bir zaman aralığında yapılmıştır. Uzunlamasına takip çalışmalarıyla bu sonuçlar teyit edilmelidir.

Sonuç olarak bu çalışmada ÖÖB bulunan çocuklarda anlamlı olarak folat ve vitamin D'nin düşük olduğu bulunmuştur. Bu vitaminlerin beynin kognitif fonksiyonlarındaki bu önemli rolleri göz önüne alındığında, ÖÖB patogenezinde de rol oynayabilecekleri düşünülebilir. Bununla birlikte bu vitamin değerlerinin rutin laboratuar ölçümlerinde bulunması, araştırılmasını kolaylaştırmaktadır. Çocukluk çağının en sık görülen psikiyatrik bozukluklarından biri olan ÖÖB bulunan çocuklarda bu testlerin yapılması ve eksikliğinde suplemantasyon tedavilerine gidilmesi önerilebilir. Bu vitaminlerin ÖÖB patogenezindeki rolleri ve suplemantasyonun etkileri konusunda daha ileri araştırmalara ihtiyaç bulunmaktadır.

KAYNAKLAR

1. APA. Diagnostic and statistical manual of mental disorders, fifth edition. American Psychiatry Association, Washington, DC, 2013.
2. Huskisson E, Maggini S, Ruf M.The influence of micronutrients on cognitive function and performance.J Int Med Res2007;35(1):1-19.
3. Bhatnagar S, Taneja S.Zinc and cognitive development. Br J Nutr2001;85:139-45.
4. Osendarp SJ, Baghurst KI, Bryan J, Calvaresi E, Hughes D, Hussaini M, et al.NEMO Study Group. Effect of a 12-momicronutrientintervention on learning and memory in well-nourished and marginally nourished school-aged children: 2 parallel, randomized, placebo-controlled studies in Australia and Indonesia.Am J Clin Nutr2007;86(4):1082-93.
5. Taras H. Nutrition and student performance at school. J Sch Health2005;75(6):199-213.
6. Wrzosek M, Łukaszkiewicz J, Wrzosek M, Jakubczyk A, Matsumoto H, Piątkiewicz P, et al.Vitamin D and the central nervous system. Pharmacol Rep2013;65(2):271-8.
7. Munger KL, Levin LI, Hollis BW, Howard NS, Ascherio A.Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA2006;296(23):2832-8.
8. Przybelski RJ, Binkley NC.Is vitamin D important for preserving cognition? A positive correlation of serum 25-hydroxyvitamin D concentration with cognitive function. Arch Biochem Biophys2007;460(2):202-5.
9. McGrath JJ, Eyles DW, Pedersen CB, Anderson C, Ko P, Burne TH, et al. Neonatal vitamin D status and risk of schizophrenia: a population-based case-control study. Arch Gen Psychiatry2010;67(9):889-94.
10. McGrath J, Eyles D, Mowry B, Yolken R, Buka S. Low maternal vitamin D as a risk factor for schizophrenia: a pilot study using banked sera. Schizophr Res2003;63(1-2):73-8.
11. Hoogendijk WJ, Lips P, Dik MG, Deeg DJ, Beekman AT, Penninx BW.Depression is associated with decreased 25-hydroxyvitamin D and increased parathyroid hormone levels in older adults. Arch Gen Psychiatry2008;65(5):508-12.
12. Gong ZL, Luo CM, Wang L, Shen L, Wei F, Tong RJ, et al.Serum 25-hydroxyvitamin D levels in Chinese children with autism spectrum disorders. Neuroreport 2014;25(1):23-7.
13. Mostafa GA, Al-Ayadhi LY.Reduced serum concentrations of 25-hydroxy vitamin D in children with autism: relation to autoimmunity. J Neuroinflammation 2012;9:201.
14. Cannell JJ, Grant WB.What is the role of vitamin D in autism? Dermatoendocrinol 2013;5(1):199-204.
15. Goksugur SB, Tufan AE, Semiz M, Gunes C, Bekdas M, Tosun M, et al.Vitamin D status in children with attention-deficit-hyperactivity disorder. Pediatr Int2014;56(4):515-9.
16. Fanjiang G, Kleinman RE.Nutrition and performance in children. Curr Opin Clin Nutr Metab Care 2007;10(3):342-7.
17. Moore E, Mander A, Ames D, Carne R, Sanders K, Watters D.Cognitive impairment and vitamin B12: a review. Int Psychogeriatr 2012;24(4):541-56.
18. Mooijaart SP, Gussekloo J, Frölich M, Jolles J, Stott DJ, Westendorp RG,De Craen AJ. Homocysteine, vitamin B-12, and folic acid and the risk of cognitive decline in old age: the Leiden 85-Plus study. Am J Clin Nutr 2005;82(4):866-71.
19. Esnafoğlu E, Yaman E. Vitamin B12, folic acid, homocysteine and vitamin D levels in children and adolescents with obsessive compulsive disorder. Psychiatry Research 2017;254: 232-237.
20. Savasir I, Sahin N. Wechsler çocuklar iciin zeka ölçeği (WISC-R). Turkish Psychological Association, Ankara. 1995 (Turkish).
21. Taşkın BD, Karalök ZS, Aydoğmuş Ü, Gürkaş E, Yoldaş M, Güven A,et al. Özgül Öğrenme Güçlüğü Olan Çocuklarda Çinko ve B12 Vitamini Düzeyleri.J Pediatr Res 2016;3(4):187-90
22. Klee GG. Cobalamin and folate evaluation: measurement of methylmalonic acid and homocysteine vs vitamin B12 and folate. Clinical chemistry 2000;46(8):1277-83.
23. Riggs KM, Spiro AIII, Tucker K, Rush D. Relations of vitamin B-12, vitamin B-6, folate, and homocysteine to cognitive performance in the Normative Aging Study. The American journal of clinical nutrition 1996:63(3):306-14.
24. Tuzcu, MS, Benli AR, Kumbasar A. B12 vitamin eksikliğinin etiyolojisinin araştırılması ve b12 vitamin düzeyi ile mcv, homosistein, folat düzeyleri ve tiroid fonksiyon testleri arasındaki ilişkinin saptanması. Investigation of Etiology of Vitamin B12 deficiency and the Association of Vitamin B12 Levels with MCV, Homocysteine, Folic Acid Levels and Thyroid Function Tests. Bozok Tıp Dergis.i 2018:8(1):25-30.
25. Selhub J, Bagley LC, Miller J, Rosenberg IH. B vitamins, homocysteine, and neurocognitive function in the elderly. The American journal of clinical nutrition. 2000:71(2);614-20.
26. Black MM. Effects of vitamin B12 and folate deficiency on brain development in children. Food and nutrition bulletin. 2008;29:126-31.
27. Cannell JJ, Grant WB. What is the role of vitamin D in autism? Dermato-endocrinology. 2013;5(1):199-204.
28. Garcion E, Wion-Barbot N, Montero-Menei CN, Berger F, Wion D. New clues about vitamin D functions in the nervous system. Trends in Endocrinology & Metabolism. 2002;13(3):100-105.

MTUS1 TÜMÖR BASKILAYICI GEN VE ONUN ANA TRANSKRİPT VARYANTI ATIP3A'NIN U2OS VE MCF-7 HÜCRELERİNDE PAKLİTAKSEL KAYNAKLI NEGATİF REGÜLASYONU

Paclitaxel-induced Negative Regulation of MTUS1 Tumor Suppressor Gene and its Major Transcript Variant ATIP3a in U2OS and MCF-7 Cells

Önder YUMRUTAS

Adiyaman University, Faculty of Medicine, Department of Medical Biology, Adiyaman, Turkey

Önder YUMRUTAS, Dr. Öğr. Üyesi

İletişim:
Dr. Öğr. Üyesi Önder YUMRUTAS
Adiyaman University, Faculty of Medicine, Department of Medical Biology, Adiyaman, Turkey
Tel: +904162231690-1499
e-mail:
oyumrutas@adiyaman.edu.tr;
yumrutasonder@gmail.com

Geliş tarihi/Received: 28.02.2018
Kabul tarihi/Accepted: 22.05.2018
DOI: 10.16919/bozoktip.399721

Bozok Tıp Derg 2018;8(3):65-70
Bozok Med J 2018;8(3):65-70

ÖZET
Artan kanıtlar, MTUS1'in meme, yumurtalık, pankreas, kolon kanseri gibi çeşitli malignitelerde düşük seviyelerde eksprese edildiğini göstermiştir. Ayrıca, fonksiyonel çalışmalar, ATIP1 ve ATIP3a/b'nin, tümör baskılayıcı aktivitelere sahip olan MTUS1'in iki büyük splice varyantı olduğunu göstermektedir. ATIP3'ün bir mikrotübül ilişkili protein bölgesine sahip olduğu, mikrotübüllerle birlikte lokalize olduğu ve mikrotübül dinamiğinin düzenlenmesinde rol alarak uzamış mitoza yol açtığı rapor edilmiştir. Buna ek olarak, paklitaksel, çeşitli kanser tiplerinde güçlü etki gösteren ve mikrotübüllerin oluşumunu indükleyen ve bozulmasını engelleyen güçlü bir antineoplastik ajantır. Dolayısıyla, bu çalışmada tümör baskılayıcı MTUS1 ve MTUS1'in majör transkript varyantı olan ATIP3'ün paklitaksel ile indüklenmiş mikrotübül stabilizasyonu ve hücre ölümündeki rolününün araştırılması amaçlanmıştır. Paklitakselin aktif dozunu saptamak için, MCF-7 ve U2OS hücrelerinin hücre canlılığı, MTT hücre canlılığı testi kullanılarak belirlenmiştir. Ayrıca, toplam MTUS1 mRNA ve ATIP3 mRNA'nın gen ekspresyonundaki değişiklikler, real-time PCR metodolojisi kullanılarak belirlenmiştir. Sonuç olarak, MTUS1 ve ATIP3 ekspresyonu, MCF-7 hücrelerinde paklitaksel uygulaması sonrasında azaldığı tespit edilmiştir. MTUS1'in ekspresyon seviyeleri U2OS hücrelerinde de azalmıştır, ancak ATIP3'ün seviyesi artmıştır. Ancak, bu değişiklikler istatistiksel olarak önemsiz bulunmuştur. Sonuç olarak, paklitaksel U2OS ve MCF-7 kanser hücrelerinde MTUS1 tümör baskılayıcı geni ve MTUS1'in majör transkript varyantı olan ATIP3'ü negatif yönde düzenlemektedir. Bu sonuçlar MTUS1 ve protein ürünü olan ATIP3'ün mikrotübül dinamiğinin düzenlenmesinde rol oynayabileceğini göstermiştir.

Anahtar kelimeler: *ATIP; Cancer; İkili fonksiyon; MTUS1; MTSG1; Tümor Supresör*

ABSTRACT
Accumulating evidence proposes that MTUS1 was expressed at low levels in a variety of malignancies such as breast, ovarian, pancreas, colon cancers. Also, functional studies indicate that ATIP1 and ATIP3a/b are the two major splice variants of MTUS1 which possess tumor suppressor activities. ATIP3 was shown to bear a microtubule-associated domain and is localized in association with microtubules and interfere with the microtubule dynamics and leads to prolonged mitosis. In addition, paclitaxel is a talented antineoplastic agent which shows potent activity on various types of cancers and induces the assembly of microtubules and inhibits their disassembly. Accordingly, in this study, we aimed to examine the key role of tumor suppressor MTUS1 and its major transcript variant ATIP3 in paclitaxel-induced microtubule stabilization and cell death. To determine active dose of paclitaxel, cell viability of MCF-7 and U2OS cells was determined by using MTT cell viability assay. Also, gene expression changes of total MTUS1 and ATIP3 mRNAs were determined by using real-time PCR methodology. As a result, the expression of MTUS1 and ATIP3 was lowered in response to paclitaxel in MCF-7 cells. Expression levels of MTUS1 were also reduced in U2OS cells but ATIP3 was increased. However, these changes were statistically insignificant. In conclusion, paclitaxel is inducing negative regulation of MTUS1 tumor suppressor gene and its major transcript variant ATIP3a in U2OS and MCF-7 cells and they might be involved in the regulation of microtubule dynamics

Key words: *ATIP; Cancer; Dual functions; MTUS1; MTSG1; Tumor Suppressor*

1. INTRODUCTION

Cancer is deadly major health situation which is estimated to be responsible for the 14.1 million new cases and 8.2 million annual deaths (1). It is clear that alterations in the proto-oncogenic and tumor suppressor signaling are the important hallmarks of cancers (2, 3). Particularly, the loss of tumor suppressor gene function is a common occasion in almost all cancers (2, 3). P53 is one of the well-known example in which the mutated p53 having lost its function to induce cellular apoptosis in harsh conditions (4). Moreover, MTUS1 is recently annotated as a novel tumor suppressor gene (5). It is first identified and characterized in pancreas cancer tumors and cells by Seibold et al (4). MTUS1 gene has been shown to be localized to 8p21.3-22 chromosomal region and approximately 150 kb in length (4). According to current knowledge, there are six different splice variants of this gene and five of them are known to produce five protein isoforms; ATIP1, ATIP2, ATIP3a, ATIP3b and ATIP4, called as angiotensin II receptor-interacting proteins (ATIPs) (6). ATIP1 is the primary identified member of this protein family and shown to be interacted with the C-terminus domain of AT2 receptor (7). Moreover, ATIP1, ATIP3a and ATIP3b variants were shown to have well tissue distribution and other members either poorly expressed or specifically expressed in some tissues (5). In addition, both ATIP3a/b were reported to be major protein isoform and ATIP1 was prominently expressed in brain tissues compared to other isoforms(5).

Furthermore, accumulating body of evidence suggests that MTUS1 was highly downregulated in a several types of malignancies such as colon, ovarian, breast, and pancreas cancers (8). Particularly, functional studies suggest that ATIP1 and ATIP3a/b have tumor suppressor activities. In addition, MTUS1 were primarily shown to be transiently stimulated in the course of initiation of quiescence and differentiation of cells (4). Furthermore, it was reported that ATIP3 has a microtubule-associated domain and is localized in association with microtubules (9, 10). Particularly, by co-localizing with microtubules, ATIP3 was shown to interfere with the microtubule dynamics and leads to prolonged mitosis (9, 10). In the confocal and fluorescence microcopy analyzes, it was shown that ATIP3 is localized in microtubule skeleton and microtubule organization centers with alpha-tubulin in cells expressing low ATIP3 (9, 10). It was also shown that elevated expression of ATIP3 triggers the formation of microtubule bundles (9, 10). This shows that ATIP3 can control the microtubules dynamic by triggering microtubule stabilization

Moreover, paclitaxel is a promising antineoplastic agent which shows potent activity on wide range of cancers (11). Paclitaxel induce the assembly of microtubules and inhibits their disassembly (11). Interestingly, assembled microtubules in the presence of paclitaxel are stable and dysfunctional and lead to cell death by disrupting the regulation of microtubule dynamics (11). Accordingly, in this study, main aim was to investigate the role of tumor suppressor MTUS1 and its major transcript variant ATIP3a in paclitaxel-induced microtubule stabilization and cell death

2. MATERIALS AND METHODS

2.1. Cell culture

U2OS and MCF-7 cancer cell line (American Type Culture Collection, VA, USA) were included in this study. Dulbecco's modified eagle's essential medium (DMEM) (GIBCO, NY, USA) supplemented with the 10% heat-inactivated fetal bovine serum (FBS) (Sigma-Aldrich, MO, USA) and penicillin (100 units/ml)/streptomycin (100 µg/ml) solution (Sigma-Aldrich, MO, USA) was used to propagate cells.

2.2. Determination of cell viability by MTT assay

Viability of cancer cells after Paclitaxel treatments were determined by using MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) cell viability assay and active doses were determined. Briefly, U2OS and MCF-7 cancer cells were treated different doses of Paclitaxel (0.03125, 0.0625, 0.125, 0.25 and 0,5 µM) (Catalog number: P3456) (Thermo Fisher Scientific Inc., Wilmington, USA) at 37ºC with 5% CO2 for 24h. After 24 hours of incubation with Paclitaxel, cells were incubated with the 1 mg/ml MTT solution for 1 hour and subsequently MTT was discarded. Plates were air-dried and purple formazan particles were dissolved using Dimethyl Sulfoxide (DMSO) (Sigma-Aldrich, MO, USA).

2.3. RNA isolation and cDNA synthesis

RNA was obtained from cultured cells using GeneJET RNA Purification Kit (Thermo Fisher Scientific Inc., Wilmington, USA) according to the manufacturer's recommended procedures. Quality and concentrations of RNA samples were determined by using NanoDrop ND-1000 spectrophotometer (Thermo Fisher Scientific Inc., Wilmington, USA). For cDNA synthesis, RevertAid First Strand cDNA Synthesis Kit (Thermo Fisher Scientific Inc., Wilmington, USA) were used. For the preparations of cDNA samples instructions of the supplier were followed and prepared samples were preserved at -80ºC in equal aliquots.

2.4. RT-qPCR experiments

Quantitative PCR (RT-qPCR) experiments were performed using Luminaris Color HiGreen qPCR Master Mix (Thermo Fisher Scientific Inc., Wilmington, USA) and the reactions were held in Rotor-Gene Q instrument (QIAGEN Sample & Assay Technologies, Germany). All experiments were studied in triplicate. Breifly, for the real-time PCR, following PCR mix were prepared for each reaction; 5 µL 2X Master Mix, 0.3 µL 10 µM Forward Primer, 0.3 µL 10 µM Reverse Primer, 1 µL cDNA and , nuclease-free water up to 10 µL. Reactions were subjected to following thermal cycling conditions; 10 min initial denaturation at 95 °C repeating 1 cycle, 15 s denaturation at 95 °C, 30 s annealing at 60 °C and 30 s Extension at 72 °C repeating 40 cycles. Also a melting curve analysis performed at the end of the reaction between 60 and 95 °C.

2.5. Analysis of data and statistical comparisons

GAPDH gene was used as internal reference control for all expression experiments. For the calculation of relative expression in qPCR experiments, 2−ΔCt (ΔCt = Target gene − Reference gene) formula was used. Also, a fold change analysis performed using the 2−ΔΔCt (ΔCt = Target gene − Reference gene) formula. Statistical analysis of the resulting data was achieved by using GraphPad Prism (v6.02, GraphPad Software, CA, USA) and SPSS (version 20, IBM, NY, USA) programs and Wilcoxon test applied. All statistical analysis was two-tailed, and $p < 0.05$ were accepted as significant.

3. RESULTS

3.1. Anti-proliferative activity of paclitaxel in U2OS and MCF-7 cells

To assess the anti-proliferative activity of paclitaxel in U2OS osteosarcoma and MCF-7 breast cancer cells, MTT cell viability assay was used. As a result, significant anti-proliferative activity of paclitaxel was observed with the increasing levels of treatment and 0.5 µM of doses of paclitaxel used was determined in both cell lines as active dose (Figure 1).

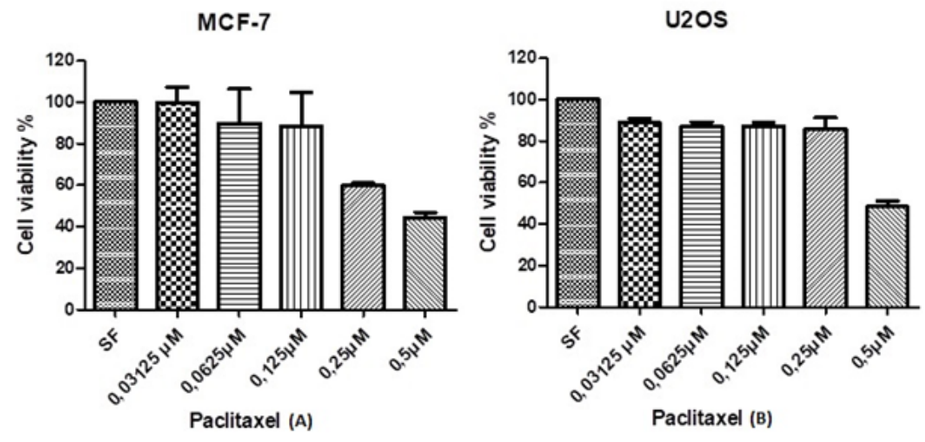


Figure 1. Anti-proliferative activity of Paclitaxel on A) MCF-7 breast cancer cells B) U2OS osteosarcoma cells.

3.2. Gene expression analysis of total MTUS1 expression levels and ATIP3a isoform

To ascertain the effect of paclitaxel on the expression of MTUS1 tumor suppressor gene and its major transcript variant ATIP3a, RT-qPCR technique was utilized. Accordingly, quantitative expression levels of total MTUS1 mRNA and ATIP3 mRNA were found to be down-regulated as result of paclitaxel treatments in MCF-7 breast cancer cells (Figure 2).

Moreover, a fold-change analysis was also performed and significant downregulation of MTUS1 and ATIP3a was observed in MCF-7 breast cancer cells (Table 1). Furthermore, while the quantitative expression levels of total MTUS1 mRNA was shown to be down-regulated as result of paclitaxel treatments in U2OS osteosarcoma cells, ATIP3a expression levels was upregulated (Figure 3).

Fold-change analysis in U2OS cell lines also confirmed these results (Table 1). Statistical analysis revealed no significant alteration in gene expressions (p>0.05).

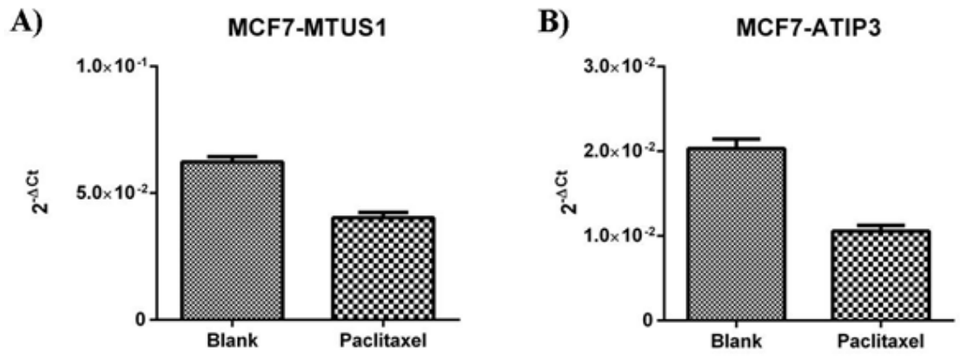


Figure 2. Differential expression of MTUS1 and its major transcript variant ATIP3a in MCF-7 breast cancer cells.

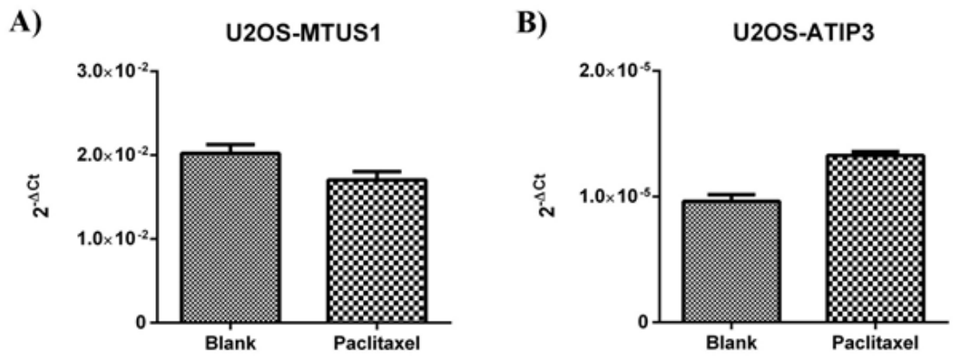


Figure 3. Differential expression of MTUS1 and its major transcript variant ATIP3a in U2OS osteosarcoma cells.

Table 1. Fold-change differences of total MTUS1 mRNA and ATIP3a transcript variant in MCF-7 breast cancer and U2OS osteosarcoma cells after paclitaxel treatments.

	MCF-7		U2OS	
	Fold change	p value	Fold change	p value
MTUS1	0.650670928	p>0.05	0.829319546	p>0.05
ATIP3a	0.52123288	p>0.05	1.328685814	p>0.05

4. DISCUSSION

Microtubules are dynamic structures which steadily transit between polymerization and depolymerization phases at their plus ends (12). This condition is actually well-known as microtubule dynamic instability which enables cells to respond various intracellular and extracellular stimuli (12). Defects in microtubule dynamic instability were shown to alter the regulation of mitotic spindle formation, chromosome segregation, migration, as well as transport of proteins and organelles within the cell (9, 12). Therefore, it leads to the formation and progression of cancer (9, 12).

The proteins that regulate microtubule dynamic instability are so called Microtubule-associated proteins (MAPs) (12). ATIP3, which is encoded by MTUS1 gene, is a recently identified MAP (12). Moreover, accumulating body of evidence suggests that MTUS1 and its transcription variants is heavily involved in the initiation, progression and metastasis of human cancers (6, 9). Studies also indicated that ATIP1 and ATIP3 is the major splice variants of MTUS1 gene and have significant tumor suppressor function in different types of human cancers (6, 9). In particular, similar to ATIP1 and ATIP3 was shown to interfere with the activation of extracellular signal-regulated kinase (ERK) signal transduction (13, 14). Particularly, recombinant overexpression of ATIP3 was shown to obstruct proliferation and migration of SACC-LM cells through downregulating the activities of ERK, and mesenchymal markers of Slug and Vimentin (14). In addition, as a microtubule-associated protein, ATIP3 was shown interact with microtubules (12, 15). Increased expression of ATIP3 has been shown to trigger the formation of microtubule bundles, thus in turn regulating microtubule dynamics (12, 15). It has also been reported that ATIP3 sediments with stabilized microtubules (12, 15). It has been also shown that microtubule dynamics are altered in cells stably expressing ATIP3 and microtubule bundles decrease nocodazole susceptibility (15). In addition, ATIP3 has shown to interact with EB1 (End-binding protein 1) and increased expression of ATIP3 suppresses EB1 accumulation at microtubule plus ends independent of microtubules (12). More recently, it was shown that ATIP3 interferes with the proliferation, migration and metastasis of breast cancer cells through altering microtubule dynamics (15). In short, these findings strongly indicate that ATIP3 interacts with microtubules and EB1 protein, regulating microtubule dynamic instability and delaying the progression of mitosis and limiting cellular migration.

Paclitaxel is a taxane drug which is routinely used to fight against various cancer types in cancer therapy. Mechanism of action of paclitaxel involves the stabilization of microtubules. Accordingly, in this particular study, it was tried to reveal the role of tumor suppressor MTUS1 and its major transcript variant ATIP3a in paclitaxel-induced microtubule stabilization and cell death. Surprisingly, expression levels of both MTUS1 and its major splice variant ATIP3 was found to be diminished in paclitaxel treated breast and osteosarcoma cancer cells. Strongly suggesting that paclitaxel is inducing negative regulation of MTUS1 tumor suppressor gene and its major transcript variant ATIP3a in U2OS and MCF-7 cells. These findings also support the notion that MTUS1 and ATIP3 splice variant might be involved in the regulation of microtubule dynamics.

5. REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. Ca-a Cancer Journal for Clinicians 2012;62: 10-29.
2. Bozgeyik E, Bayraktar E, Chavez-Reyes A, Rodriguez-Aguayo C. Oncolncs: Long non-coding rnas with oncogenic functions. Mol Biol 2016;5: 1-13.
3. Hanahan D, Weinberg RA. Hallmarks of cancer: The next generation. Cell 2011;144: 646-74.
4. Seibold S, Rudroff C, Weber M, Galle J, Wanner C, Marx M. Identification of a new tumor suppressor gene located at chromosome 8p21.3-22. Faseb Journal 2003;17: 1180-+.
5. Di Benedetto M, Bieche I, Deshayes F, Vacher S, Nouet S, Collura V, et al. Structural organization and expression of human MTUS1, a candidate 8p22 tumor suppressor gene encoding a family of angiotensin ii at2 receptor-interacting proteins, atip. Gene 2006;380:

127-36.
6. Rodrigues-Ferreira S, Nahmias C. An atipical family of angiotensin ii at2 receptor-interacting proteins. Trends in Endocrinology and Metabolism 2010;21: 684-90.
7. Nouet S, Nahmias C. Signal transduction from the angiotensin ii at(2) receptor. Trends in Endocrinology and Metabolism 2000;11: 1-6.
8. Kara M, Kaplan M, Bozgeyik I, Ozcan O, Celik OI, Bozgeyik E, et al. MTUS1 tumor suppressor and its mirna regulators in fibroadenoma and breast cancer. Gene 2016;587: 173-7.
9. Bozgeyik I, Yumrutas O, Bozgeyik E. MTUS1, a gene encoding angiotensin-ii type 2 (at2) receptor-interacting proteins, in health and disease, with special emphasis on its role in carcinogenesis. Gene 2017;626: 54-63.
10. Rodrigues-Ferreira S, Di Tommaso A, Dimitrov A, Cazaubon S, Gruel N, Colasson H, et al. 8p22 MTUS1 gene product ATIP3 is a novel anti-mitotic protein underexpressed in invasive breast carcinoma of poor prognosis. Plos One 2009;4: e7239.
11. Weaver BA. How taxol/paclitaxel kills cancer cells. Mol Biol Cell 2014;25: 2677-81.
12. Velot L, Molina A, Rodrigues-Ferreira S, Nehlig A, Bouchet BP, Morel M, et al. Negative regulation of eb1 turnover at microtubule plus ends by interaction with microtubule-associated protein ATIP3. Oncotarget 2015;6: 43557-70.
13. Nouet S, Amzallag N, Li JM, Louis S, Seitz I, Cui TX, et al. Trans-inactivation of receptor tyrosine kinases by novel angiotensin ii at2 receptor-interacting protein, atip. J Biol Chem 2004;279: 28989-97.
14. Zhao TT, He QT, Liu ZH, Ding XQ, Zhou XF, Wang AX. Angiotensin ii type 2 receptor-interacting protein 3a suppresses proliferation, migration and invasion in tongue squamous cell carcinoma via the extracellular signal-regulated kinase-snai2 pathway. Oncol Lett 2016;11: 340-44.
15. Molina A, Velot L, Ghouinem L, Abdelkarim M, Bouchet BP, Luissint AC, et al. ATIP3, a novel prognostic marker of breast cancer patient survival, limits cancer cell migration and slows metastatic progression by regulating microtubule dynamics. Cancer Res 2013;73: 2905-15.

PALYATİF BAKIM MERKEZİNDE YATAN KANSER HASTALARININ BESLENME NRS-2002 SKORLARI İNFLAMASYONLA İLİŞKİLİ MİDİR?

Are the Nutritional Nrs-2002 Scores of Cancer Patients at the Palliative Care Center Related to Inflammation?

Deniz AVCI

Sağlık Bilimleri Üniversitesi Kayseri Eğitim ve Araştırma Hastanesi, Palyatif Bakım Merkezi, KAYSERİ

Deniz AVCI, Uzm. Dr.

İletişim:
Uzm. Dr. Deniz AVCI,
Sağlık Bilimleri Üniversitesi Kayseri Eğitim ve Araştırma Hastanesi,
Palyatif Bakım Merkezi, KAYSERİ
Tel: 05053964878
e-mail:
denav38@gmail.com

Geliş tarihi/Received: 27.02.2018
Kabul tarihi/Accepted: 01.08.2018
DOI : 10.16919/bozoktip.399229

Bozok Tıp Derg 2018;8(3):71-5
Bozok Med J 2018;8(3):71-5

ÖZET

Amaç: Bu çalışmada, NRS-2002 tarama skorları ile hematolojik inflamasyon belirteçleri sayılan nötrofil/Lenfosit oranı (NLR), platelet/lenfosit oranı (PLR) ve ortalama trombosit hacmi (MPV) arasındaki olası ilişkilerin ortaya konulması amaçlandı.

Gereç ve Yöntemler: Palyatif bakım merkezinde takip edilmiş olan çeşitli tanılardaki kanser hastalarının NRS-2002 skorları ile NLR, PLR ve MPV arasındaki olası korelasyonlar araştırıldı. Ayrıca, taburcu olanlar ve palyatif ünitede ölen hastalar olmak iki grup oluşturuldu ve bu inflamatuvar belirteçler gruplararasında yönünden de karşılaştırıldı.

Bulgular: Toplam 64 hastanın yaş ortalamaları 66,5±13,1 yıldı. Hastaların NRS-2002 skorlarıyla NLR arasında pozitif yönde, hafif düzeyde, istatistiksel olarak anlamlı bir korelasyon vardı (r=383, p=0,002). Hastaların NRS-2002 skorlarıyla PLR arasında pozitif yönde, hafif düzeyde, istatistiksel olarak anlamlı bir korelasyon vardı (r=341, p=0,006). Hastaların palyatif bakım ünitesinden taburcu edildikten sonraki sağkalım süreleri ile PLR arasında negatif yönde, orta düzeyde, istatistiksel olarak anlamlı bir korelasyon vardı (r=0,501, p=-0,021). Hastaların palyatif bakım ünitesine yattığı andan ölümüne kadar geçen süre ile MPV arasında negatif yönde, hafif düzeyde, istatistiksel olarak anlamlı bir korelasyon vardı (r=-285, p=0,029). Hastaların palyatif bakıma yattıktan sonraki sağkalımları ile (yatış günü 1.gün olarak kabul edildi) NLR arasında negatif yönde, hafif düzeyde, istatistiksel olarak anlamlı bir korelasyon vardı (r=-279, p=0,025).

Sonuç: Bu çalışmanın sonuçlarına göre NLR ve PLR'nin NRS-2002 skorlarıyla korelasyon içerisinde olduğu söylenilebilir. Bu karşılaştırmalar palyatif bakım merkezleri özelinde ilk kez yapılmıştır.

Anahtar Kelimeler: *Palyatif bakım; Kanser; İnflamasyon*

ABSTRACT

Objective: In this study, it was aimed to determine the possible relationships between the NRS-2002 screening scores and the neutrophil / lymphocyte ratio (NLR), platelet / lymphocyte ratio (PLR) and mean platelet volume (MPV), which are considered to be hematologic inflammation markers.

Materials and methods: Possible correlations between NRS-2002 scores and NLR, PLR, and MPV were investigated in the various cancer patients followed up at the palliative care center. In addition, two groups of patients who were discharged and those who died in the palliative unit were formed and compared in terms of the groups of these inflammatory markers.

Results: The mean age of 64 patients was 66.5 ± 13.1 years. There was a statistically significant correlation between the NRS-2002 scores of the patients and the NLR in the positive direction (r = 383, p = 0,002). There was a statistically significant correlation between the NRS-2002 scores of the patients and PLR in the positive direction (r = 341, p = 0.006). There was a moderate, statistically significant correlation between the survival times after discharge from the patients' palliative care unit and PLR (r = 0,501, p = -0,021). There was a mild, statistically significant correlation between MPV and the time from the onset of death to the palliative care unit of the patients (r = -285, p = 0.029). There was a mild, statistically significant correlation (r = -279, p = 0.025) between the survival of the patients after palliative care and the NLR on the negative side (day 1 was accepted as the day of admission).

Conclusion: According to the results of this study, it can be said that NLR and PLR are in correlation with NRS-2002 scores. These comparisons were made for the first time in the area of palliative care centers.

Key Words: *Palliative care; Cancer; İnflammation*