Practical Application of Biogenic Amine Profiles for the Diagnosis of Patients with Ischemic Stroke

Natalia Miękus, PhD,*,† Ilona Olędzka, PhD,* Piotr Kowalski, PhD,* Paweł Miękus, MD, PhD,‡ and Tomasz Baczek, Prof*

Background: Ischemic stroke (IS) is still one of the major issues in medicine. Still, early diagnosis and misdiagnosis remain the main barriers for proper patient treatment and follow-up. Exploring new potential diagnostic biomarkers for IS is relevant to decrease patient morbidity and the occurrence of poststroke diseases. Biomedical analysis could bring new light to the background of IS and—in such a way—propose new bioanalytical tools for the early diagnosis, prognostication, and monitoring of IS. *Materials and Methods:* This research aimed to present a discussion on the employment of biogenic amines (BAs), as well as their precursory amino acids and main metabolites, as a new panel of biomarkers for IS. Preliminary patient data were presented and the patients were described with respect to their clinical history and examination records, as well as scientific data gained from the liquid extraction-capillary electrophoresis determination of BAs in the patients' urine samples. *Results:* The results showed the potential of BA screening using the developed sample preparation and analysis methods in urine during IS, and this will be further studied on a more numerous group of patients with IS to reveal the usefulness of BAs as a new panel of biomarkers for early IS diagnosis and prognostication. *Conclusions:* To our best knowledge, this methodology for the first time has been used for the simultaneous analysis of multiple small molecular biomarkers. In addition, the factors that might influence the determination of BAs in real samples were pointed out. **Key Words:** Biogenic amines—diagnosis—biomarkers—capillary electrophoresis—ischemic stroke.
© 2017 National Stroke Association. Published by Elsevier Inc. All rights reserved.

Introduction

Omics sciences are a powerful approach to studying basic biology as well as obtaining clinical information about various life-threatening diseases.[1] Omics sciences relay, among other things, through the genes (genomics), proteins (proteomics), or small molecules (metabolomics), analyses for the evaluation of new, potential biomarkers of disease for early diagnosis and prognostication, for new therapeutic targets, or for monitoring a patient's therapy.[2-4] Due to the improvement of the omics analytical platform, many serious diseases might be deeply investigated in terms of basic biology, the verification of new drug candidates, and early diagnosis. Thus, the hope of a rapid improvement in patient care is becoming a reality.

Stroke remains a significant problem worldwide. In the United States, approximately 700,000 strokes occur

From the *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University of Gdańsk, Gdańsk, Poland; †Department of Animal and Human Physiology, University of Gdańsk, Gdańsk, Poland; and ‡Department of Cardiology, Voivodeship Hospital, Gdynia, Poland.

Received April 20, 2017; revision received October 3, 2017; accepted October 31, 2017.

This project was supported by the National Science Centre Poland on the basis of decision DEC-2013/09/D/NZ4/01658 and for the statutory R&D activities of the Department of Animal and Human Physiology at the University of Gdańsk.

Address correspondence to Tomasz Bączek, Prof, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University of Gdańsk, Gen. J. Hallera 107, Gdańsk, 80-416, Poland. E-mail: tbaczek@gumed.edu.pl.

1052-3057/$ - see front matter

© 2017 National Stroke Association. Published by Elsevier Inc. All rights reserved.

https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.10.041

annually, whereas in China, current statistics show that around 1.3 million people experience strokes each year. Most of these strokes are ischemic.[5,6] A brain ischemia leads to a reduction in glucose and in oxygen supply, among other things, and initiates changes at a cellular level. Ischemic stroke (IS) is a serious pathological stage of the organism that, if not captured early, could lead to various undesirable events in the body, such as damage to the blood–brain barrier, immunosuppression, and elevated morbidity.[7-9] Using omics sciences might be beneficial for both basic knowledge about IS and to propose new, potential omics biomarkers for its prevention, detection, and the monitoring of therapy. Determining a new panel of biomarkers for the diagnosis and prognostication of IS could be done by the qualitative and quantitative studies of small molecules such as biogenic amines (BAs) in body fluids.

BAs greatly influence communication within the human body. Indoleamines (serotonin [5-HT]) and catecholamines (adrenalin [A], noradrenaline [NA], and dopamine [DA]) serve as hormones and neurotransmitters in the peripheral and central nervous systems. Nowadays, much effort is paid to determine those small molecules in the blood, urine, cerebrospinal fluid (CSF), or other biological matrices, because disturbances in BA content are connected to numerous life-threatening diseases such as tumors (neuroblastoma and pheochromocytoma) and neurodegenerative or psychiatric disorders of the brain (such as Alzheimer's disease and depression).[10-12] Nevertheless, the low concentration and dynamic range of BAs in body fluids, as well as their physicochemical properties (sensitivity to light exposure and high temperature, among others), have forced scientists to optimize sophisticated bioanalytical methods for their unbiased quantitative and qualitative determination in biological samples.[13] Often robust sample pretreatment procedures must be employed as well. Therefore, there is still a need to develop new methods or to improve already existing methods for the simultaneous identification and quantification of BAs from body fluids. A great clinical improvement would also be to analyze Bas, together with their precursory amino acids (L-tryptophan [L-Trp], L-tyrosine [L-T], levodopa [L-DOPA]) and main acidic metabolites (such as homovanillic acid [HVA], vanillylmandelic acid, and 3,4-dihydroxyphenylacetic acid [DOPAC]), because possessing knowledge of the concentration of multiple biomarkers could underline the background of IS.

Current scientific data demonstrated disturbances in the catecholamine concentration in the body in samples derived from patients with IS. Schulze et al pointed out a concentration of altered amines when the immune response is induced by ischemia. The pathological stage of the organism not only influences the immune system itself and causes a patient's susceptibility to infections, but also could destroy the balance in the production, storage, and release of BAs. Catecholamines promote the release of the head shock protein 72, which serves as a cell stress biomarker.[14,15] Moreover, the high concentration of catecholamines is known to induce lymphocyte apoptosis.[16] There is strong evidence that the increase in BAs early after a stroke might be a marker of the immunological defects that can supposedly develop. Furthermore, Ormstad group data revealed that the reduced capacity for the biosynthesis of brain catecholamines might be the effect of stroke-derived proinflammatory effects. The precursor amino acids were also studied in patients with stroke. Lower levels of L-Trp and L-T were demonstrated, which indicated the increased oxidation of those amino acids in acute IS.[17] The deregulation of the degradation of L-Trp could be detected in the serum, CSF, and brain tissue in several diseases, such as cancer, rheumatoid arthritis, and stroke.[18] The screening of BA metabolites in the CSF samples obtained from patients with acute IS were mentioned years ago, and the importance of studying BA metabolites in the first week after a stroke was mentioned.[19] Another study demonstrated that, even after 25 days after a stroke, the HVA concentration correlated with the clinical course of the stroke. The authors pointed out the necessity to create 2 subgroups of patients, taking into account that the ischemia existed in the right or left cerebral hemisphere.[20]

Taking all the previously mentioned findings into account, more attention must be paid to the study of those small molecules nowadays. Our task in the presented pilot study was to qualitatively and quantitatively determine 11 potential biomarkers: 4 BAs (A, NA, DA, and 5-HT), together with their precursory amino acids and main metabolites (HVA, vanillylmandelic acid, L-DOPA, DOPAC, L-T, L-Trp, and L-DOPA) in biological samples derived from patients suffering from IS. Urine was chosen as the biological matrix because its collection is less invasive (especially when compared to CSF collection) and more desirable (less traumatic) for both patients and doctors. We previously demonstrated the usefulness of the investigation of BAs in urine for patients with neuroblastoma and would like to shed light on the monitoring of urine for patients with IS.[21]

Materials and Methods

Materials and Reagents

Precautionary steps were undertaken when working with biological material and toxic reagents (protective laboratory coats, glasses, and gloves). Reagents, such as sodium tetraborate decahydrate (borax) and α-cyclodextrin were delivered from Merck (Darmstadt, Germany). Methanol was supplied by POCh (Gliwice, Poland). All chemicals were of analytical grade and were applied without further purification. Highly pure water was obtained from Milli-Q equipment (Millipore, Bedford, MA). Analytical standards of DA, epinephrine (A), norepinephrine (NA), serotonin (5-HT), tyrosine (L-TY), 3,4-dihydroxyphenylalanine (L-DOPA), tryptophan (L-T), HVA,

Download English Version:

https://daneshyari.com/en/article/8595145

Download Persian Version:

https://daneshyari.com/article/8595145

Daneshyari.com