Rivastigmine for Relatively Younger Alzheimer’s Disease Patient

Kentaro Horiuchi,1 Koji Hori1*, Misa Hosoi1, Kimiko Konishi1,2, Hiroi Tomioka1 and Mitsugu Hachisu3

1Department of Psychiatry, Showa University Northern Yokohama Hospital, Kanagawa, Japan
2Tokyo Metropolitan Tobu Medical Center for Persons With Developmental/Multiple Disabilities, Tokyo, Japan
3Department of Clinical Pharmacology, School of Pharmaceutical Sciences, Showa University, Tokyo, Japan

*Corresponding author: Koji Hori, Department of Psychiatry, Showa University Northern Yokohama Hospital, 35-1 Chigasaki-kicho, Tsuzuki-ku, Yokohama-City, Kanagawa, 224-8503, Japan, Tel: +81-45-949-7000; Fax: +81-45-949-7927; E-mail: kojihori@med.showa-u.ac.jp

We presented the patient with relative younger Alzheimer’s disease (AD) whose clinical symptoms and cognitive functions were responsive not to donepezil but to rivastigmine. Age of initial visit our memory clinic of this patient was relatively younger. It is considered that in relative older patient both AD pathology and aging cause cognitive dysfunctions. However, in relative younger patient not aging but only AD pathology causes cognitive dysfunctions.

Abstract

We presented the patient with relative younger Alzheimer’s disease (AD) whose clinical symptoms and cognitive functions were responsive not to donepezil but to rivastigmine. Age of initial visit our memory clinic of this patient was relatively younger. It is considered that in relative older patient both AD pathology and aging cause cognitive dysfunctions. However, in relative younger patient not aging but only AD pathology causes cognitive dysfunctions.

Keywords: Alzheimer’s disease; Butyrylcholinesterase; Rivastigmine; Relative younger patient

Introduction

In Japan, two cholinesterase inhibitors (ChEIs), galantamine and rivastigmine, are marketed in 2011 in addition to donepezil. As one ChEI is not allowed to be combined with other ChEI, we should select one of three ChEIs for the patient Alzheimer’s disease (AD). Among the ChEIs, rivastigmine is unique in its characteristics to inhibit not only acetylcholinesterase (AChE) but also butyrylcholinesterase (BuChE) [1]. Therefore, this action causes more potent upregulation of acetylcholine (ACh). Here we report a case of an AD patient showing amelioration by rivastigmine. Informed consent of reporting was obtained by this patient and his wife.

Case Presentations

Patient was a 69-year-old male patient who came to the memory clinic of our hospital complaining of memory deterioration. He had been experiencing amnesia 4 years age. Then he could not manage his finance 2 years age. He showed apathy, irritability and temporal disorientation 1 year before. On initial examination at our clinic, the patient’s Mini-Mental State Examination (MMSE) [2] score was 20 and magnetic resonance imaging (MRI) showed periventricular high density, however, there was no prominent atrophy in his brain. We diagnosed our patient with mild AD [3] because his cognitive function was mildly deteriorated, and he complained of memory disturbances and apathy. We prescribed donepezil at 5 mg daily and soon after starting this treatment, his memory disturbances and apathy were ameliorated. However, he showed apathy again. Seven months later, his MMSE score was down to 19. We considered that donepezil was not effective because his wife complained that his demented state was not changed. We prescribed rivastigmine instead of donepezil. Five months later, his MMSE score became 25. His wife said that the progression of his dementia became slow and his apathy was ameliorated. At 2 years from first visit, his MMSE score became 27. At that time, his wife said that he was vivid and his memorial disturbance was ameliorated, i.e. rivastigmine was also effective.

Discussion

We considered the patient with relative younger AD was responsive to not donepezil but rivastigmine because his clinical symptoms especially apathy were ameliorated and his cognitive function was improved with the prescription of rivastigmine instead of donepezil.

Main finding of neurotransmitter change in AD is downregulation of ACh [6]. The downregulation of ACh is related to cognitive dysfunctions such as memory disturbance and disorientations [3,7]. However, it is considered that ACh also regulates inflammatory system, i. e., referred to as antiinflammatory pathway [8,9]. Therefore, we speculated that some cytokines caused by upregulations of inflammations have anticholinergic activity (AA), which accelerated AD pathology (amyloids and tau) [10-12]. Generally speaking, AD progresses more rapidly in moderate stage than in mild stage [13]. We also speculated that when downregulations of ACh reached critical
level, AA generated by upregulations of inflammations accelerated AD pathology [12]. Therefore, it is important not to downregulate ACh so as not to generate AA and not to accelerate AD pathology.

In normal brain, main enzyme degrading ACh is AChE [14], which exists in nervous cells. However, in AD, glia cells and amyloids proliferate and nervous cells shrink. BuChE exists in glia cells and amyloids [15]. Therefore, when AD progresses, AChEs decrease and BuChEs increase. Accordingly the ratio of BuChEs/AChEs increases. In MCI stage, even when AD pathology is burdened, nervous cells are almost normal. Therefore, main enzyme which catalyses ACh is AChE. However, in mild stage in AD, when nervous cells decrease and glia cells and amyloids increase, main enzymes those catalyse ACh are not only AChE but also BuChE. In fact Perry et al. reported that when AD progresses, AChEs decrease with finer fashion and BuChEs increase with sigmoid fashion [16]. Moreover, BuChE is considered to accelerate the numbers of amyloids, i.e., BuChE is considered to accelerate AD pathology [17]. Therefore, when at mild stage such as our patient, not donepezil but rivastigmine which has inhibiting actions on both AChE and BuChE was suitable.

Moreover, age of initial visit to our memory clinic of our patient was relative younger. It is considered that in relative older patient both AD pathology and aging cause cognitive dysfunctions [16]. However, in relative younger patient not aging but only AD pathology causes cognitive dysfunctions. Therefore, AD pathology was thought to be more pronounced in our patient than relative older patients with same cognitive disturbances. There might be a possibility that the lost potency of donepezil might result from drug resistance due to repetitive usage, however, it might not happen to rivastigmine with prolonged treatment because rivastigmine showed efficacy for 1 year and 5 months.

We considered that from these three points of view, our patient was responsive not to donepezil but to rivastigmine and that when relatively younger AD patient at middle stage receive the treatment of AD, not donepezil but rivastigmine which has inhibiting actions to both AChE and BuChE was suitable.

Conflicts of Interest

Acknowledgement
Funding for this study was received from Eisai Co., Ltd., Daiichi Sankyo Inc. and Ono Pharmaceutical Co., Ltd.

References