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Cognitive Behaviour Therapy Combined Fluoxetine Treatment Superior to Cognitive Behaviour Therapy Alone for School Refusal

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Abstract: School Refusal (SR) is a serious problem that will interfere with daily life and future of children and adolescents. To date, two ways including psychotherapy and medication are taken into consideration to treat SR. It has been reported that Cognitive Behavior Therapy (CBT) might be effective for SR. SR frequently combines with depression and anxiety and we therefore assume that fluoxetine combined with CBT may increase the efficiency of CBT for SR. Our study investigated the efficacy of CBT combined fluoxetine treatment and CBT alone for School Refusal (SR). A total of 75 patients with SR were randomized into two groups: CBT group (n = 36) and CBT plus Fluoxetine group (n = 39). Treatment was done for 12 weeks. The Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale, Clinical Global Impression-Severity scale (CGI-S) and percentage of school attendance were used for evaluation before and after treatment. The therapeutic efficacy was compared between two groups. After 12 weeks, in the CBT group, the SAS score, SDS score and CGI-S score were significantly decreased ($p < 0.01$) and the percentage of school attendance was 72.2%; in the CBT plus Fluoxetine group, the SAS score, SDS score and CGI-S score were significantly decreased ($p < 0.01$) and the percentage of school attendance was 82.1%. There were no significant differences in the SAS score, SDS score, CGI-S score and the percentage of school attendance after 12-week treatment between two groups ($p < 0.01$). Our results demonstrated that the CBT combined Fluoxetine treatment has comparable therapeutic efficacy to CBT alone for SR, but was not superior to CBT alone.

Key words: School refusal, cognitive behavior therapy, fluoxetine

INTRODUCTION

In order to ensure a fair education for every people, compulsory education law has been issued in many countries. However, the School Refusal (SR) has attracted the public attention. SR has been recognized since it was put forward by Hersov (Berg, 1997; Wu and Liu, 2006) in 1960 who defined it as a phenomenon that students were unwilling to go to school due to psychological problems or mental disorders. In Berg (1997) formally defined SR as a problem that students refuse or avoid going to school due to emotional disorders, especially anxiety and depression.

Epidemiological study has shown that more than 1% children and adolescents have SR and about 5% of children and adolescents who go to hospital for medical treatment suffer from SR (King and Bernstein, 2001). The prevalence of SR is similar between males and females and not associated with the economic and social status

(King and Bernstein, 2001). This problem is frequently found in subjected aged 6-7 and 10-12 years. To date, epidemiological study on SR has not been conducted in China. It was reported that, in some cities of China, SR was the first reason for counseling psychologists in children and the number of SR cases was yearly increasing (Jiang *et al.*, 2003).

SR is not a mental disease in the Diagnostic and Statistical Manual of Mental Disorders (4th Edition; DSM-IV) and International Classification of Diseases (ICD-10). The diagnostic criteria for SR were summarized: due to mood disorders, (1) He/she refuses to school, (2) He/she can not maintain the study in the school, (3) Parents and school staffs know that fact that he/she does not go to school and (4) He/she stays at home after leaving school. It might disturb family function and social function to different extents. According to the severity of SR, it can be divided into seven grades (Kearney, 2003; Maric *et al.*, 2012), (1) Grade 1: Threat or cry out aiming to

not go to school (2) Grade 2: Avoid going to school repeatedly in the morning, (3) Grade 3: Act shamelessly in the morning and not go to school unless they are accompanied, (4) Grade 4: Not go to school or withdraw from class sometimes (5) Grade 5: Not go to school or withdraw from class repeatedly for a period of time, (6) Grade 6: Not go to school in a semester and (7) Grade 7: Not go to school completely for a long time.

In the short term, SR may influence the patient's emotion, the school achievement and the friendship with schoolmates, leading to the performance decline and disturbance in the social and family function (Wu and Liu, 2006; Iwata *et al.*, 2012). In the long term, it may affect the further education and employment when they are in adulthood. In addition, it is a risk factor for future psychotics (Kendall *et al.*, 2004). SR is considered to be a predictor of serious anxiety in children and teenagers. The anxiety in childhood is an aura symptom of adult depression, suicide, square phobia and panic attacks (Kendall *et al.*, 2004). Thus, effective treatment for SR can provide an opportunity for preventing or controlling serious mental diseases.

Psychological intervention: The efficacy of psychological treatments for SR (such as Psychodrama therapy, psychodynamics therapy and family therapy) is not clear at present (Gullone, 2000). Cognitive Behavioral Therapy (CBT) was put forward by Araron Beck and his colleagues in late 1970s or early 1980s and has been a main treatment of anxiety, depression and other mental illnesses. Its effectiveness has been proved in SR in clinical trials in the past decade. Two randomized controlled trials on SR treatment were successively done at Monash University of Australia. In one study (King *et al.*, 1998) (n = 34), results showed that CBT was effective for SR and the rate of backing to school, anxiety scale and self-reported depression in the CBT group were obviously better than those the control group. The other study (n = 61) compared three treatments on SR: CBT alone, combination therapy with attendance of teachers and parents (Heyne *et al.*, 2002). It was found that all treatments were effective after 20-week treatment, about 60% of SR subjects were back to school and there was no remarkable difference in three groups. Long-term follow up showed that the symptoms of depression and anxiety resolved in 69% of SR subjects.

Pharmacotherapy: Tricyclic antidepressants (TCAs) are effective in the treatment of anxiety and depression of adults. However, they have potential heart side effects or even may cause death in children and adolescents. Thus, some experts advise not to use them in children and

teenagers (Hazell *et al.*, 2002). Selective serotonin reuptake inhibitors (SSRIs), a new generation of antidepressants, have been developed and gradually replace TCAs in the treatment of anxiety and depression in adults. Studies have showed that the side effects of SSRIs are significantly reduced when compared with TCAs (Cheung *et al.*, 2005). Fluoxetine is the first SSRIs approved by the FDA to be used in children and adolescents with depression (Cheung *et al.*, 2005). Some study has revealed that Fluoxetine is effectively for SR in children and adolescent aged 6-17 years and the rate of back to school is as high as 72.22% (Wu *et al.*, 2007).

Combination therapy: Bernstein *et al.* (2000) applied both Clomipramine treatment and CBT for SR in children and teenagers aged 12-18 years. Results showed the rate of back to school in the Clomipramine+CBT group was 54%, which was significantly higher than that in the CBT+placebo group (17%). Investigators concluded that CBT was an effective treatment for SR and CBT containing combination therapy would increase the therapeutic effect.

As mentioned above, CBT treated SR effectively and TCAs could increase the rate of back to school to 50%. However, TCAs have serious side effects in children and adolescents. Thus, it is imperative to develop new antidepressants such as SSRIs to treat SR safely. The purpose of our study is to test the efficacy of fluoxetine combined CBT for SR and find out a best way for the treatment of SR.

MATERIALS AND METHODS

Subjects: Children and adolescents aged 6-18 years who had SR were recruited from 2006-2009 from the Department of Children and Adolescents Psychiatry, the People's Hospital of Guangxi Zhuang Autonomous Region.

Inclusion criteria: Diagnostic criteria for SR (1) Symptoms standard: He/she has trouble in going to school due to mood disorders and presents with psychological symptoms (such as fear of going to school, loss of temper, somatic symptoms of avoiding to go to school). He/she refuses to go to school, can't maintain the study in the school and stays at home after leaving school, all of which have known by the parents and school staffs. Stealing, lying, destroying the public property and anti-social behaviors are not present, (2) Criteria for SR course: Absence from school for at least 2 weeks in 4 weeks (>50% of time) before assessment (Iwata *et al.*, 2012).

Exclusion criteria: Patients were excluded from the study if the following conditions were present, (a) epilepsy, bipolar disorders and conduct disorder (b) Substance abuse and mental retardation (c) Treatment with antidepressants and other psychological treatment (d) Absence of SSRI antidepressant treatment for two times, (e) Serious organic diseases. f) Abnormalities in electrocardiogram (ECG), (g) Intellectual problems or language disability in patient or parents and (h) Unwilling to participate in study. i) Serious suicide and/or self-injury tendency.

Withdraw criteria: Patients should be withdrawn from this study if the following conditions were present, (a) Participants strongly wanted to withdraw, (b) Manic symptoms, serious suicidal tendencies and suicidal behavior that require to be treated in hospital were present and (c) Severe drug toxicity or suspicious acute 5-hydroxytryptamine amine syndrome was present.

Study population: A total of 93 subjects were referred to our department, a bipolar disorder was observed in 1 subjects, schizophrenia in 2, conduct disorder in 1, substance abuse in 1, pervasive developmental disorder in 3 and truancy in 3. 11 of 93 were excluded. The remaining 82 subjects met the diagnostic criteria for SR and were then randomly divided into two groups: CBT group and CBT+Fluoxetine group. Then, informed consent was obtained before study.

CBT treatment: According to the guideline for CBT of SR at the Monash university of Australia (Heyne *et al.*, 2002), CBT treatment was performed for 45-50 min each time for a total of 12 times. Acute treatment was done for 12 weeks, supportive CBT therapy for one month and maintenance treatment once monthly for 3 months. The patient, parents and teachers also involved in the treatment. The strategies for CBT included relaxation training, cognitive therapy, problem-solving training, regulation of emotional training, training of social communication skill and systematic desensitization therapy. The strategies for parents included the training of impulsive behavior controlling, training of incident handling and problem-solving, training of parenting skills and training of tips to help children to school and self-relieve anxiety and depression. The school teachers were interviewed one time in the course of the treatment to discuss the plans and requirements for back to school and how to help patients in school.

Fluoxetine treatment: The initial dose was 10 mg day⁻¹ for one week and thereafter increased gradually to

20-40 mg day⁻¹ and the highest dose was 60 mg day⁻¹. Acute treatment was done for 12 weeks, followed by 12-week maintenance therapy.

Evaluations: Self-rating Anxiety Scale (SAS) (Zhang, 2003): SAS was developed by Zhang (2003) and is used to measure the severity of anxiety and the changes in mental state. It has been translated into Chinese. It contains 20 items and 4 levels: no or very little time, some time, quite a lot of time and most or all the time. The scores are 4,3,2 and 1, respectively. The higher the score, the more obvious the anxiety tendency. Evaluation was done before treatment and at 2 weeks after the last treatment.

Self-rating depression scale (SDS) (Zhang, 2003): SAS was developed by Zung in 1965 and is used to measure the severity of depression and changes in the psychological state. It contains 20 items on the symptoms and the frequency of depression, which are divided into 4 levels: no or very little time, some time, quite a lot of time and most or all the time. The scores are 4, 3, 2 and 1, respectively. The higher the score, the more obvious the depressive tendency. Evaluation was done before treatment and at 2 weeks after the last treatment.

The clinical global impression (CGI) (Zhang, 2003): CGI has been widely used in clinical studies on psychotropic drugs in children and adolescents for evaluation of anxiety and depression. It is a comprehensive tool to assess the therapeutic efficacy and the severity of diseases. In this study, the subscale of CGI (severity of Impression Scale; [CGI-S]) was employed for evaluation. The CGI-S included 7 levels to assess the severity of diseases. Evaluation was done before treatment and at 2 weeks after the last treatment.

The rate of back-to-school: The rate of Back-to-school refers to the percentage of SR subjects who return to school successfully. "Return to school successfully" means that SR subjects spend the = 80% of school time in school in 4 weeks. The rate of Back-to-school = the number of patients returning to school successfully/the number of patients in each group×100% (Heyne *et al.*, 2002). Evaluation was done before treatment and at 2 weeks after the last treatment.

Assessment of adverse effects: According to the guideline for medication, the SR patients should come to clinic once weekly during the acute treatment and once monthly during the maintenance therapy, to assess the adverse effects. The adverse effects were evaluated with New York state psychiatric institute side effects form in each patient (Klein, 1994).

Statistical analysis: The SPSS 13.0 software program for Windows was used. Quantitative variables were described as Mean±SD. Categorical variables were expressed as numbers and percentages. Analysis of t-test, covariance were used to compare quantitative data. Chi-squared test was used to compare categorical variables. Statistical significance was defined at p-values of <0.05.

RESULTS

In present study, a total of 75 patients with SR were randomized into two groups: CBT group (n = 36) and CBT+Fluoxetine group (n = 39). After treatment, in two groups, the SAS score, SDS score and CGI-S score were significantly decreased (p<0.01) and the percentage of school attendance was 72.2% in CBT group and 82.1% in CBT+Fluoxetine group. There were no significant differences in the SAS score, SDS score, CGI-S score and the percentage of school attendance after 12-week treatment between two groups (p<0.01).

Patient data: Eighty two subjects met the inclusion criteria. During the treatment, 7 subjects withdrew from this study, the reasons were as follows: worrying about side effects of Fluoxetine in 2 subjects of CBT+Fluoxetine group, complaining about treatment effect in 1 case of each group, unsatisfying the research program in 1 case of CBT group, treatment failure in 1 case of CBT+Fluoxetine group and non-compliance in 1 case of CBT group. There was no significant difference of withdrawing numbers between the tow group, P>0.05. Finally, 75 subjects completed all clinical trials Including 40 males and 35 females. The average age was 13.44±2.99 years (range: 8-18). The 15-year-old patient accounted for the largest number, followed by the 12-year-old, 18-year-old The average time of not going to school was 18.99±24.87 weeks (range: 2 weeks-2.5 years).

Among 75 subjects, there were 36 in the CBT group and 39 in the CBT+Fluoxetine group. In the CBT group, the average age was 13.58±2.97 years old and the mean time of absence from school was 18.97±27.07 weeks. In the CBT+Fluoxetine group, the average age was 13.31±3.04 years and the mean time of absence from school was 19.00±23.00 weeks. Before treatment, SAS score was 56.36±12.94 in the CBT group and 56.26±13.24 in the CBT+Fluoxetine group. The pre-treatment SDS score was 58.36±12.51 in the CBT group and 57.28±12.69 in the CBT+Fluoxetine group. The CGI-S score was 4.42±1.65 in the CBT group and 4.72±1.69 in the CBT+Fluoxetine group before treatment. There were no significant differences in the age

Table 1: General information of subjects in 2 groups (t-test)

Variables	Group	n	Average	SD	t-value	p-value
Age	CBT	36	13.58	2.97	0.396	0.693
	CBT+Fluoxetine	39	13.31	3.04		
Time of absence from to school	CBT group	36	18.97	27.07	-0.005	0.996
	CBT+Fluoxetine	39	19.00	23.01		
SAS	CBT group	36	56.36	12.94	0.035	0.972
	CBT+Fluoxetine	39	56.26	13.24		
SDS	CBT group	36	58.36	12.51	0.370	0.712
	CBT+Fluoxetine	39	57.28	12.69		
CGI-S	CBT group	36	4.42	1.65	-0.782	0.437
	CBT+Fluoxetine	39	4.72	1.69		

Table 2: SR related mental disorders in different groups

Clinical diagnosis	CBT	CBT+Fluoxetine	Total
Major depression/dysthymia	16	18	34
Specific phobia	9	8	17
Separation anxiety disorder	7	8	15
Social phobia	3	10	13
Panic disorder	7	2	9
Attention deficit hyperactivity disorder	6	3	9
Obsessive-compulsive disorder	2	5	7
Learning disabilities	4	3	7
No	5	4	9
Total	59	57	120

Table 3: Adverse effects of fluoxetine

Order	Side effects	No.	System	Percentage (%)
1	Dry mouth	5	GI	20.8
2	Dizziness	4	CNS	16.7
3	Attention problems	3	CNS	12.5
4	Nausea	3	GI	12.5
5	Sleep disorders	3	CNS	12.5
6	Sleepiness	2	CNS	8
7	Headache	2	CNS	8
8	Increased appetite	1	GI	4
9	Bellyache	1	GI	4

(p = 0.693), the time of absence from school (p = 0.996), the pre-treatment SAS score (p = 0.972), the pre-treatment SDS score (p = 0.712) and the pre-treatment CGI-S score (p = 0.437) between the two groups (Table 1).

SR and related mental disorders: Among 75 subjects, 66 had at least one comorbidity with mental disorder accounting for 88.00%, 31 of them had one mental disorder and 35 developed two or more mental disorders (Table 2). 9 subjects had no a diagnosis of mental disorders, including 5 in the CBT group and 4 in the CBT+Fluoxetine group.

Adverse effects: There were 10 of 39 subjects in the CBT+Fluoxetine group complaining the side effects (a total of 24 times). The gastrointestinal symptoms and neurological symptoms were the most frequently observed. The side effect with highest incidence was dry mouth, followed by dizziness and concentration problems (Table 3).

Table 4: Comparative study of SAS, SDS and CGI-S score before and after treatment

Within-group design ($\bar{x}\pm\text{sec}$)						
Variables	Group	n	Before treatment	After treatment	t-value	p-value
SAS score	CBT	36	56.36±12.94	37.92±12.94	5.69	0.000
	CBT+Fluoxetine	39	56.26±13.24	39.49±14.27	5.56	0.000
SDS score	CBT group	36	58.36±12.51	35.14±9.960	8.94	0.000
	CBT+Fluoxetine	39	57.28±12.69	38.72±13.16	5.56	0.000
CGI-S score	CBT group	36	4.42±1.650	1.28±1.090	11.60	0.000
	CBT+Fluoxetine	39	4.72±1.690	1.26±1.270	11.54	0.000

Table 5: Comparative study of SAS, SDS and CGI-S score difference before and after treatment between-group design ($\bar{x}\pm\text{sec}$)

Group	n	SAS score difference	SDS score difference	CGI-S score difference
CBT group	36	-18.39±2.35	-23.22±15.59	-3.14±1.62
CBT+Fluoxetine	39	-16.82±2.25	-18.56±17.58	-3.46±1.90
F		0.23	1.78	0.08
p-value		0.631	0.186	0.773

Score difference: The score before treatment-the score after treatment

Table 6: Comparisons of therapeutic efficacy between-group design (multiple comparisons of analysis of covariance)

Scales	(I)	(J)	Mean Difference (I-J)	SDE	p-value	95% confidence interval for difference	
						Lower bound	Upper bound
SAS	CBT	CBT×Fluoxetine	-1.571	3.25	0.631	-8.06	4.91
SDS	CBT	CBT×Fluoxetine	-3.644	2.73	0.186	-9.08	1.80
CGI-S	CBT	CBT×Fluoxetine	0.077	0.27	0.773	-0.46	0.61

SAS, SDS and CGI-S Scale evaluation before and after treatment within-group design: After treatment, the SAS score, SDS score and CGI-S score in the CBT group was markedly reduced, $p < 0.01$ and the SAS score, SDS score and CGI-S score in CBT+Fluoxetine group was also significantly decreased, $p < 0.01$ (Table 4).

Comparative study of SAS, SDS and CGI-S score difference before and after treatment between-group design: It was found from the scatterplot that the difference between the scores before and after treatment of SAS, SDS and CGI-S were all in linear correlation (R^2 value was between 0.45~0.60). The results show that all the scores before treatment of SAS, SDS and CGI-S were respectively related to the therapeutic efficacy significantly, the SAS was ($F = 62.669$, $p = 0.000$), the SDS was ($F = 72.501$, $p = 0.000$) and the CGI-S was ($F = 98.989$, $p = 0.000$). There was no significant difference in slope of the scores before treatment between 2 groups, the SAS was ($F = 0.326$, $p = 0.570$), the SDS was ($F = 0.029$, $p = 0.866$) and the CGI-S was ($F = 0.264$, $p = 0.007$). So the covariance analysis could be used to further data analysis. However, the age and the time of absence from to school were not in linear relation ($R^2 < 0.07$), could not be made to the analysis of covariance (Table 5).

The results of the covariance analysis showed that, after adjustment of the SAS, SDS and CGI-S score before and after treatment between two groups, the difference of SAS score in the CBT group was -1.571 points lower than

that in the CBT+Fluoxetine group, but there was not statistical difference ($p = 0.631$), the difference of SDS score in the CBT group was -3.644 points lower than that in the CBT+Fluoxetine group but there was not statistical significance ($p = 0.186$) and the difference of CGI-S score in the CBT group was 0.077 points higher than that in the CBT+Fluoxetine group without statistical significance ($p = 0.773$) (Table 6).

Rate of back to school: There were 26 subjects in the CBT group staying in school for more than 80% of school time in school in 4 weeks after treatment and the rate of back to school was 72.2%. In addition, 32 subjects in the CBT+Fluoxetine group were back to school and the rate of back to school was 82.1%. There was no significant difference in the rate of back to school between two groups ($\chi^2 = 1.032$, $P = 0.310$). It means that both CBT and CBT+Fluoxetine treatment can successfully help SR patients back to school. CBT+Fluoxetine treatment had a slightly higher rate of back to school when compared with CBT.

DISCUSSION

Clinical features of SR: The subjects of this study were mainly from the Nanning city locating in the Guangxi Zhuang Autonomous Region in the south part of China. This study showed that the peak age of subjects with SR was 12, 15 and 18 years, which were different from findings in other counties (6-7 and 10-12 years)

(King and Bernstein, 2001). And SR children aged 6-7 years were not present in our study, which may be attributed to following reasons (1) there is a low incidence of SR at this age in this area and (2) Children at this age do not come for treatment. In addition, the parents of children at this age might not timely recognize the presence of SR and the requirement for treatment. Of note, subjects aged 12, 15 and 18 years exactly take part in the entrance examinations that may increase the pressure on these students. However, the specific reasons are required to be elucidated in future investigations. So it suggested that there would be differences in presentation of SR among different countries under various culture background (Lyon and Cotler, 2007).

In our study, 31 subjects were diagnosed as one of mental disorders and 35 developed two or more concomitant mental disorders (such as major depression, social phobia, specific phobia and separation anxiety disorder), which has been reported previously (King *et al.*, 2001). According to the DSM-IV, SR is divided into four subtypes including social phobia, specific phobia, separation anxiety disorder and depression. However, 9 subjects had no mental disorder(s). The mechanism was still unclear and whether it affects the therapeutic efficacy was poorly understood. Further studies are required to confirm this.

CBT treated SR effectively: Our study showed that 26 subjects backed to school successfully and stayed in school for = 80% of school time in the CBT group and the rate of back to school was 72.22%. This result was similar to previously reported (70%). In addition, the scores of CGI-S, SDS and SAS were significantly lowered after treatment. Thus, the CBT is an effective treatment for SR and can reduce the associated anxiety and depression in SR subjects.

CBT was one of psychological treatments proposed by Araron Beck and colleagues in late 1970s and early 1980s. Extensive clinical studies in the past decade have confirmed the effectiveness of CBT. It has become a major tool for psychological intervention of anxiety, depression and many other mental illnesses in adults. Some experts recommend that different strategies of CBT should be applied depending on the type of dysfunction and subtypes. If the patients' fear and anxiety are related to the school settings, the relaxation training, step by step exposure or systematic desensitization can be used. When SR sufferers are fear for school or other social situations, the behavior rehearsal exposure and cognitive reconstruction may be effective. The communication skill training and challenging distorted thinking may help them return to school. When concerns and worries are from

family members (such as parents), the parents' attendance may help these patients and parents to achieve goals and the behavioral management of parents may encourage patients to go to school. As to SR patients who seek positive stimulation behaviors out of campus, parents attending CBT treatment is also effective. Assertiveness training may help patients to deal with conflicts and stress in school finally to return to school.

Fluoxetine did not further improve the efficacy of CBT for SR. Our study showed that the rate of back to school was 82.1% in the CBT+Fluoxetine group, which was only slightly higher than that in the CBT group ($p>0.05$). This result was similar to previously reported (Heyne *et al.*, 2002; Wu *et al.*, 2007). In addition, the CGI-S score, SDS score and SAS score were significantly lowered after treatment. In order to determine whether Fluoxetine could further improve the efficacy of CBT, covariance analysis was applied and results showed the pre-treatment CGI-S score, SDS score and SAS score were related to the therapeutic efficacy of both treatments. After adjustment of scores of CGI-S, SDS and SAS before and after treatment in two groups, there were no marked differences in these scores between two groups ($p>0.05$), suggesting that the combination treatment fails to further increase the therapeutic efficacy of CBT. Fluoxetine is one of SSRIs and can selectively inhibit the presynaptic reuptake of 5-HT and slightly influence the reuptake of norepinephrine. It is one of anti-depressants of new generation, having the characteristics of anti-anxiety and anti-depression. It has been used in the treatment of depression and anxiety in children and adolescents. However, our findings did not find that Fluoxetine further improve the efficacy of CBT.

The subjects withdrawing from this study were also analyzed. Severe subjects withdraw during the acute treatment. Two patients complained the side effects of Fluoxetine in the CBT+Fluoxetine group. One parent was unsatisfactory with the research program in the CBT group and one unsatisfactory with the therapeutic efficacy in the CBT+Fluoxetine group. In addition, 1 patient had no compliance in the CBT group. There was no significant difference in the number of subjects withdrawing from the study (Table 1). However, due to small sample size, Fluoxetine leading to withdrawing can not be excluded.

Adverse effects of Fluoxetine: In the CBT+Fluoxetine, 10 of 39 subjects developed adverse effects of different extents (a total of 24 times). Symptoms of the digestive system and central nervous system were frequently found. Symptoms of urinary system, cardiovascular system and other systems were not found. The side effect

with the highest incidence was dry mouth, followed by dizziness and attention abstraction (Table 4). Our results revealed that, during the first week of treatment, adverse effects were more common. Some patients experienced more than two different symptoms which were mild to moderate. Most of patients could tolerate these side effects which resolved within 1-2 weeks.

CONCLUSION

The SR in children and young people should be paid attention to and it has different clinical features in different countries and regions. Studies have shown that CBT and CBT+Fluoxetine treatment can effectively treat SR, while our results fail to show Fluoxetine can further increase the efficacy of CBT for SR.

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