotomy, superior mesenteric artery was exposed and primary suturization of the skin with 3/0 silk. Second group, superior mesenteric artery clamped for 45 minutes with buldog clamp for transient mesenteric ischemia model (n=8),and third group, sutured with 3/0 silk sutures for permanent mesenteric ischemia model (n=8). At the end of the experimental protocol, 3ml of blood sample obtained intracardiacally from all rats under anesthesia at 12th hour of laparatomy and ileal resection (10cm) performed for histological assessment for all rats in all 3 groups.

Blood samples were evaluated to determine serum urea, creatinine, omentin and C-reactive protein (CRP) levels. A blinded histological examination performed with the same histologist for hemotoxileneosine painted ileal tissue samples. Ischemic morphologic changes were graded with the scoring system described by Chiu et al (15). The grades according to the scoring system are the following: grade 0: normal mucosa, grade 1: villous subepithelial detachment formation accompanied by capillary congestion, grade 2: subepithelial detachments exerted and moderate amount of upward push on the mucosa epithelium, grade 3: large subepithelial detachments exerted a massive amount of upward-push on the mucosa epithelium along the villi and few denuded villus tips were observed, grade 4: the villi were denuded to the level of lamina propria and dilated capillaries, grade 5: presence of ulceration, disintegration of lamina propria, and hemorrhage. Sections photographed by NICON 50i photomicroscobe and NIS elementary programme.

Statistical analyses

All statistical analyses were performed using the SPSS program 17.0 SPSS Inc. Chicago, III, USA for Windows XP. Unless otherwise stated values are expressed as the means ± SD. Variance analyses performed with Kruskall-Wallis test. Mann Whitney U test used for pairwise comparisons after Bonferonni corrections. The Spearman test used for correlation analyses.

Results

Serum omentin level in the sham group (27.5±4.67) was significantly elevated compared to rats in the group2 (10.9±9.01). The difference reached the statistical significance (p=0.004). CRP levels of the groups were not significantly different between groups.

Tab. 1. Laboratory data of the groups.

Groups	Urea (mean±SD)	Creatinine (mean±SD)	CRP (mean±SD)	Omentin (mean±SD)
1	53±4.40	0.58±0.02	0.2	27.5±4.67
2	55±15.89	0.57±0.04	0.2	10.9±9.01
3	31±5.31	0.50±0.02	0.2	19.6±7.22

Tab. 2. Comparison of the p values of laboratory parameters between groups.

Compared groups	Urea	Creatinine	cRP	Omentin
Grup I–II	0.833	0.460	1	0.004
Grup I–III	0.001	0.001	1	0.037
Grup II–III	0.001	0.004	1	0.173

Tab. 3. Chiu scores of the rats.

Groups	Chiu Scores							
	Rat1	Rat2	Rat3	Rat4	Rat5	Rat6	Rat7	Rat8
Control	0	0	1	1	0	0	1	1
Transient Ischemia	2	2	3	2	3	1	2	3
Permanent Ischemia	4	4	5	5	5	5	4	5

On the other hand, serum urea and creatinine levels of the rats in the group 3 were significantly lower than the rats in both group 1 and 2. Table1 shows the mean urea, creatinine, CRP and omentin levels of the groups. Table2 shows the comparison of the p values of laboratory parameters for group 1, 2 and 3.

In histological examinations of the biopsy specimens, the Spearman correlation test was performed for detection the possible correlation between laboratory parameters. Serum omentin levels were not correlated to urea, creatinine or CRP levels. Chiu scores of the rats are summarized in Table 3.

Figure 1 shows the intestinal mucosa of the rats in the control group. Figure 2 a, b shows the intestinal mucosa of the rats in the transient ischemia group. Figure 3 a, b shows the intestinal mucosa of the rats in the permanent ischemia group.

Discussion

We found that serum levels of omentin were significantly reduced after a transient mesenteric ischemia ($p<0.04$). Although serum omentin levels were lower in the permanent ischemia group than the control group, interestingly, the difference could not reached the statistically significant level. Permanent mesenteric ischemia may not be associated with serum omentin levels. We also found that serum urea and creatinine levels were not different in patients with transient ischemia and controls. However, the mean urea and creatinine levels were lower in the permanent ischemia group than both controls and the transient ischemia group.

Shibata et al found that omentin levels were significantly decreased in patients with coronary artery disease(CAD) compared to controls(16). Omentin has been found to be promoting revascularization after ischemia(17). Alcelik et al reported that serum omentin levels of patients with chronic kidney disease were significantly elevated compared to control subjects(18). Omentin is present in blood stream in humans, and plasma omentin levels are decreased in obese individuals (19).Conversely, circulating omentin concentrations are increased in obese subjects after weight reduction(20). Reduced levels of plasma omentin were also observed in overweight insulin-resistant women with polycystic ovary syndrome(21). Recently, circulating omentin concentrations were reported to be associated with endothelium-dependent vasodilation in patients with impaired glucose tolerance(22).Mechanisms of the association of omentin-1 with CAD have not been elucidated;

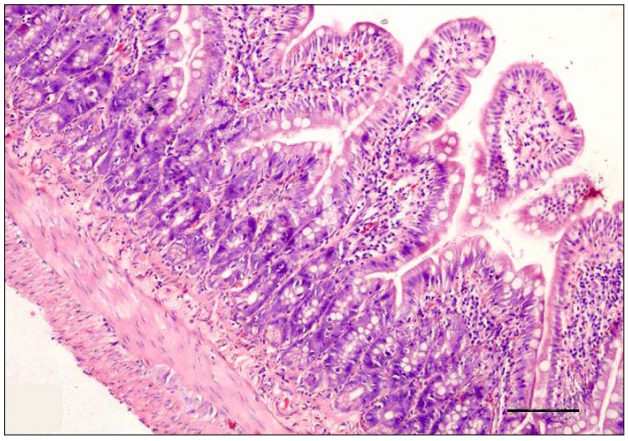

Fig. 1. Intestinal mucosa of the control rats (H&E strain).

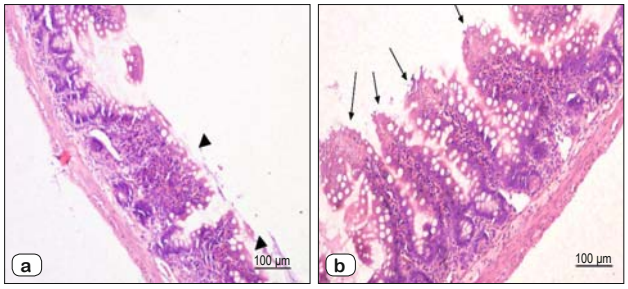

Fig. 2a, b. Intestinal mucosa of the rats in transient ischemia group. Shortened villi (►)and epithelialdesquamation of the villi in transient ischemic rats (H&E).

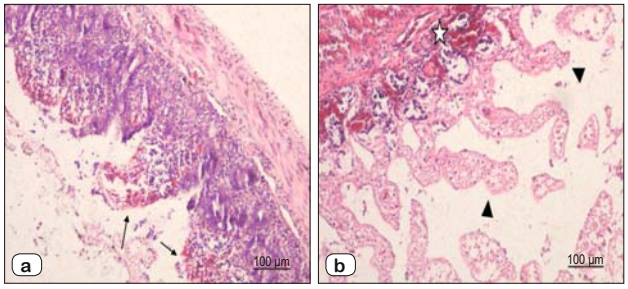

Fig. 3 a,b. Intestinal mucosa of the rats in permanent ischemia group(H&E strain) 3a: hemorrhageand epithelial desquamation and inflammatory cell infiltration in lamina propria (arrows) in permanent ischemia group3b: totally desquamated villi (►) and hemorrhageand destructed glands in lamina propria (*).

however, one could consider several possibilities. First, omentin induces endothelium-dependent relaxation via endothelium-derived Nitric Oxide(NO) through phosphorylation of endothelial nitricoxidesynthetase (eNOS) in rat isolated aorta(23). Coronary artery disease (CAD) may also be associated with impaired endothelium-dependent coronary dilatation(24). Therefore, omentin may participate in CAD development at least in part through regulation of coronary contractility. Second, omentin has been shown to increase insulin sensitivity(25). Rodrigues et al(26) recently named insulin resistance as one of the most important risk factors for subclinical atherosclerosis and reported an association with coronary artery calcification in patients with type 1 diabetes mellitus (T1DM).

Circulating omentin concentration correlated negatively with BMI, leptin, waist circumference, fasting insulin, and homeostasis model assessment and positively with adiponectin and high-density lipoprotein in 94 healthy Amish subjects(19).

Ischemic colitis (IC), first described by Boley et al, is the most common form of ischemic injury to the gastrointestinal tract representing more than half of the cases with gastrointestinal ischemia(27, 28). The incidence of IC is underestimated because it often has a mild and transient nature. Moreover, many cases are misdiagnosed as suffering from other diseases such as inflammatory bowel disease or infectious colitis.

An acute, self-limited compromise in intestinal blood flow which is inadequate for meeting the metabolic demands of a region of the colon is the underlying pathophysiology(29).Approximately 90 % of cases of colonic ischemia occur in patients over 60 years of age although younger patients may also be affected(30). This idiopathic or “spontaneous” form is generally thought to be related to localized nonocclusive ischemia of the bowel(21, 31). In younger patients, a predisposing cause is more easily recognized. Vasculitides, estrogens, cocaine and methamphetamine use, psychotropic drugs, sickle cell disease, long-distance running and heritable disorders of coagulation should be considered(32, 33).

Various laboratory markers of ischemia have been investigated such as: lactate, LDH, CPK, amylase levels, leucocytes, alkaline phosphatase, inorganic phosphate, intestinal fatty acid binding protein and alfa-glutathione S-transferase(34). These markers have been studied mainly in acute bowel ischemia, and none has been found to be sufficiently specific to diagnose IC. They are uncommon in mild ischemia and only increase with advanced and severe ischemic damage, late in the course of the disease. Treatment depends on acuteness and severity of presentation. Most cases of IC are transient and resolve spontaneously. Such patients do not require specific therapy.

Our results are compatible with literature, we also found that an ischemia in mesenteric vessels may cause a reduction in serum levels of omentin. In conclusion, omentin levels may be a biochemical indicator to detect acute mesenteric ischemia.

Learning points

Omentin should be a marker for detecting early mesenteric ischemia.

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