Advance Research Journal of medical and clinical science
Received 26 May 2021 | Revised 6 June 2021 | Accepted 15 June 2021 | Published Online 19 June 2021

DOI: https://doi.org/10.15520/arjmcs.v7i06.327
ARJMCS 07 (06), 597–602 (2021)
ISSN (O) 2455-3549 IF:1.6

ORIGINAL ARTICLE

Effects of Galectin-3 And Mif Proteins on Angogenic Factors in Patients with Prostat Cancer

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Abstract

Introduction: Galectin-3 has a wide range of effects on tumor development, including cell proliferation, apoptosis, cell adhesion, invasion, angiogenesis, and metastasis. Macrophages migration inhibitory factor is a pleiotropic inflammatory cytokines found in many cell processes and especially in cancer. It has been said to interact with many tumor cells. For these reasons, we aim to explain the relationship between Galectin-3 and MIF proteins in the serum of blood samples of prostate cancer patients on VEGF and IL-6 release in prostate cancer patients in this study.

Methods: Our study group consists of Healthy control, Bening prostatic hyperplasia, prostate cancer, operated prostate cancer and metastatic prostate cancer group (each group will consist of 20 people). Protein levels were then measured using the Eliza analyse in these collected blood.

Results: A statistical increase in VEGF, MIF, Galectin-3 and IL-6 levels was observed in patients with cancer benign prostatic hyperplasia, radical prostectomy and metastasis in the control group. In the cancer group, there was a statistically significant decrease in VEGF, MIF, Galectin-3 and IL-6 levels in patients with benign prostatic hyperplasia and radical prostectomy, while a statistically significant increase was observed in VEGF, MIF, Galectin-3 and IL-6 levels in the metastasis group. In patients with radical prostectomy, MIF and Galectin-3 levels decreased statistically, while VEGF and IL-6 levels increased statistically.

Conclusions: These markers may be a new marker in the diagnosis and monitoring of treatment of prostate patients. We think we should do more studies on this subject.

Keywords: Prostate Cancer, Galectin-3, MİF, IL-6, VEGF

1 | INTRODUCTION

Galectin-3 is a multifunctional protein and a member of the beta galactosidase binding lectin (1). It has been found in high amounts in many studies in human malignancies (1) , (2). Galectins are found mainly in the nucleus and cytosol and are not defined as 14 members. Galectins are basically divided into 3 subgroups. These are (a) prototype (galectin-1, -2, -5, -7, -10, -11, -13, and -14); (b) chimera type (galectin-3); and (c) tandem repetitive type (galectin-6, -8, -9, and -12) (3)). Galectin-3 expression is increased in neoplastic cell types. Galectin-3 is associated with the development process of tumors, including cell growth, adhesion, proliferation, and metastasis (4), (5).

Angiogenesis is essential for the growth and development of neoplastic diseases (6), (7). The most important angiogenic factor is VEGF. VEGF, nitric oxide synthetase, tyrosine protein kinase, sarcoma mitogen-activating kinase and phosphoinositol 3 kinase-protein kinase B binding to VEGF receptor 2 in the signaling pathway affect vascular permeability, endothelial migration, proliferation, and survival of endothelial cells (VEGFR2) (8), (9). Galectin-3, which is bound to the carbohydrate recognition domain (CRD), has been shown to bind directly to endothelial cells because the competing disaccharide could be specifically inhibited by lactose polysaccharide and mineralized citrus pectin (10), (11), (12). The response of EC to galectin-1 and -3 treatment is dependent on the presence of VEGFR1 or VEGFR2 levels on the cell surface (13). Increase in circulating galectin-3 in cancer patients (14), (15). induces the release of metastatic secreting cytokines such as interleukin-6 (IL-6) and colony stimulating factor (G-CSF) from the blood vascular endothelium in vivo and in vitro.

Macrophage migration inhibitory factor is a pleiotropic inflammatory cytokine found in many cell processes and especially in cancer. (16). In addition to immune functions, it also has an effect on angiogenesis and tumor growth. Galectin-3 has an effect on tumor growth by reducing cell loss through apoptosis, but may also be a critical marker during metastasis (17), (18). According to the data we obtained during our screening, we think that Galectin-3 and MIF can be a good marker especially for cancer patients. How Galectin-3 and MIF affect the angiogenic protein VEGF and IL-6 cytokines in prostate cancer patients, understanding the pathogenesis of diseases and associating them with treatment, development of new treatment protocols and even elimination of risk factors in healthy people before diseases occur. Is extremely important and emerges as a subject that needs to be researched. For these reasons, we aim to explain the relationship between Galectin-3 and MIF proteins in the serum of blood samples of prostate cancer patients on angiogenesis and the release of cytokines in prostate cancer patients.

2 | MATERIAL AND METHOD

He was selected from the patient group who applied to the hospital due to prostate cancer in Manisa Celal Bayar University Faculty of Medicine, Urology Department. Our study group consists of Healthy control, Being pro static hyperplasia, prostate cancer, operated prostate cancer and metastatic prostate cancer group (each group will consist of 20 people). Volunteers who do not have a chronic disease and want to participate in the study were included in the study. Persons who have these standards and want to participate in the study were included in this study by signing a consent form. The collected blood was stored in deep freez at -80 degrees until the collection of all blood to be allocated to the collected blood serum was completed. The stored blood is analyzed by applying the sandavish elisa method. Galectin-3, MIF, VEGF and IL-6 levels were measured using this ELISA method.

Statistical analyses

Supplementary information The online version of this article (https://doi.org/10.15520/arjmcs.v7i06.327) contains supplementary material, which is available to authorized users.

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The data obtained from the research were analyzed using the statistical package for social sciences (SPSS) for Windows, version 15.0. The value of p <0.05 was deemed statistically significant in comparisons. Mean + standard deviation (SD), number percentage distribution, Mann-Whitney U test analyes was performed to evaluate the data collected in accordance with the purpose of the study.

3 | RESULTS

In our study, we aimed to investigate the relationship between Galectin-3 and MIF proteins in the serum of blood samples of prostate cancer patients on VEGF and IL-6 release in prostate cancer patients.

A statistical increase in VEGF, MIF, Galectin-3 and IL-6 levels is observed in patients with cancer benign prostatic hyperplasia, radical prostectomy, and metastasis in the control group (Table I).

Table 1*: Galectin-3, MIF, VEGF and IL-6 levels in groups*

Groups	Galectin-3 (ng/ml)	IL-6 (pg/ml)	MIF (ng/ml)	VEGF (pg/ml)
Control	0,033±0,03*	10,73±0,32*	3,90±0,195*	180,71±6,37*
Cancer	0,33±0,02*	20,60±0,32*	9,98±0,23*	248,25±2,21*
Bening prostate	0,19±0,05*&	18,30±0,60*&	6,00±0,17*&	237,52±2,20*&
Radical prostektomy	0,29±0,009*&β	21,62±0,34*&β	8,25±0,22*&β	271,4667±2,13*β&
Metastasis	0,42±0,02*&β≠	25,15±0,37*β≠&	12,72±0,28*β&≠	305,73±6,53*&β≠

* According to the control group p<0.05

& According to the cancer group p<0.05

β According to the Bening prostate group p<0.05

≠ According to the Radical prostektomy group p<0.05

In the cancer group, there was a statistically significant decrease in VEGF, MIF, Galectin-3 and IL-6 levels in patients with benign prostatic hyperplasia and radical prostectomy, while a statistically significant increase in VEGF, MIF, Galectin-3 and IL-6 levels was observed in the metastasis group. In patients with radical prostectomy, MIF and Galectin-3 levels decreased statistically, while VEGF and IL-6 levels increased. A statistical increase in VEGF, MIF, Galectin-3 and IL-6 levels was observed in patients with benign prostatic hyperplasia compared with patients with radical prostectomy and metastasis. Similarly, a statistically significant increase was observed in VEGF, MIF, Galectin-3 and IL-6 levels in patients with radical prostectomy compared with patients with metastasis (Figure I).

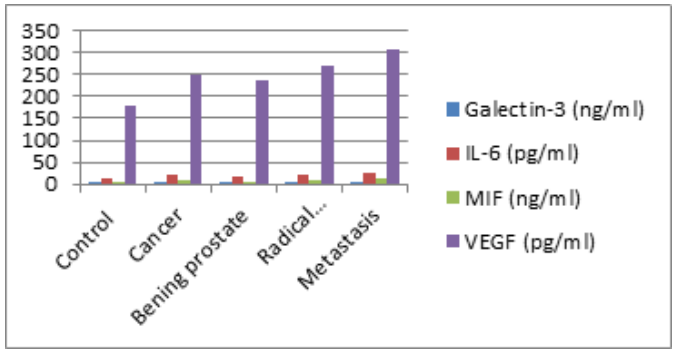

FIGURE 1: *Galectin-3, MIF, VEGF and IL-6 levels in groups*

4 | DISCUSSION

The prostate is the largest accessory gland of the male genital system and forms the initial part of the male urethra (1). The zonal anatomy of the prostate gland is particularly important clinically, since many carcinomas originate from the peripheral zone. However, benign prostatic hyperplasia involves the transitional zone. The central zone surrounding the ductus ejaculatory is rarely affected by diseases (19), (20).

Prostate carcinoma is the most common internal malignancy in the male sex. It ranks second in cancer-related deaths. Hormonal factors are important in its development. It is usually a disease of men over the age of 50. Incidental carcinoma foci of microscopic size that do not cause symptoms with advancing age are observed at a rate of up to 70% in autopsy studies (21). Microscopically, the majority of prostate carcinomas are of the adenocarcinoma type and can develop in a spectrum ranging from highly differentiated to poorly differentiated forms (22). PSA is the most important tumor marker used in the diagnosis, staging, and follow-up of patients with prostate cancer (23).

Free oxygen radicals are the basis of many diseases (eg, inflammatory diseases, neurodegenerative diseases, atherosclerosis, cancer) (24). It has been argued that oxidative stress products produced by inflammatory cells are one of the leading mechanisms in the formation of prostate cancer, similar to other epithelial cancers such as liver and gastric (25). Oxidative stress affects the development of prostate cancer and also hypoxia and inflammation are frequently due to DNA base lesions (26).

Cellular response to DNA damage occurs through aging of cells, apoptosis, damage repair, and cell cycle blocking (27). In studies conducted, reactive oxygen species (ROS) can cause DNA damage such as broken bonds, changes in thiamine and guanine bases and DNA crosslinks (28).

Malignant diseases are classically known as diseases in which uncontrolled excessive cell proliferation occurs. However, in addition to excessive proliferation, decreased apoptotic cell death rate has also been found to contribute to the development of malignancy (29).

Galectin-3 has a broad impact on tumor development, including cell proliferation, apoptosis, cell adhesion, invasion, angiogenesis, and metastasis (5). In order for the tumor to grow, it must pass from the prevascular to the vascular phase, in which activation of the angiogenic structure is required (6) . Some of the proangiogenic growth factors are secreted by the tumor, and the excess of molecules is regulated by destruction and care of perivascular cells and extracellular matrix, as well as stimulated endothelial cell division and migration (7). Galectin-3 has been reported to affect angiogenesis (10). Markowska et al reported in their study that Galectin-3 modulates VEGF- and bFGF-mediated angiogenesis. They reported that galectin-3 CRD binds to GnTV-modified N-glycans as a multimer and on $\alpha v\beta 3$ integrin, this binding is cross-linking, pathways that modulate endothelial cell migration in the angiogenic cascade activate FAK-mediated signals and cluster integrins (11). This group also reported that galectin-3 binds VEGFR2 and inhibits internalization causing an increased angiogenic response to VEGF-A (12). D'Haene et al. Reported that galectin-3 and 1 have an increased effect on angiogenesis and a decreased effect on receptor endocytosis through VEGFR1 activation (13).

The increase in circulating galectin-3 in cancer patients (14), (15). induces the release of metastatic secreting cytokines such as interleukin-6 (IL-6) and colony stimulating factor (G-CSF) from the blood vascular endothelium in vivo and in vitro.

MIF is the first protein to activate the formation of cytokines. There are studies showing an increase in IL-6 cytokines, especially in patients with prostate cancer (16). It has been said to interact with many tumor cells. MIF is thought to affect cancer by several mechanisms. These mechanisms cause immunomodulation by increasing the prevalence of immunosuppressive cells, neoangogenesis by binding to HIF-1 and ultimately provide transendothelial migration in cancer. Similar to other proinflammatory cytokines, it does not just modulate.

Among the identified proteins, interleukin-8 (IL-8), macrophage migration inhibitory factor (MIF), galectin-1, midkine (MK), IL-18, galectin-3, VEGF-A, hepatoma-derived growth factor (HDGF), osteopontin (OPN), connective tissue growth factor (CTGF) and granulin (GRN) are known to be involved in angiogenesis (30) . How Galectin-3 acts on the angiogenic protein VEGF and IL-6 cytokine in cancer patients is extremely important to understand the pathogenesis of diseases and to associate them with treatment, to develop new treatment protocols and even to eliminate risk factors in healthy people before diseases occur and It emerges as a subject that needs to be investigated.

In conclusion, the increase in VEGF, MIF, Galectin-3 and IL-6 levels in patients with cancer, metastatic, benign prostatic hyperplasia and radical prostectomy compared to the control group in our study seems to support our study. The reason for the statistical decrease in VEGF, MIF, Galectin-3 and IL-6 levels in patients with benign prostatic hyperplasia and radical prostectomy, according to the cancer group, suggests that the prostectomy performed is beneficial and will decrease more depending on the time. In addition, the decrease in MIF and Galectin-3 levels in patients with radical prostectomy compared to the cancer group made us think that the increased Il-6 and VEGF, which were activated by galectin-3

and MIF, would decrease depending on time. These markers may be a new marker in the diagnosis and monitoring of treatment of prostate patients. We think we should do more studies on this subject.

Conflict of interests

The authors have no conflicts of interest to declare.

Financial Disclosure

Celal Bayar University supported by scientific research project coordination

Ethical approval

Celal Bayar University etchic comitte is approved

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How to cite this article: D.F.K., G.T.E.M.E.L.T.A.S., O.U.C.E.R., T.M.U.E.Z.Z.I.N.O.G.L.U., U.B.A.S.A.R.A.N. **Effects of Galectin-3 And Mif Proteins on Angogenic Factors in Patients with Prostat Cancer**. Advance Research Journal of medical and clinical science . 2021;597−602. https://doi.org/10.15520/arjmcs.v7i06.327