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Effect of riluzole (Rilutek) treatment on plasma amino acid percentages in amyotrophic lateral sclerosis patients

Abstract The aim of the study was to investigate the effect of riluzole (Rilutek) treatment on plasma amino acids (AA) percentage capacity in amyotrophic lateral sclerosis (ALS) patients. Excitatory AA may be important in the pathogenesis of ALS. Riluzole is a neuroprotective drug that blocks glutamatergic neurotransmission in the central nervous system. The study was conducted at the Department of Neurology, University School of Medicine in Lublin. The study comprised 20 ALS patients. Plasma AA were measured by automated ion-exchange chromatography before and after 3 months of riluzole treatment. The study has shown a significant decrease in serine percentage capacity and a significant increase in isoleucine percentage capacity in the plasma of the ALS patients, however the plasma excitatory AA percentage capacity was not significantly changed after 3 months of the riluzole treatment. Our investigations revealed that riluzole does not significantly influence the majority of plasma AA percentage capacity in ALS patients.

Key words Amino acids • Amyotrophic lateral sclerosis • Riluzole

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Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by a loss of upper and lower motor neurons, leading to a progressive loss of motor function [1]. Glutamate is a principal excitatory neurotransmitter in the central nervous system but it is also a neurotoxin that may cause motor neuron degeneration [2]. Riluzole (Rilutek), a neuroprotective drug, blocks glutamatergic neurotransmission in the central nervous system. It has a complex mechanism of action: blockage of glutamate release, noncompetitive inhibition of excitatory amino acid receptors, inactivation of the voltage-sensitive sodium channels, activation of G-protein-dependent processes, and influence on the uptake of many neurotransmitters, all of which are involved in neurodegeneration. Riluzole has also neurotrophic, antioxidative, and antiapoptotic effects [3]. The aim of this study was to examine the effect of riluzole on plasma AA percentages in ALS patients after 3 months of the treatment.

Materials and methods

Twenty ALS patients (11 men/9 women) with an average age of 56 were diagnosed according to the El Escorial criteria [4] and included in the study. The average duration of ALS was 18 months (3 months – 4 years). AA analysis of 6% sulfosalicylic-treated plasma samples was performed by automated ion-exchange chromatography with lithium-based buffers on an AAA 400 automatic amino acid analyzer (Ingos, Czech Republic). For statistical analysis the Wilcoxon test was used. P values <0.05 were considered significant. The study was conducted according to the principles established in Helsinki and was approved by the Ethics Committee of University School of Medicine in Lublin.

Results

Our study shows a significantly decreased percentage of serine and a significantly increased percentage of isoleucine after 3 months of riluzole treatment. The changes in the tyrosine, aspartate, and alanine percentages were close to statistical significance. The plasma glutamate percentage had not changed after 3 months of riluzole treatment. The data are shown in Table 1.

Discussion

The altered metabolism of AA in ALS has been previously reported [5]. A defect in this metabolism may cause degeneration of motor neurons. Iwasaki et al. [6] demonstrated a significant elevation in plasma levels of the excitatory amino acids aspartate and glutamate and the inhibitory amino acid glycine. It has been suggested that an altered level of glycine in ALS may potentiate activation of spinal cord NMDA receptors, resulting in neurotoxicity [7]. Niebrój-Dobosz et al. [8] confirmed that serum glutamate and aspartate is increased in patients with severely progressing ALS. Our study shows a significantly decreased percentage of serine and significantly increased percentage of isoleucine. Plasma excitatory AA percentages were not significantly changed after 3 months of the riluzole treatment; however, the antiglutamatergic mechanism is only one of the neuroprotective mechanisms of the riluzole action. Riluzole did not cause significant changes in the majority of plasma AA percentages in the ALS patients after 3 months of the treatment. The conclusions are limited, however, due to the very short study period.

Table 1 The plasma amino acid (AA) percentage capacity (%) in amyotrophic lateral sclerosis (ALS). *p** statistical significance according to Wilcoxon test

Aminoacid	Before treatment	After 3 months	Significance
Valine	6.88±0.49	7.73±0.92	*p*=0.09
Methionine	0.49±0.30	0.50±0.27	*p*=1.0
Glutamine	16.93±4.13	16.77±3.83	*p*=0.88
Isoleucine	1.81±0.48	2.49±0.42	*p*=0.02*
Leucine	4.28±0.86	4.40±0.69	*p*=0.77
Phenylalanine	2.30±0.67	2.23±0.29	*p*=1.0
Tyrosine	1.88±0.32	2.17±0.40	*p*=0.06
Aspartate	1.95±0.28	1.71±0.31	*p*=0.06
Alanine	13.17±2.02	15.52±2.02	*p*=0.06
Taurine	3.09±1.35	2.68±0.83	*p*=0.40
Serine	5.81±0.75	4.82±0.29	*p*=0.01*
Glutamate	5.92±4.15	4.14±2.09	*p*=0.40
Glycine	8.95±2.56	8.80±2.28	*p*=0.88
Lysine	6.67±0.54	6.67±0.68	*p*=0.77
Histidine	2.87±0.36	2.76±0.21	*p*=0.57
Citrulline	0.71±0.45	0.83±0.39	*p*=0.67
Arginine	5.70±2.50	4.79±1.22	*p*=0.67
Threonine	4.52±0.98	4.36±0.44	*p*=0.88
Ornithine + NH3	5.14±1.52	4.67±0.73	*p*=0.57
Ethanolamine	2.06±0.31	1.90±0.35	*p*=0.17

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