ORIGINAL ARTICLE

The relationship between prognosis of patients with traumatic brain injury and microRNA biogenesis proteins

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ABSTRACT

BACKGROUND: This study aims to investigate whether the expression levels of proteins involved in microRNA (miRNA) biogenesis vary in early- and late-stage traumatic brain injury (TBI) patients and to evaluate its effect on prognosis.

METHODS: Dicer, Drosha, DiGeorge Syndrome Critical Region eight (DGCR8), Exportin5 (XPO5), and Argonaute2 (AGO2) levels were measured in the blood samples of severe TBI patients collected 4–6 h and 72 h after the trauma and compared with the control group. Prognostic follow-up of the patients was performed using the Glasgow Coma Scale score.

RESULTS: There were no statistically significant changes in the expression of the miRNA biogenesis proteins Dicer, Drosha, DGCR8, XPO5, and AGO2 in patients with severe TBI. However, the expression of Dicer increased in the patients who improved from the severe TBI grade to the mild TBI grade, and the expression of AGO2 decreased in most of these patients. The Dicer expression profile was found to increase in patients discharged from the intensive care unit in a short time.

CONCLUSION: MicroRNAs and their biogenesis proteins may guide prognostic and therapeutic decisions for patients with TBI in the future.

Keywords: Traumatic brain injury; prognosis; MicroRNA; MicroRNA biogenesis.

INTRODUCTION

Traumatic brain injury (TBI) has become a significant health and socioeconomic problem worldwide. It is one of the leading causes of mortality and morbidity in young adults.[1] The heterogeneity of TBI severity and clinical presentation combined with the paucity of validated objective tools hinders optimal immediate and long-term patient care. Unlike routine fluid-based diagnostic tests for heart failure, pregnancy, or diabetes, the clinical use of brain-derived blood biomarkers for TBI is limited. In addition to clinical examination, patient demographics, and radiological information, biomarkers are required for the timely identification of the prognosis after TBI and the early estimation of short and long-term outcomes in patients with moderate-to-severe brain injury. TBIs can be categorized into mild, moderate, and severe based on clinical factors, such as the duration and severity of consciousness (if present), the presence of amnesia and neurological symptoms, and the results of structural brain imaging (such as computed tomography [CT] or magnetic resonance imaging [MRI]). At present, no biomarker that can reliably be used for the diagnosis and prognosis of TBI patients in the clinical practice has been identified.[2] At present, the diagnosis of concussion relies on subjective assessment.[3] There are only a few biologi-

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cal measures available which can be used to tailor treatment and guide decision-making. The lack of sensitive and objective assessment tools limits the ability of doctors to provide accurate diagnoses and effective treatments.[4,5] Therefore, identifying biomarkers for TBI could have a significant impact on the diagnosis and management of concussion.[6,7] Recent evidence suggests that microRNAs (miRNAs) may be able to fulfill this clinical need.

MiRNAs are small, endogenous, and non-coding ribonucleic acid (RNA) molecules that consist of 19–28 nucleotides and regulate protein synthesis at the post-transcriptional level. The miRNA biogenesis is a two-step process in both the nucleus and the cytoplasm. Specialized proteins are involved in this process. The most specific ones are the Drosha enzyme and its cofactor DiGeorge syndrome critical region eight (DGCR8), which are the members of the RNAase III family; Exportin5 (XPO5), a transport receptor; Dicer endonuclease, another enzyme of the RNAase III family; and the argonaute protein, which provides a stable chain selection. It is well documented that the function of the targeted miRNA is impaired if the proteins involved in miRNA synthesis cannot perform their functions correctly.[8]

miRNAs play a key role in the pathophysiology of many diseases and are critical for neurodevelopment and brain function. [9] Through regulation of gene activity, miRNAs control cellular processes such as differentiation, proliferation, apoptosis, and metabolism, which are essential in neuronal damage and repair.[10,11]

Numerous studies have demonstrated that peripheral miRNA profiles fluctuate across the primary and secondary phases of TBI.[12-14] At present, diagnosing TBI poses a significant challenge, as available tools are limited in effectiveness. However, recent studies have highlighted the potential of miRNAs as biomarkers for TBI. A distinct advantage of miRNAs is their ability to cross the blood-brain barrier and remain stable in peripheral biofluids, making them ideal for diagnosis and prognosis. Furthermore, the role of miRNAs in neuronal communication may provide unique insights into the damaged brain, further increasing their potential as a diagnostic tool. Identification of miRNAs that respond rapidly to injury could enhance the diagnostic capabilities for TBI, aiding in therapeutic decision-making. Despite ongoing gaps in TBI biomarker research, miRNAs show potential for a significant breakthrough in the diagnosis and management of TBI.

Clinical and experimental studies have demonstrated many prognostically and diagnostically valuable miRNAs expressed in TBI; however, there is a limited number of data regarding the levels of proteins implicated in the miRNA biogenesis in TBI patients.[15] In the present study, we aimed to investigate whether the expression levels of proteins involved in miRNA biogenesis vary in the early- and late-stage TBI patients and to evaluate its effect on prognosis.

MATERIALS AND METHODS

Study Design and Sample

This prospective and clinical study was conducted at the anesthesiology intensive care unit (ICU) of a tertiary care center between July 2017 and April 2019. Twenty-one patients with severe TBI (Glasgow Coma Scale [GCS] score ≤8) aged ≥18 years were included in the study. In the presence of epidural, subdural, or intracerebral hematoma, microhemorrhages, contusion, diffuse or focal axonal damage, laceration, or subarachnoid hemorrhage in post-traumatic patients, these patients were considered to have a TBI. Demographic variables and injury characteristics consisted of age, gender, medical history, trauma type, trauma severity scores, and ICU stay times. Severity scores have included the injury severity score and abbreviated injury scales (AIS). Major extracranial trauma was defined as AIS ≥3 in one or more body regions other than the head.

The first blood samples of the patients were collected from the peripheral blood during the first 4–6 h after trauma. A second set of blood samples was collected at 72 h after trauma.

The variables about interventions and treatment were collected as length of hospital and ICU stay, insertion of an intracranial pressure catheter, sedation, and mechanical ventilation at the ICU. Brain-specific treatments such as osmotherapy (mannitol or hypertonic saline), vasopressive medication to maintain cerebral perfusion pressure, hyperventilation, cerebrospinal fluid drainage, hypothermia (body temperature <35°C), and use of barbiturates were also recorded.

The control group consisted of 21 patients aged ≥18 years that sustained a trauma but did not have a history of clinical or radiological brain injury, amnesia or syncope, and a deficit in the neurological examination. Peripheral blood samples were taken from the control group at the same time as the case group. Patients with alcohol, substance, or drug addiction, a history of neurological or psychiatric disease, intracranial operation, neoplastic disease, and patients operated during follow-up were excluded from the study.

A written informed consent was obtained from all participants and/or their legal guardians. The study was approved by the Institutional Ethics Committee (Date: March 01, 2017, No: 2012-KAEK-20) and conducted in accordance with the principles of the declaration of Helsinki.

Study of Gene Expression Profiles of Target Molecules by Real-time Polymerase Chain Reaction (RT-PCR)

The RNA isolation was performed in peripheral blood samples of all study groups using the AccuZol™ Total RNA extraction kit (Bioneer Corp., Daejeon, South Korea), and the RNAs were translated to complementary deoxyribonucleic acid (cDNA) with high-capacity cDNA reverse transcription kit (Thermo Fisher Scientific, MA, USA).

Each cDNA sample was analyzed for gene expressions in Exi-Cycler™ 96 Quantitative-PCR device (Bioneer Corp., Daejeon, South Korea) by RT-PCR using the K-6253 AccuPower®

Table 1. Primer sequences used to amplify a specific gene region

Primer sets	Sequences
DGRC8	F: GCAAGATGCACCCACAAAGA
	R: TTGAGGACACGCTGCATGTAC
Argonaute2	F: TCGCACTATCACGTCCTCTG
	R: ATGGCTTCCTTCAGCACTGT
DICER1	F: TACCCCGTTCCCCTGTGCGA
	R: TCGGAGGCCTCTTCTTGCTGCT
DROSHA	F: TTCCCTCCCTTGGCCCAGCTT
	R: CTATAAAAGGCTCTCGGGCCGC
Exportin5	F: CACAACGAGAGGTGATGAG
	R: AAGGTGAGAAGACGGAACAGAG

2X GreenStar™ Master Mix kit (Bioneer Corp., Daejeon, South Korea) and specific primers designed with reference to the literature on DICER1 (Dicer), Drosha, DGCR8, XPO5, and AGO2 (Table 1).[16-18]

Study of Protein Expression Profiles of Target Molecules by Protein Isolation and Western Blot Analysis

Protein quantification of each sample was performed using the Bradford-based DeNovix DS-11 spectrophotometer (DeNovix Inc., DE, USA). A WesternBreeze™ Kit (Thermo Fisher Scientific, MA, USA) containing an anti-Dicer antibody (rabbit), anti-Drosha antibody (rabbit), anti-DGCR8 antibody (rabbit), anti-XPO5 antibody (rabbit), and anti-AGO2 antibody (rabbit) was used in specific protein analysis. Finally, blotting was performed using the Hoefer™ TE70XP (Hoefer Inc., MA, USA), and the results were analyzed using the SynGene GeneTools software version 4.3.9.0 (Synoptics Ltd., Cambridge, UK).

Statistical Analysis

Statistical analysis was performed using the SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). The ΔΔCt (Fold Change: Fold change in mRNA expression levels) equation was used for normalization and comparative quantification.[19]
ΔCT = CT (target) – CT (reference, i.e., GAPDH) ΔΔCT = ΔCT (sample) – ΔCT (control)
2–ΔΔCT (fold increase in target gene amount normalized to endogenous reference)
where CT indicates cycle threshold defined as the number of cycles required for the fluorescent signal to cross the threshold that refers to the exponential increase in the log-linear phase of PCR and ΔCT indicates the difference between the target and reference thresholds.
Normalized gene expressions and expression changes were calculated using the 2–ΔΔCT method. Paired-samples t-test for normally distributed groups and Wilcoxon signed-ranks test for not normally distributed groups were performed. P<0.05 was considered statistically significant.

RESULTS

Forty-two individuals, including 21 patients with severe TBI (patient group) and 21 control group patients, were included in the study. Demographic characteristics of the study population are shown in Table 2. There was no statistically significant difference in the demographic data of the patients regarding sex medical history and trauma severity between the TBI patients and control groups, while age (P=0.03), cause of trauma, and ICU stay were significantly different between the groups (P<0.001) (Table 2). Furthermore, interventions and treatments done in the TBI patients group are shown in Table 3.

The mean GCS scores were 6.1±1.7 on admission and 11.9±4.3 on day 30 during follow-up in the TBI patients group. The increase in the GCS scores in the TBI patients group was statistically significant (P<0.05). The total GCS scores of the control group were 15 on admission and 15 on day 30, indicating no statistically significant difference (P>0.05).

There was no significant difference in the TBI patients group between the normalized gene expressions measured at 4–6 h and 72 h after trauma (Dicer P=0.13; Drosha P=0.41; XPO5 P=0.18; DGCR8 P=0.29; and AGO2 P=0.57) (Fig. 1a). Similarly, there was no significant difference in the control group between the normalized gene expressions measured at 4–6 h and 72 h after trauma (Dicer P=0.74; Drosha P=0.98; XPO5 P=0.78; DGCR8 P=0.17; and AGO2 P=0.94) (Fig. 1b). The Dicer, Drosha, XPO5, DGCR8, and AGO2 showed no statistically significant difference in the normalized gene expression levels and fold increases between the TBI patients group and control groups (P>0.05) (Figures 1c and d).

Eleven of 21 patients with severe TBI improved to mild TBI at the end of 30 days (P2, P3, P4, P5, P7, P8, P9, P13, P16, P20, and P21). No significant correlation was found between grade change and increases in the Dicer, Drosha, XPO5, DGCR8, and AGO2 gene expression levels (Dicer P=0.42; Drosha P=0.71; XPO5 P=0.35; DGCR8 P=0.3; and AGO2 P=0.41). However, the Dicer protein expression levels increased in all of these 11 patients, while AGO2 decreased in eight of these patients (Figures 2a and b). The mean partial arterial oxygen pressure in these 11 patients was 106.4±31.8 mmHg.

Five patients (P3, P5, P8, P13, and P20) showed a rapid recovery in a short period of 1 week and were discharged from the ICU. The individual evaluation of protein expression levels revealed an increased Dicer expression in all of these patients. The mean partial arterial oxygen pressure values of this patient group were 112.8±36 mmHg during follow-up.

In this study, the GCS scores of patient 18 and patient 19 deteriorated during clinical follow-up. Among the protein expression profiles of these patients, Dicer was decreased and DGCR8 was increased.

The gene expression profile was confirmed by the western

Table 2. Demographic variables and injury characteristics of the patient and control groups

Variable	Traumatic brain injury patient group	Control group	P-value
Age	40.2±19	53.8±20.7	0.03
Sex (F/M)	5/16	7/14	0.50
Medical history, n (%)			
Non-specific	8 (38)	13 (61.9)	0.12
ASA Class I	13 (61.9)	8 (38)	
Trauma type n (%)			
Pedestrian accident	11 (52.3)	2 (9.5)	0.001
Road traffic accident	6 (28.5)	3 (14.2)	
Fall	4 (19)	16 (76.1)	
Abbreviated injury scores			
Head/Neck	3.40±1.15	2.94±1.08	<0.001
Face	1.80±0.43	1.77±0.45	0.107
Thorax	2.58±0.87	2.63±0.78	0.305
Abdomen	2.67±0.94	2.69±0.94	0.171
Extremity	2.14±0.58	2.31±0.56	<0.001
External	1.20±0.58	1.21±0.58	0.988
Injury severity score	9±3	9±2	0.5
ICU stay	26±19	19±12	<0.05

Data are given in mean±standard deviation or number and percentage, unless otherwise stated. ASA: American Society of Anesthesiologists, ICU: Intensive care unit.

Table 3. Interventions and treatments in traumatic brain injury patients group

Interventions and treatments	n
ICU management	
Mechanical ventilation	17
Sedation	16
ICP Monitoring	None
Osmotherapy	8
Vasopressive use	7
Hyperventilation	None
CSF drainage	None
Hypothermia	None
Barbiturates	None

ICU: Intensive care unit; ICP: Intracranial pressure; CSF: Cerebrospinal fluid.

blot analysis, which showed the expression at the protein level.

DISCUSSION

The number of patients hospitalized in the ICU due to severe brain injury has been increasing every year. In addition to the clinical and radiological parameters used to estimate the prognosis of these patients, miRNAs have become the target of many studies in recent years.[15,20] However, the heterogeneous nature of both the injury itself and the populations in which TBI is occurred can explain why biomarkers have not yet been discovered and incorporated into clinical practice.

In the past decade, several novel categories of blood biomarkers, for example, extracellular vesicles, miRNAs, and cellular metabolites, have emerged and have the potential to accurately gauge the severity of neural injury and neurodegenerative progression.[9,15] Redell et al.[21] were the first to describe altered hippocampal miRNA levels in rats exposed to controlled cortical effects. Using microarray techniques to evaluate over 400 miRNAs, they confirmed changes in eight miRNAs with RT-PCR (RT-PCR; miR-107, miR-130a, miR-223, miR-292-5p, miR-433- 3p, miR-451, miR-541, and miR-711). Liu et al.[22] extended these miRNA findings to the rat cerebral cortex and found that miRNA levels changed dynamically within the first 72 h after TBI. The authors identified one miRNA (miR-21) that remained chronically elevated following the initial injury.

The biochemical cascade that occurs during brain injury and mechanical damage consists of oxidative stress, apoptotic cell death, subacute repair, and chronic remodeling.[23] The miR-21 and miR-16, identified in both human and animal TBI studies, are biomarker candidates that can regulate apoptosis as described in animal studies.[24,25] In addition, miR-16 has criti-

cal targets in cell cycle regulation, including b-cell lymphoma 2 (Bcl-2) and cyclin-dependent kinase. These molecules may facilitate neurogenesis and acute repair responses following TBI.[26] Unlike proteins that typically increase after TBI, some miRNAs are downregulated after injury (e.g., miR-107 and miR-27a). The decrease in miR-107 may activate inflammatory processes by allowing the transcription of granulin.[27] Similar to miR-27a, its decrease may facilitate programmed cell death by enabling the expression of pro-apoptotic Bcl-2 proteins.[28]

The exact underlying mechanisms that drive individual miRNA alterations after TBI have not been fully understood, yet. Such as proteins that increase in the circulation due to damage to endothelial cells and astrocytes forming the blood-brain barrier after trauma, or due to axonal involvement of neurons, miRNAs may be also released, increasing their amount in the peripheral blood.[29] Furthermore, peripheral blood concentrations of peripheral miRNAs may vary in response to sympathetic, hormonal, or neuroimmune mechanisms which regulate the physiological response to TBI. Through this mechanism, miRNAs may play a key role in neuroplasticity, and altered miRNA expression in the subacute period among TBI patients may indicate the long-term prognosis.[30] Whether miRNA alterations are passive artifacts of the primary injury or integral players in the secondary injury response, their dynamic expression and multifaceted role in the human brain provide a distinct opportunity to measure the central nervous system's response to trauma. Clinical and experimental studies have demonstrated many prognostically and diagnostically valuable miRNAs measured in TBI; however, data on the levels of proteins involved in miRNA biogenesis in TBI patients are limited.

In the present study, we investigated biogenesis proteins independently of any miRNA. We prospectively measured the differences in protein expression levels of Dicer, Drosha, DGCR8, XPO5, and AGO2, which are involved in miRNA biogenesis, in TBI patients and compared them with the control group. At the end of 30 days, we observed that Dicer protein expression levels increased in all patients who were classified as mild TBI (GCS≥14) (n=11), whereas AGO2 de-

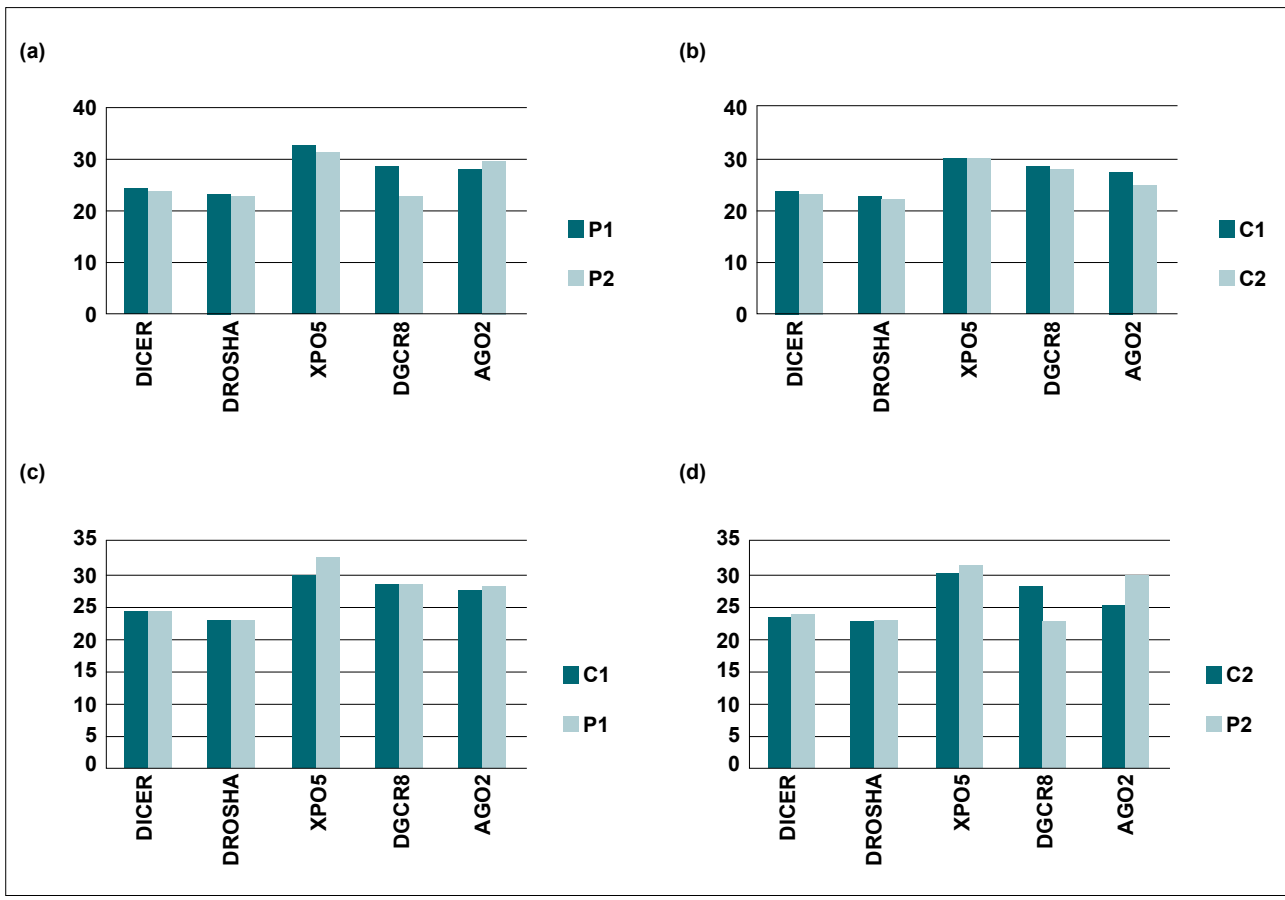

Figure 1. Cycle threshold of miRNA biogenesis proteins. **(a)** Comparison of mean Ct values of the patient group (P1: 4–6 h after trauma, P2: At 72 h after trauma) (P>0.05), **(b)** Comparison of the mean Ct values of the control group (C1: 4–6 h after trauma, C2: at 72 h after trauma) (P>0.05), **(c)** Comparison of the mean Ct values of the patient and control groups at 4–6 h after trauma (C1: Control group, P1: Patient group) (P>0.05), **(d)** Comparison of the mean Ct values of the patient and control groups at 72 h after trauma (C2: Control group and P2: Patient group) (P>0.05). Ct: Cycle threshold.

Figure 2. MiRNA biogenesis protein expression levels of patients with mild TBI. **(a)** Protein expression profiles at 4–6 h after trauma of the patients classified in the mild TBI category at the end of 30 days. **(b)** Protein expression profiles at 72 h after trauma of the patients classified in the mild TBI category at the end of 30 days. P: Patient. (Each patient has been numbered, e.g. P2, P3, etc.) TBI: Traumatic brain injury.

creased in 72% (n=8) of these patients. While there was a statistically significant increase in the 30-day GCS scores of the patients, no statistically significant correlation between the increased GCS and protein expression levels was found.

In the literature, there are studies examining the proteins involved in miRNA biogenesis in the brain tissue and neural stem cells.[31] In addition to preclinical studies, there are studies investigating these proteins in cancer, neurodegenerative diseases, and renal transplant patients.[8,31,32] However, our study is the first to identify the clinical relationship of proteins involved in miRNA biogenesis with TBI.

Dicer has been identified as a member of the RNase III family enzymes that specifically, cleaves long double-stranded RNA (dsRNA) substrates into short, defined-length dsRNA fragments.[33] This evolutionarily conserved and universally expressed protein[33,34] has crucial physiological roles,[35] and its absence is associated with various stages of disease development.[32,36] In recent years, the Type III RNase Dicer has emerged as a key regulator of adaptive cellular response to fluctuation of metabolic homeostasis and catabolic processes. This further supports the concept that Dicer may mediate beneficial metabolic effects in balancing systemic energy. Autophagy is a cellular catabolic process that directs cyto-

plasm components such as macromolecules or damaged organelles to the lysosome for degradation to maintain energy homeostasis and combat cellular stress. It has been proposed that Dicer, which regulates autophagy in response to multiple sources of cellular stress that may occur after TBI, such as nutrient deprivation,[37] hypoxia,[38,39] DNA damage,[40] and heat shock,[41] may have a central role in helping cellular survival through its participation in stress-induced catabolic metabolism.[42] The increase in Dicer protein in recovering patients and the decrease in worsening patients in our study indicate that the hypoxia and catabolic processes following TBI may be regulated in a way that positively affects the prognosis of the patient in the presence of Dicer.

It has been proven by many studies that hypoxia, which is a secondary injury factor in TBI, increases morbidity and mortality, impairs cognitive functions, and prolongs the length of ICU stay.[43,44] Several studies have shown that Dicer is downregulated under hypoxic conditions.[45] In the present study, we observed an increase in Dicer levels in patients who recovered and discharged within 1 week after TBI and a decrease in these levels in two patients whose GCS scores worsened during clinical follow-up. Based on these findings, we can speculate that the increased expression of Dicer protein in recovering patients can be used as a predictor of good prognosis; similarly, the application of synthetic Dicer protein can be viewed as a therapeutic target in the treatment of severe TBI, particularly in hypoxic patients.

Argonaute2 is one of the key proteins with miRNA-related mRNA synthesis or translational inhibition activity.[38] There are no data in the literature showing the effect of changes in the level of AGO2 protein, but it is more likely described to define the miRNA to which it is bound, on tissue damage. While some authors have shown an increase in AGO2 protein expression level in hypoxic conditions,[45] some others have not shown any changes.[46] We believe that the decreased AGO2 protein expression in 8 (72%) of 11 patients who improved to mild TBI from severe TBI in our study can be considered a positive prognostic marker. However, further studies are needed to gain a better understanding of the mechanism of the pathophysiological effects of AGO2 on damaged cerebral tissue.

The previous studies have demonstrated that Drosha, Dicer, DGCR8, and XPO5 levels do not change after temporary middle cerebral artery occlusion in rats.[47] However, DNA replication, protein translation, cell cycle progression, and DNA damage repair are impaired due to the deletion of the DGCR8 protein in neural stem cells.[48] The insufficient expression of Dicer and DGCR8 in mice has been shown to cause changes in synaptic protein expression, synaptic transmission, learning, and memory.[49,50] In our study, we found no significant change in the expressions of the DGCR8, Drosha, and XPO5.

In the present study, the GCS scores were evaluated at the time of admission and after 30 days to evaluate the prognosis of the patients. Since treatments such as sedation and neuromuscular blockade impair the optimization of the GCS score, the GCS evaluation of the patients was made after ensuring that such treatments were not applied or the effect period expired.

The rate of TBI was found to be higher in motor vehicle accidents in our study. There are studies with compatible results in the literature; however, there are also publications reporting that fall-related injuries are more common in the etiology of TBI.[1]

Furthermore, patients who underwent surgery within the first 3 days after trauma were excluded from our study. Therefore, we attempted to optimize patient standardization by eliminating one of the additional factors that may affect the levels of proteins involved in miRNA biogenesis in both the patient and control groups.

The collection of late blood samples at the post-traumatic 72 h in the patient and control groups is based on the previous animal studies demonstrating that the protein permeability of the blood-brain barrier increases biphasically 4–6 h and 2–3 days after trauma.[51,52]

The small sample size is the main limitation of this study. Despite the small sample size, however, we observed changes in some of the protein expressions in individual cases. Relatively, short follow-up (30 days) is another limitation. Further studies are needed to evaluate the long-term outcomes of patients after discharge from the ICU and hospital. Finally, baseline biogenesis protein levels of the patients before injury are unknown. In future studies, the association between baseline protein levels and post-TBI prognosis should be addressed. Nonetheless, it is a prospective study for the1st time investigating the levels of synthesis proteins that may affect all miRNA levels. Since the existing literature lacks similar studies on this subject, we believe that this study is valuable as it provides additional contributions to the management of TBI patients.

CONCLUSION

Our study did not show significant changes in the expression of proteins involved in miRNA biogenesis in patients with severe TBI at the first 4–6 h or 72 h after trauma compared to trauma patients without head trauma. However, Dicer expression increased in patients with a significant GCS score improvement and AGO2 expression decreased in many of these patients. The Dicer expression profile also increased in patients discharged from the ICU in a short time. Based on these findings, miRNAs and their biogenesis proteins can guide diagnostic, prognostic, and therapeutic decisions for patients with TBI in the future. Nevertheless, further, well-designed, large-scale, long-term, and prospective studies are warranted to shed light into the pathophysiological processes implicated in TBI.

Ethics Committee Approval: This study was approved by the Faculty Of Medicine, Akdeniz University Ethics Committee (Date: 01.03.2017, Decision No: 139).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Travmatik beyin hasarlı hastalarda prognoz ile mikroRNA biyogenez proteinleri arasındaki ilişki

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AMAÇ: Bu çalışmanın amacı erken ve geç dönem travmatik beyin hasarı (TBH) hastalarında mikroRNA (miRNA) biyogenezinde yer alan proteinlerin ekspresyon düzeylerinin farklılık gösterip göstermediğini araştırmak ve bunun prognoza etkisini değerlendirmektir.
GEREÇ VE YÖNTEM: Şiddetli TBH hastalarından, travmadan 4 ila 6 saat ve 72 saat sonra alınan kan örneklerinde Dicer, Drosha, DiGeorge Sendromu Kritik Bölge 8 (DGCR8), Exportin5 (XPO5) ve Argonaute2 (AGO2) seviyeleri ölçüldü ve kontrol grubuyla karşılaştırıldı. Hastaların prognostik takibi Glasgow Koma Skalası skoru kullanılarak yapıldı.
BULGULAR: Şiddetli TBH'li hastalarda miRNA biyogenez proteinleri Dicer, Drosha, DGCR8, XPO5 ve AGO2'nin ekspresyonunda istatistiksel olarak anlamlı bir değişiklik yoktu. Ancak şiddetli TBH derecesinden hafif TBH derecesine düzelen hastalarda Dicer ekspresyonu artmış ve bu hastaların çoğunda AGO2 ekspresyonu azalmıştır. Yoğun bakımdan kısa sürede taburcu olan hastalarda Dicer ekspresyon profilinin arttığı görüldü.
SONUÇ: MikroRNA'lar ve biyogenez proteinleri, gelecekte TBH'li hastalar için prognostik ve terapötik kararlara rehberlik edebilir.

Anahtar sözcükler: Travmatik beyin hasarı, Prognoz, mikroRNA, mikroRNA biyogenezi

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