# Tiapride is more effective and causes fewer adverse effects than risperidone in the treatment of senile dementia

Y. YUAN<sup>1</sup>, L.H. LI<sup>2</sup>, Y.J. HUANG<sup>2</sup>, L.F. LEI<sup>2</sup>

<sup>1</sup>Department of Neurology, Xiangya Hospital, Central South University, Changsha, Hunan, China <sup>2</sup>Department of Neurology, the 3<sup>rd</sup> Xiangya Hospital, Central South University, Changsha, Hunan, China

**Abstract.** – OBJECTIVE: We wanted to compare the effects of tiapride and risperidone in treating behavioral and psychological symptoms of senile dementia.

PATIENTS AND METHODS: 108 patients with senile dementia received respective treatments (54 patients per treatment, either with 100 mg/day risperidone or 2.0 mg tiapride/day) for 2 months. Outcomes included the positive and negative syndrome scale (PANSS) scores, the curative rate of senile dementia, and prevalence of adverse effects (somnolence, headache, loss of weight, extrapyramidal system response, irritation and insomnia).

**RESULTS:** PANSS scores before treatment were comparable between treatment groups. On days 7, 15, 30, and 60 of the treatment, the differences between two treatment groups became evident. Thus, curative rates in patients treated with risperidone were 74.1% and in those treated with tiapride 88.9% (p < 0.05). Prevalence of adverse reactions was significantly lower in the latter group (9.3% vs. 25.9% in patients treated with risperidone; p < 0.05).

CONCLUSIONS: Tiapride is more effective in improving clinical symptoms of senile dementia and causes fewer adverse effects.

Key Words:

Tiapride, Risperidone, Senile dementia, Clinical effect.

# Introduction

Senile dementia is a disease caused by degeneration of neurological function in the elderly<sup>1-3</sup>. This disease mainly manifests as a decrease of intelligence and presence of psychiatric symptoms, including irritation, aggression, illusion and delusion<sup>1-4</sup>. The treatment most commonly utilizes antipsychotic drugs. Unfortunately, their long-term administration can aggravate the consciousness disturbance and cause adverse reactions, thus negatively affecting the curative effect of senile dementia<sup>5-8</sup>.

Risperidone and tiapride are novel antipsychotic drugs and exhibit some advantages in treating senile dementia<sup>7,8</sup>. Our study aimed at analyzing the efficacy and safety of these drugs in the treatment of senile dementia, with the overall goal of providing the reference for drug selection.

In the present study, patients with senile dementia were treated with either risperidone or tiapride. Our observations demonstrate that tiapride has a better efficacy and safety profile, than risperidone, in the treatment of senile dementia.

# **Patients and Methods**

# **Patients**

One hundred and eight patients with senile dementia, who received treatment in our Hospital between June 2010 and May 2013, were selected. The patients included 64 male and 44 female patients aged between 62 and 78 ([mean  $\pm$  SD] 70.4  $\pm$  4.68) years. The patients were divided into control and study groups (54 patients each) according to administered psychiatric drugs. Specifically, patients in control group received risperidone at 100 mg/day, while patients in study group were treated with tiapride at 2.0 mg/day. The treatment cycle was 2 months.

The control group comprised 32 male and 22 female patients aged between 62 and 77 (70.1  $\pm$  4.34) years. The study group included 32 male and 22 female patients (63-78, 70.8  $\pm$  5.25 years). Patient age and gender distribution did not significantly differ between both groups.

# **Outcomes**

We evaluated treatment efficacy by assessing the change of the Positive and Negative Syndrome Scale (PANSS) score after the treatment with either antipsychotic drug. The treatment was ranked as

Table I. PANSS scores before and after the treatment.

	Control group (risperidone treatment; n = 54)	Study group (tiapride treatment; n = 54)	p
Before treatment	$96.3 \pm 10.75$	$96.6 \pm 9.89$	N.S.
7 days after treatment	$75.6 \pm 8.14$	$58.6 \pm 7.87$	< 0.05
15 days after treatment	$62.2 \pm 7.86$	$52.8 \pm 6.87$	< 0.05
30 days after treatment	$51.4 \pm 6.75$	$41.6 \pm 5.78$	< 0.05
60 days after treatment	$42.4 \pm 6.43$	$32.6 \pm 5.68$	< 0.05

Footnote: Data are mean ± SD. N.S.: not-significant.

follow<sup>9</sup> <sup>10</sup>: recovery (PANSS score decreased >75% and clinical symptoms were improved), improvement (PANSS score decreased between 50% and 75%, and most of clinical symptoms improved), effective (PANSS score decreased between 25% and 50%; clinical symptoms were slightly improved), and lack of effect (PANSS decreased by <25%; clinical symptoms and neurological function did not recover or even deteriorated). Total treatment efficacy was calculated as a sum of cure, improvement, and effective outcomes.

In addition, we compared the prevalence of adverse reactions (somnolence, headache, loss of weight, extrapyramidal system response, irritation and insomnia) between two treatment groups.

# Statistical Analysis

The SPSS16.0 software (IBM, Beijing, China) was used for data analysis. Categorical data were compared using the chi-square test, and quantitative data analyzed by the *t*-test. A *p* value of less than 0.05 was considered as statistically significant.

# Results

#### Treatment Efficacy

PANSS scores before the treatment were comparable between control and study groups (respectively, risperidone at 100 mg/day and

tiapride at 2.0 mg/day; Table I). However, these scores were significantly lower in the patients of study group at all tested time points (7-60 days) of the treatment (p < 0.05; Table I).

We next calculated the treatment efficacy. Patient of control group demonstrated treatment efficacy of 74.1%, which was significantly lower than in study group (88.9%, p < 0.05; Table II).

#### Adverse Reactions

The prevalence of common adverse reactions (somnolence, headache, loss of weight, extrapyramidal system response, irritation and insomnia) was much lower in patients on tiapride (9.3%) compared with risperidone-treated patients (25.9%). The observed difference was statistically significant (p < 0.05; Table III).

# Discussion

As our society becomes older, the prevalence of senile dementia increases<sup>11-14</sup>. Senile dementia mainly manifests as disturbance of memory and intelligence, and is often complicated with aberrant behavioral and psychological symptoms<sup>15,16</sup>. A significant change of 5-hydroxytryptamine in the brain of senile dementia patients causes anxiety, fidget, depression, delusion and illusion<sup>17,18</sup>. Senile dementia significantly affects the quality of

**Table II.** Treatment efficacy in patient groups.

Treatment efficacy	Control group (risperidone treatment; n = 54)	Study group (tiapride treatment; n = 54)	P
Before treatment	$96.3 \pm 10.75$	$96.6 \pm 9.89$	N.S.
7 days after treatment	$75.6 \pm 8.14$	$58.6 \pm 7.87$	< 0.05
15 days after treatment	$62.2 \pm 7.86$	$52.8 \pm 6.87$	< 0.05
30 days after treatment	$51.4 \pm 6.75$	$41.6 \pm 5.78$	< 0.05
60 days after treatment	$42.4 \pm 6.43$	$32.6 \pm 5.68$	< 0.05

**Table III.** Adverse reactions in patient groups.

Adverse effect	Control group (risperidone treatment; n = 54)	Study group (tiapride treatment; n = 54)	p
	Absolute number (%)	Absolute number (%)	
Somnolence	3 (5.56)	1 (1.85)	
Headache	2 (3.70)	2 (3.70)	
Loss of weight	1 (1.85)	0 (0)	
Extrapyramidal system response	e 3 (5.56)	1 (1.85)	< 0.05
Irritability	3 (5.56)	1 (1.85)	
Insomnia	2 (3.70)	0 (0)	
Total prevalence (%)	25.9	9.3	

life of these patients, poses a significant burden on the families, and increases costs of medical care. It is not surprising that treatment of behavioral and psychological symptoms of senile dementia is in the focus of current investigations<sup>19</sup>. Earlier, conventional antipsychotics were widely administered to treat senile dementia<sup>20,21</sup>. However, these cause substantial adverse reactions. As the new generation of antipsychotics drugs, both tiapride and risperidone exhibit significantly increased treatment efficacy and decreased prevalence of adverse effects. For this reason, both these drugs are commonly used in the clinic<sup>22-24</sup>. At present, there is little data about the efficacy and safety of either of these drugs in the treatment of senile dementia. We analyzed the efficacy and safety such treatments in the present study.

Patients with senile dementia received the treatment with either tiapride or risperidone. The PANSS scores of patients receiving tiapride treatment were significantly lower than in those on risperidone treatment. In addition, the prevalence of adverse effects was lower in patients treated with tiapride. Both these observations agree with the conclusions by other researchers<sup>20,23</sup>.

Risperidone is a benzisoxazole derivative and is a new generation antipsychotic drug. It has a high affinity for dopamine D<sub>2</sub> receptor and it is a strong D<sub>2</sub> receptor antagonist<sup>25,26</sup>. It can improve the symptoms of schizophrenia, and its adverse effects are less severe than those by conventional antipsychotic drugs<sup>27</sup>. Tiapride is a neuropsychiatric drug that blocks the mesencephalic limbic dopamine receptor. It is used for the treatment of behavioral and psychological symptoms in patients with senile dementia. An advantage of this drug is that it exerts low toxicity. The drug is essential for the treatment of senile dementia and has been shown to markedly improve the quality of life in these patients<sup>28,29</sup>.

## Conclusions

Tiapride shows better treatment efficacy and causes a fewer adverse reaction, compared with risperidone, in patients with senile dementia.

#### **Conflict of Interest**

The Authors declare that they have no conflict of interests.

## References

- SADHU A, UPADHYAY P, AGRAWAL A, ILANGO K, KARMAKAR D, SINGH GP, DUBEY GP. Management of cognitive determinants in senile dementia of Alzheimer's type: therapeutic potential of a novel polyherbal drug product. Clin Drug Investig 2014; 34: 857-869.
- KAWAHARA M, MIZUNO D, KOYAMA H, KONOHA K, OHKAWARA S, SADAKANE Y. Disruption of zinc homeostasis and the pathogenesis of senile dementia. Metallomics 2014; 6: 209-219.
- MIZUNO D, KAWAHARA M. The molecular mechanisms of zinc neurotoxicity and the pathogenesis of vascular type senile dementia. Int J Mol Sci 2013; 14: 22067-22081.
- UKAI K, MIZUNO Y. Physical complications for elderly inpatients with senile dementia in the Imaise Branch of Ichinomiya City Hospital. Psychogeriatrics 2009; 9: 167-172.
- PANI L. The need for individualised antipsychotic drug therapy in patients with schizophrenia. Eur Rev Med Pharmacol Sci 2009; 13: 453-459.
- WARNOCK CA, FERGUSON ID, LAM J. Psychotropic drug prescribing survey in a Canadian rehabilitation and complex care facility. Consult Pharm 2014; 29: 387-399.
- PALMER KT, D'ANGELO S, HARRIS EC, LINAKER C, COG-GON D. The role of mental health problems and common psychotropic drug treatments in accidental injury at work: a case-control study. Occup Environ Med 2014; 71: 308-312.

- THAKKAR KB, JAIN MM, BILLA G, JOSHI A, KHOBRAGADE AA. A drug utilization study of psychotropic drugs prescribed in the psychiatry outpatient department of a tertiary care hospital. J Clin Diagn Res 2013; 7: 2759-2764.
- STOCHL J, JONES PB, PLAISTOW J, REININGHAUS U, PRIEBE S, PEREZ J, CROUDACE TJ. Multilevel ordinal factor analysis of the positive and negative syndrome scale (PANSS). Int J Methods Psychiatr Res 2014; 23: 25-35.
- 10) ORTIZ BB, GADELHA A, HIGUCHI CH, PITTA JC, KAGAN S, VONG MR, NOTO C, HALLAK JE, BRESSAN RA. What are the PANSS items most related with global improvements in patients with schizophrenia? Toward a reduced version of the PANSS. Schizophr Res 2014; 158: 277-278.
- 11) KUYUMCU ME, YESIL Y, OZTURK ZA, CANKURTARAN M, UL-GER Z, HALIL M, YAVUZ BB, SAIT B, AKYOL O, VURAL H, KARA Y, ARIOGUL S. AN ALTERNATIVE WAY FOR THE EVAIUAtion of zinc status in the elderly; nail zinc levels and relationship with Alzheimer's disease. Eur Rev Med Pharmacol Sci 2013; 17: 1467-1471.
- SINGH S, KUSHWAH AS, SINGH R, FARSWAN M, KAUR R. Current therapeutic strategy in Alzheimer's disease. Eur Rev Med Pharmacol Sci 2012; 16: 1651-1664.
- 13) MAHDY K, SHAKER O, WAFAY H, NASSAR Y, HASSAN H, HUSSEIN A. Effect of some medicinal plant extracts on the oxidative stress status in Alzheimer's disease induced in rats. Eur Rev Med Pharmacol Sci 2012; 16 Suppl 3: 31-42.
- 14) CHAUDHURI K, SAMARAKOON SM, CHANDOLA HM, KU-MAR R, RAVISHANKAR B. Evaluation of diet and life style in etiopathogenesis of senile dementia: A survey study. Ayu 2011; 32: 171-176.
- MOHAMD EM, AHMED HH, ESTEFAN SF, FARRAG AE, SALAH RS. Windows into estradiol effects in Alzheimer's disease therapy. Eur Rev Med Pharmacol Sci 2011; 15: 1131-1140.
- 16) ISHIDA C, KOBAYASHI K, KITAMURA T, UJIKE H, IWASA K, YAMADA M. Frontotemporal dementia with parkinsonism linked to chromosome 17 with the MAPT R406W mutation presenting with a broad distribution of abundant senile plaques. Neuropathology 2015; 35: 75-82.
- Mushtao R, Shoib S, Shah T, Mushtao S. 5-Hydroxy tryptamine transporter (5HTT) gene promoter region polymorphism in anxiety and depressive disorders. Med J Islam Repub Iran 2014; 28: 127.
- SHILPA J, PRETTY MA, ANITHA M, PAULOSE CS. Gamma aminobutyric acid B and 5-hydroxy tryptamine 2A receptors functional regulation during enhanced liver cell proliferation by GABA and 5-HT chitosan nanoparticles treatment. Eur J Pharmacol 2013; 715: 154-163.
- SHOYAMA M, UKAI S, SHINOSAKI K. Evaluation of regional cerebral blood flow in patient with atypical senile dementia with asymmetrical calcification. Psychogeriatrics 2015; 15: 272-276.

- BALLARD C, CORBETT A, HOWARD R. Prescription of antipsychotics in people with dementia. Br J Psychiatry 2014; 205: 4-5.
- 21) PIERSANTI M, CAPANNOLO M, TURCHETTI M, SERRONI N, DE BERARDIS D, EVANGELISTA P, COSTANTINI P, ORSINI A, ROSSI A, MAGGIO R. Increase in mortality rate in patients with dementia treated with atypical antipsychotics: a cohort study in outpatients in Central Italy. Riv Psichiatr 2014; 49: 34-40.
- 22) NOZAKI I, FURUKAWA Y, KATO-MOTOZAKI Y, IKEDA T, TAGAMI A, TAKAHASHI K, ISHIDA C, KOMAI K. Neuroleptic malignant syndrome induced by combination therapy with tetrabenazine and tiapride in a Japanese patient with Huntington's disease at the terminal stage of recurrent breast cancer. Intern Med 2014; 53: 1201-1204.
- Bogalsky M. Galantamine versus risperidone treatment of neuropsychiatric symptoms in patients with probable dementia: an open randomized trial. Am J Geriatr Psychiatry 2014; 22: 951.
- 24) TERANISHI M, KURITA M, NISHINO S, TAKEYOSHI K, NU-MATA Y, SATO T, TATENO A, OKUBO Y. Efficacy and tolerability of risperidone, yokukansan, and fluvoxamine for the treatment of behavioral and psychological symptoms of dementia: a blinded, randomized trial. J Clin Psychopharmacol 2013; 33: 600-607.
- 25) TAKEUCHI H, SUZUKI T, BIES RR, REMINGTON G, WATANABE K, MIMURA M, UCHIDA H. Dose reduction of risperidone and olanzapine and estimated dopamine D(2) receptor occupancy in stable patients with schizophrenia: findings from an openlabel, randomized, controlled study. J Clin Psychiatry 2014; 75: 1209-1214.
- 26) KIMURA H, KANAHARA N, KOMATSU N, ISHIGE M, MUNEOKA K, YOSHIMURA M, YAMANAKA H, SUZUKI T, KOMATSU H, SASAKI T, HASHIMOTO T, HASEGAWA T, SHIINA A, ISHIKAWA M, SEKINE Y, SHIRAISHI T, WATANABE H, SHIMIZU E, HASHIMOTO K, IYO M. A prospective comparative study of risperidone long-acting injectable for treatment-resistant schizophrenia with dopamine supersensitivity psychosis. Schizophr Res 2014; 155: 52-58.
- 27) KIMURA H, KANAHARA N, WATANABE H, IYO M. Potential treatment strategy of risperidone in long-acting injectable form for schizophrenia with dopamine supersensitivity psychosis. Schizophr Res 2013; 145: 130-131.
- 28) KARIA S, SHAH N, DE SOUSA A, SONAVANE S. Tiapride for the treatment of auditory hallucinations in schizophrenia. Indian J Psychol Med 2013; 35: 397-399.
- 29) NOBILIS M, VYBIRALOVA Z, SZOTAKOVA B, SLADKOVA K, KUNES M, SVOBODA Z. High-performance liquid chromatographic determination of tiapride and its phase I metabolite in blood plasma using tandem UV photodiode-array and fluorescence detection. J Chromatogr B Analyt Technol Biomed Life Sci 2011; 879: 3845-3852.