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Pharmacotherapy for visual hallucinations: A review focusing on Charles Bonnet syndrome

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ABSTRACT

Charles Bonnet syndrome (CBS) consists of vivid visual hallucinations which occur in otherwise psychologically normal people with insight. We reviewed the literature associated with pharmacotherapy for CBS. According to the limited data, antipsychotics such as risperidone, mood stabilizers such as valproate, antidepressants such as mirtazapine and Chinese medicine such as Yi-gan san are candidate treatments for visual hallucinations. Since existing data is solely derived from case reports, further controlled studies are required to establish pharmacotherapy for CBS.

***Keywords*: Charles Bonnet syndrome, CBS, valproate, risperidone, mirtazapine, Yi-gan san**

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INTRODUCTION

Visual hallucinations have been reported in a wide range of clinical and non-clinical circumstances. Clinical diseases such as narcolepsy-cataplexy syndrome, delirium tremens, Parkinson's disease, Lewy body dementia, intoxication with psychoactive substances, temporal lobe epilepsy and other conditions have been reported to be associated with visual hallucinations [1]. As for non-clinical situations, hypnopompic and hypnagogic phenomena or sensory deprivation may produce visual hallucinations even in healthy individuals.

Among a variety of visual hallucinations, a unique disorder, Charles Bonnet syndrome (CBS), was named by de Morsier after the Swiss philosopher Charles Bonnet who first described the occurrence of vivid complex hallucinations in his visually impaired, otherwise psychologically normal 89-year-old grandfather (Charles Lullin) in 1760 [2]. CBS is characterized by the occurrence of complex visual hallucinations, predominantly in normal elderly people. There have been several sets of diagnostic criteria for CBS [3]. Several authors proposed the following criteria: (1) the presence of formed and complex, persistent or repetitive visual hallucinations; (2) full or partial retention of insight; (3) absence of delusions; and (4) absence of hallucinations in other sensory modalities. The prevalence of CBS ranges from 0.4 to 14% of patients attending eye clinics (Cammaroto et al, 2008), but these values are difficult to interpret because of differences in the diagnostic criteria for CBS and in the methods used

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to evaluate visual hallucinations.

With regard to etiology, Ffytche et al [4] studied CBS patients by using functional magnetic resonance imaging (fMRI) and found that visual hallucinations of color, faces, textures and objects were associated with cerebral activity in ventral extrastriate visual cortex, and that the content of the hallucinations reflected the functional specializations of the region, and that patients who hallucinated had increased ventral extrastriate activity, which persisted during hallucinations. Kazui et al [5] reviewed neuroimaging studies in CBS patients and suggested that there may be a fundamental dysfunction in occipital visual cortices, especially primary and secondary cortices (Brodmann area (BA) 17 and BA 18), with transient cortical activation occurring during the appearance of hallucinations in the inferior lateral temporal cortex, mainly fusiform gyrus (BA37), which is one of visual association cortices such as BA19.

As for pharmacotherapy for CBS, there have been several reports. In this review, these reports are reviewed to provide some insight into pharmacotherapy for CBS.

MATERIALS AND METHODS

Pubmed (Medline) research was performed to identify articles dealing with pharmacotherapy for CBS by using two key words "Charles Bonnet syndrome" and "treatment" in February 2010. As a result, 86 articles were identified. Of the articles, only 16 were found to be associated with pharmacotherapy for CBS. The other 70 articles were qualitative reviews and case reports without description of pharmacotherapy or other articles. Of the 16 related to pharmacotherapy, all were case reports and there were no randomized, controlled studies.

RESULTS

As shown in Table 1, the 16 case reports had 20 patients. Their mean age was 69.5 years old and consisted of 7 men and 13 women. To treat the CBS symptoms 6 types of psychotropics were administered. These were antipsychotics (4 case reports [6-9] with 6 patients; 1 of risperidone, 1 of olanzapine, 3 of melperone, and 1 of haloperidol), mood stabilizers (5 case reports [10-14] with 6 patients; 3 of valproate, 2 of carbamazepine, and 1 of gabapentin), antidepressants (3 case reports [15-17] with 3 patients; 1 of clomipramine, 1 of citalopram, and 1 of mirtazapine), Chinese medicine (2 case reports [18,19] with 2 patients; 2 of Yi-gan san), donepezil (1 case report [20] with 1 patient), and cisapride (1 case report [21] with 2 patients). Although the doses of these drugs were relatively small, there were clear effects on visual hallucinations of CBS in all the patients (Table 1).

DISCUSSION

Unfortunately, there were only 16 case reports of 20 patients dealing with pharmacotherapy for CBS. There were no open studies or randomized, placebo-controlled studies. Taking placebo effects into consideration, it is unclear whether these case reports showed true pharmacological effects of each drug on CBS as in some reports the other drugs could not bring about effects and thereafter visual hallucinations improved. Therefore, it seems less likely that placebo had major role in alleviating visual hallucinations in such cases. With regard to donepezil, Terao and Collinson [22] suggested that visual hallucinations consistent with CBS may occur in the early stage of Lewy body dementia. Ukai et al [20] described a patient with CBS, responding to donepezil without symptoms of Lewy body dementia. On the other hand, Hanyu et al [18] reported a patient with CBS, responding to Yi-gan san but later diagnosed as suffering from Lewy body dementia. Thus, it should be kept in mind that some patients with CBS may develop Lewy body dementia, and that the purportedly efficacious drug such as donepezil may indirectly improve visual hallucinations via its direct action on the process of dementia.

Table 1. Pharmacotherapy for Charles Bonnet syndrome: A Summary of 16 Case Reports

author (publication year)	patient	visual hallucinations	drug (mg/day)	effects
Maeda et al (2003)	57-year-old woman	scenes from her childhood	risperidone (1 mg/day)	Visual hallucinations disappeared.
Colleti Moja M et al (2005)	62-year-old man	unfamiliar human faces, bizarre animals, small grotesque figures with hats on their heads, colourful road maps	olanzapine (2.5-5 mg/day)	Visual hallucinations disappeared.
Batra et al (1997)	83-year-old man	grotesque and well-shaped faces, light green flowers, floral arrangements in impressive colours	melperone (67.5 mg/day)	Visual hallucinations disappeared.
	81-year-old man	ghosts, chinese men with open, moving mouths, tall grass growing in his bedroom, waving fields of grass divided by rivers in the kitchen	melperone (25 mg/day)	Visual hallucinations disappeared.
	61-year-old woman	a woman, dressed in a light blue dress with a flowered pattern, who was sitting on a chair	melperone (100 mg/day)	A clear and persistent symptomatic improvement was observed.
Chen et al (1996)	69-year-old woman	a few children, aged approximately 2-5 years old with colorful clothes, engaging in some age-appropriate activities	haloperidol (0.5 mg/day)	A reduction in the frequency of visual hallucinations was reported.
Hori et al (2000)	73-year-old woman	a doll dancing and a black bug coming around a decorated ball in her bedroom	valproate (800 mg/day)	Visual hallucinations disappeared.
	77-year-old woman	her dead husband or several men in her bedroom	valproate (400 mg/day)	Visual hallucinations disappeared.
Segers (2009)	85-year-old woman	monstrous figures	valproate (300 mg/day)	Visual hallucinations disappeared.
Bhatia et al (1992)	38-year-old man	beautiful unfamiliar faces, public places including both familiar and unfamiliar persons, frightening pictures of burning houses, flooded cities, contries affected by famines or wars	carbamazepine (300 mg/day)	Visual hallucinations disappeared.
Chen et al (2001)	56-year-old woman	Chinese and English characters, vegetables, small animals penetrating into her abdomen	carbamazepine (800 mg/day)	Visual hallucinations disappeared.
Paulig and Mentrup (2001)	86-year-old woman	medieval women, knights in bright colours, torsos, isolated heads	gabapentin (300 mg/day)	Visual hallucinations disappeared.
Murai and Takagi (2004)	49-year-old man	familiar or unfamiliar human faces, downtown scenes where many people walking around, theater scenes	clomipramine (60 mg/day)	Visual hallucinations became less disgusting and well-formed.
Lang et al (2007)	78-year-old woman	faces, geometrical figures, animals	citalopram (20 mg/day)	Visual hallucinations disappeared.
Siddiqui et al (2004)	59-year-old man	groups of people, farm animals	mirtazapine (7.5 mg/day)	Visual hallucinations disappeared.
Hanyu et al (2008)	81-year-old woman	no description	Yi-gan san	A reduction in the frequency and severityof visual hallucinations was reported.
Miyaoka et al (2009)	73-year-old woman	cross stripes, a group of life-sized japanese people such as a colorfully dressed nobility, an aged man riding with a sword and flag, and a middle-aged woman with beautiful flowers	Yi-gan san (7.5 g/day)	Visual hallucinations disappeared.
Ukai et al (2004)	73-year-old woman	black and round objects flying, colourful flowers or leaves, colourful lattice patterns	donepezil (5 mg/day)	A size of the hallucinations did not change but their colour and brightness had diminished remarkably.
Ranen et al (1999)	75-year-old woman	children dressed in plaid winter clothing walking in her bedroom, stuffed animals coming up from the floor, frightening soldiers marching before her, women dressed in 19-century garb riding bicycles	cisapride (40 mg/day)	Visual hallucinations were markedly reduced.
	74-year-old man	arms, legs, bodies, body images engaging in sexual relations	cisapride (40 mg/day)	Visual hallucinations were markedly reduced.

The limitation of the present review should be mentioned. Only Pubmed (Medline) was used to seek relevant articles. Although Pubmed can access most papers in the world, it is not perfect and other search systems such as EMBASE should be used in the future. In fact, it is noteworthy that Pubmed could not identify our previously published case report on pharmacotherapy for CBS [23]. Notwithstanding this limitation, at the moment it is clear that present case reports provide only limited information about pharmacotherapy for CBS.

According to the limited data, when CBS patients consult us, antipsychotics such as risperidone, mood stabilizers such as valproate, antidepressants such as mirtazapine and Chinese medicine such as Yi-gan san are candidates in the treatment of visual hallucinations. Of course, since the power of evidence of such case reports is weak, further controlled studies are required to establish pharmacotherapy for CBS.

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