ORIGINAL ARTICLE

Evaluation of the Effectiveness of Withania Somnifera Root Extract on the Anxiety Symptoms among children with ADHD in Mashhad

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ABSTRACT

Background: The aim of this study was to investigate the effect of Withania somnifera root extract on the symptoms of anxiety among children with ADHD.
Methods: In total, 28 children referred to Ibn Sina Hospital in Mashhad were randomly assigned into intervention (Withania somnifera root extract) and control groups (placebo). The participants were selected according to the results of a clinical interview conducted by a child and adolescent psychiatrist based on the criteria of the diagnostic and statistical manual of mental disorders.
The data were collected using the Revised Children's Manifest Anxiety (RCMA) and Attention Deficit Hyperactivity Disorder Rating Scale questionnaires at the beginning of the study and on the third and sixth weeks after the intervention.
Results: The mean age of the participants in the intervention and control groups was 9.71 and 9.29 respectively. There were no significant differences between the two groups in terms of the patient's clinical features, such as age, and gender (P>0.05). The total result of RCMA showed a decrease in the scores of both groups during the third and sixth weeks, compared to the beginning of the study. Moreover, the difference between the intervention and control groups was statistically significant.
Conclusion: The use of Withania somnifera root extract among ADHD children suffering from anxiety symptoms reduced the symptoms of physiological anxiety, sensitivity, social concerns (i.e., hypersensitivity and centralization), and an overall score of RCMA.
Keywords: ADHD, Anxiety disorder, Withania somnifera

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is a psychiatric disorder that affects children, adolescents, and adults all over the world. Its prevalence is estimated at 7.2% in the general population[1]. This disorder characterized by stable patterns of reduced attention and increased impulsivity and hyperactivity. The ADHD affects about 5%-8% of school-age children. The individuals suffering from ADHD most frequently exhibit significant degradation in academic performance and interpersonal as well as social situations.

The ADHD process is highly variable and its sustainability can be predicted by different factors, including its association with other psychiatric disorders[2,3,4,5]. The prevalence rate of this disorder among children in the USA was estimated at 2%-20%. However, it was obtained less than 1% in the UK[5]. The studies conducted in Iran on the prevalence of ADHD among children and adolescents have reported different prevalence rates ranged from 9% to 14.2%[6,7]. Moreover, the incidence rate of this disorder is estimated at 4.4% in adulthood[8].

Many children with ADHD also have other psychiatric disorders, such as anxiety disorders with the prevalence rate ranged from 25% to 30%[9,10]. This simultaneously affects the prediction of therapeutic responses among this population[11]. Some studies have suggested that children with ADHD and comorbid anxiety disorders are more sensitive to the side effects of medications which lead to more limited responses[12].

Medical therapy is the cornerstone for ADHD treatment[13]. The multidisciplinary treatment of anxiety disorders among children includes medical treatment with selective serotonin reuptake inhibitors, tricyclic antidepressants, and benzodiazepines[5].

Some factors persuade researchers to find new treatments with fewer side effects. They include the limited number of approved drugs, drug side effects, lack of adequate studies regarding the use of these drugs among children and adolescents, and the ineffectiveness of drugs on 20-35% of cases[5,9].

Withania somnifera is an important medicinal plant with therapeutic properties. Moreover, this herb benefits cardiovascular, endocrine, and central nervous systems due to its anti-inflammatory and anti-anxiety effects[14]. It is cultivated in some countries such as Iran, Spain, Italy, Greece, and China[15]. To the best of our knowledge, very few research has been done on the anti-anxiety effects of Withania somnifera in Iran and throughout the world. Therefore, the aim of this study was to investigate the effect of Withania somnifera root extract on the symptoms of anxiety among children with ADHD.

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MATERIALS AND METHODS

In this study, 34 children were diagnosed with ADHD and anxiety symptoms in Ibn Sina Hospital in Mashhad. The results of a clinical interview conducted by a child and adolescent psychiatrist based on the DSM-V diagnostic criteria were applied as the diagnostic approach. After the parents had provided written informed consent, 28 children entered the study based on the inclusion and exclusion criteria (Fig. 1). The inclusion criteria were children with: 1) ADHD according to DSM-V diagnostic criteria, 2) the age range of 7-12, 3) no other psychiatric illnesses, and 4) at least 3 months of standard medical treatment.

On the other hand, the children who were unwilling to continue the study and those with systemic diseases and psychiatric interventions were excluded from the study.

Patients were randomly assigned into two groups using the table of random numbers, namely the anti-ADHD treated group and the Withania somnifera capsule (intervention group), and the anti-ADHD treated group and placebo (control group). The participants consumed 10 mg Withania somnifera once daily for six weeks.

The patients were evaluated before the intervention and after 3 and 6 weeks of treatment using Revised Children's Manifest Anxiety (RCMA) and ADHD Rating Scale-IVAD (HD-RS).

Revised children's manifest anxiety questionnaire: This questionnaire consists of 37 self-reported items designed to be applied to children and adolescents aged between 5 and 19 years. Moreover, it evaluates the general and non-specific characteristics of anxiety. Out of 37 items, 28 questions measure anxiety in three areas, including physiological anxiety, anxiety-sensitivity, and social concerns (i.e., hypersensitivity and centralization). The other nine items measured the respondents' truthfulness using lie scales.

Attention deficit hyperactivity disorder rating scale questionnaire: This questionnaire includes 18 items, of which nine questions deal with hyperactivity problems and the other nine items concern with the attention-deficit issues. The children were asked to complete the RCMA and ADHD-RS questionnaires with the help of their parents on the third and sixth weeks. A psychiatry assistant prepared a medical history in terms of the clinical complications (e.g., nausea, vomiting, diarrhea, headache, drowsiness, and blurred vision), medication acceptance and compliance.

Data analysis: The normality of data was determined using one-sample Kolmogorov-Smirnov test with Lilliefors correction. In addition, the normal data were analyzed by the student test. In addition, the Mann-Whitney U test, Friedman, and Wilcoxon tests were utilized for non-normal data analysis. The data were analyzed in SPSS software (version 20) and p-value less than 0.05 was considered statistically significant.

This double-blind randomized clinical trial was approved by the Research Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran in 2017. The trial was registered at the Iranian registry of clinical trials (www.irct.ir; registration number: IRCT201506215280N18).

RESULTS

In this study, 28 children were randomly selected and assigned into the intervention and control groups. According to Table 1, there are no significant differences between the two groups in terms of age, gender, and educational status.

In the present study, two groups were compared in terms of anxiety, social concerns (i.e., hypersensitivity and centralization), and lie scale. The results showed a decrease regarding the scores for all factors between both groups three and six weeks after the treatment. Moreover, this reduction was higher in the intervention group.

According to Table 2, a decrease was observed between the two groups in terms of anxiety and hypersensitivity scores in the sixth week. However, the scores of centralization between the two groups were significant on the third and sixth weeks.

Although there was a decrease regarding the lie scale scores in both groups during the study, it was not significant ($P>0.05$).

The reduction of scores in terms of physiological anxiety was observed in two groups after 3 and 6 weeks of intervention, compared to the beginning of the study. However, this reduction was more significant in the intervention group. Furthermore, the anxiety scores decreased by 37.25% and 19.84% after three weeks and 67.02% and 24.56% after six weeks in the intervention and control groups, respectively (Fig. 2).

With regard to the hypersensitivity scores, higher reduction levels were observed in the intervention group. Figure 3 illustrates a decrease in the intervention group in terms of hypersensitivity scores three (37.55%) and six (63.11%) weeks after the beginning of the study. This difference was significant during the study ($P< 0.05$).

As shown in Figure 4, a reduction was observed in two groups in terms of centralization scores during the study. However, the difference between the two groups was significant only on the sixth week. The reduction in terms of centralization scores in the intervention and control groups was 51.71% and 18.88%, respectively. The intervention and control groups were asked to complete the ADHD questionnaire, Friedman and Wilcoxon tests before the intervention and on the third and sixth weeks. The results showed a significant decrease within each group, compared to the beginning of the study ($P<0.05$). However, the difference between the two groups was not significant ($P>0.05$, Fig.5).

Moreover, the result of RCMA showed that the anxiety scores decreased significantly in both groups on the third and sixth weeks, compared to the beginning of the study (Fig. 6).

Fig. 1: Randomly selected children in the intervention and control groups

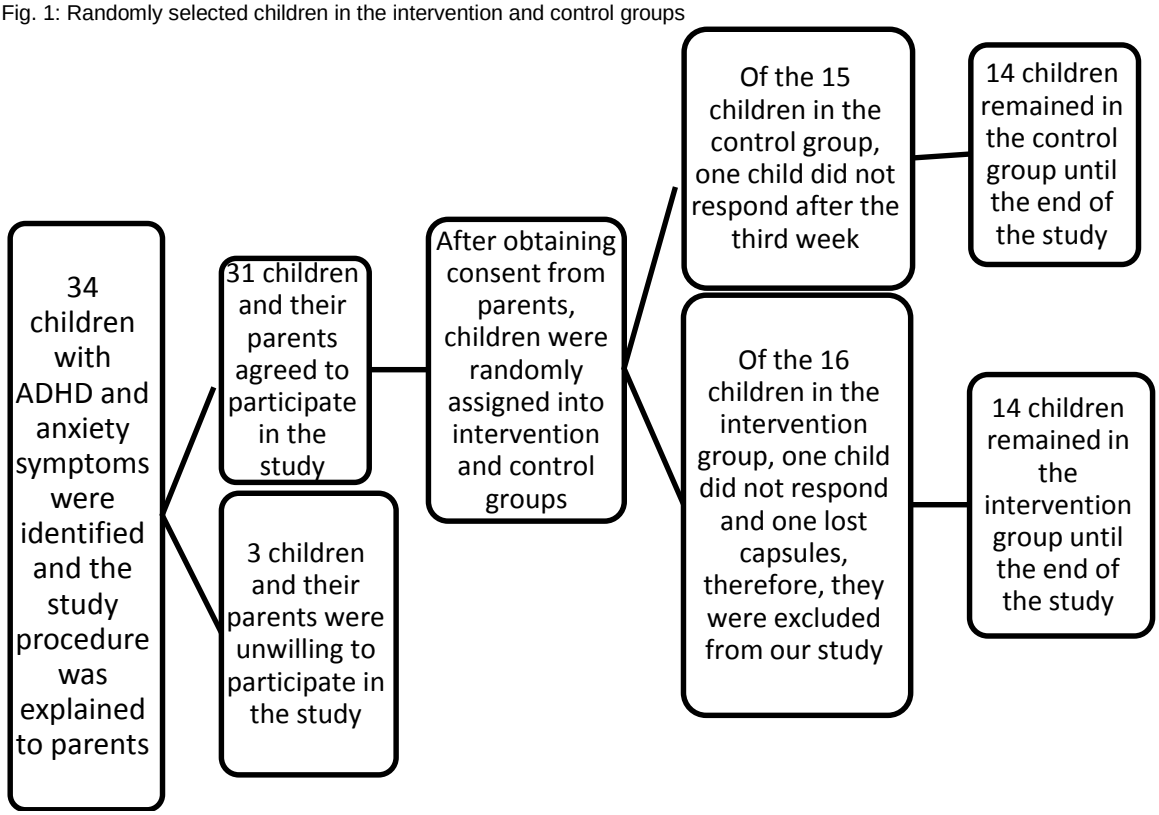

Fig. 2: Results of anxiety in intervention and control groups on the third and sixth weeks, compared to the beginning of the study

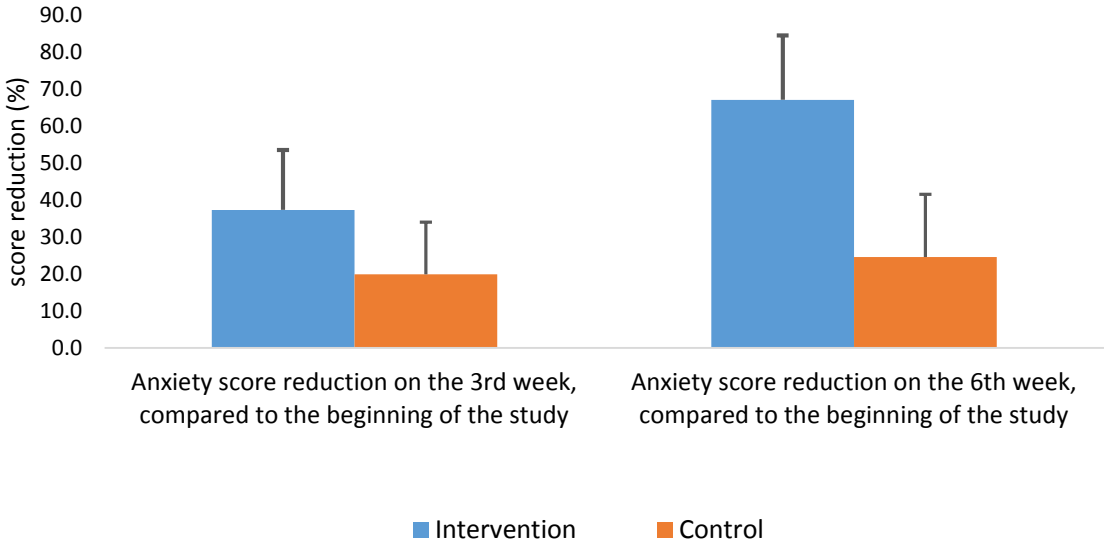

Fig. 3: Result of social concern (i.e., hypersensitivity) in intervention and control groups on the third and sixth weeks, compared to the beginning of the study

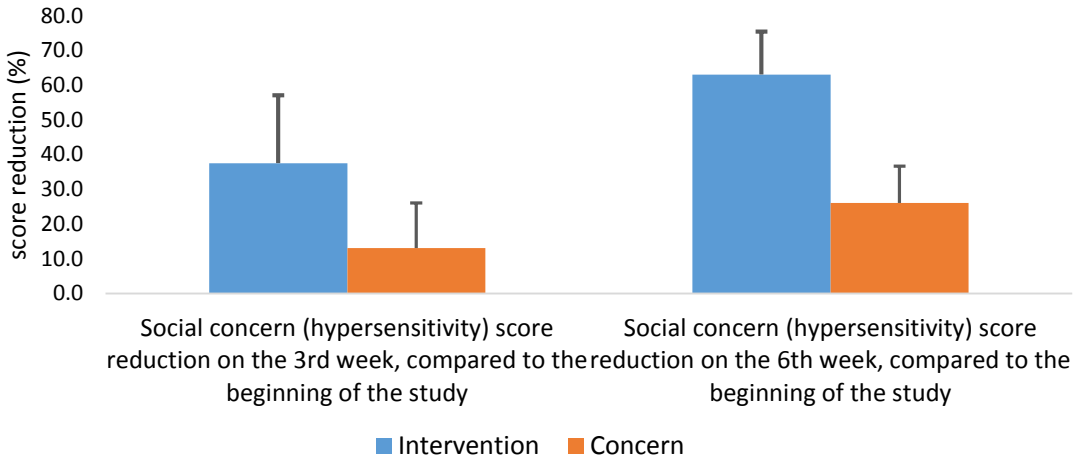

Fig. 4: The result of social concern (i.e., centralization) in intervention and control groups at 3rd and 6th weeks compared to the beginning of the study

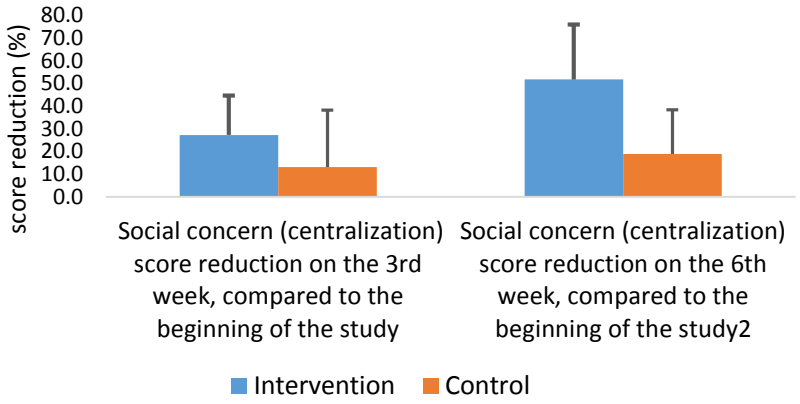

Fig. 5: Comparison of the two intervention and control groups after completing the ADHD-RS questionnaire before intervention and on the third and sixth weeks

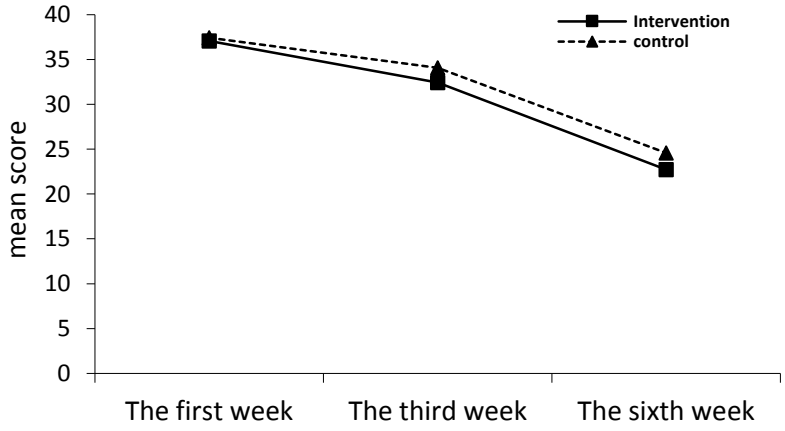

Fig. 6: Total result of RCMA in intervention and control groups on the third and sixth weeks, compared to the beginning of the study

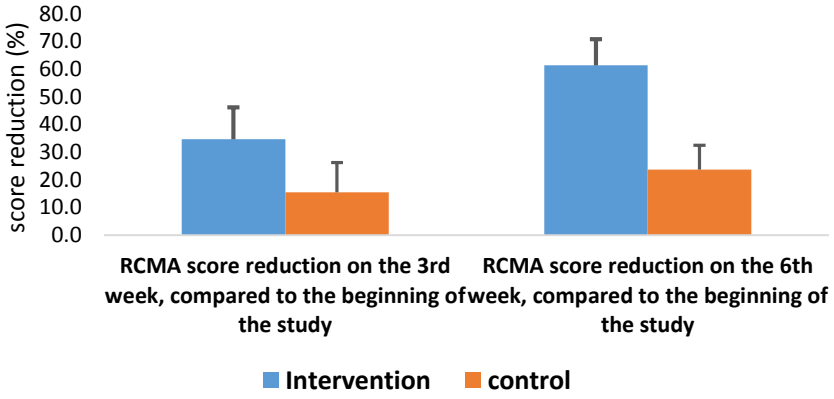

Table 1: Age, gender, and education status in the intervention and control groups

Variables	Group				P-value	test
	Intervention		Control			
Age (year)	9.71±1.77		9.29±1.44		0.489	t†=0.703
Gender (%)	Female	42.9	Female	35.7	0.699	Likelihood Ratio††=0.150
	Male	57.1	Male	64.3		
Educational status	3.71±1.77		3.36±1.50		0.570	t†=0.576

††) χ^2

†) Student's t-test

Table 2: Distribution of physiological anxiety, social concerns, and lie scale scores among children with ADHD referring to children's psychiatric clinic of Ibn Sina Hospital in Mashhad

Factor	Time/Group		ADHD score		
			Mean±SD	p-Value	Test
Concern (hypersensitivity)	Before intervention	Intervention	8.86±1.10	0.104	t†=1.69
		control	7.93±1.73		
	The third week	Intervention	5.5±1.83	0.056	t†=-2.00
		control	6.93±1.94		
	The sixth week	Intervention	3.29±1.27	<0.0001**	t†=-4.78
		control	5.86±1.56		
Physiological anxiety	Before intervention	Intervention	6.29±1.33	0.227	U††=-1.24
		control	5.64±1.34		
	The third week	Intervention	4.00±1.41	0.482	U††=-0.75
		control	4.57±1.70		
	The sixth week	Intervention	2.07±1.00	<0.0001**	U††=-3.53
		control	4.29±1.54		
Concern (centralization)	Before intervention	Intervention	6.07±1.33	0.296	t†=-1.07
		control	6.64±1.50		
	The third week	Intervention	4.43±1.45	<0.046*	U††=-1.99
		control	5.57±1.28		
	The sixth week	Intervention	2.93±1.54	<0.001**	U††=-3.35
		control	5.29±1.44		
lie scale	Before intervention	Intervention	4.86±1.99	0.485	t†=0.71
		control	4.29±2.27		
	The third week	Intervention	3.50±1.74	0.689	U††=-0.40
		control	3.93±1.77		
	The sixth week	Intervention	2.93±1.38	0.841	U††=-.20
		control	2.86±1.10		

†) Student's t-test ††) Mann-Whitney U Test

DISCUSSION

In this study, the anxiety, hypersensitivity, and centralization levels decreased in intervention and control groups for six weeks. However, the reduction levels were higher in the intervention group receiving Withania somnifera root extract. Some studies showed a positive effect of Withania somnifera on the reduction of stress, anxiety, and depression levels[16,17,18].

Moreover, a review study was conducted on Withania somnifera with different dosages (125 mg QD, 125mg BID, 250 mg BID) in 2014. This study employed the Perceived Stress Scale (PSS), Hamilton Anxiety Rating Scale (HAS), and Bioelectrical Impedance Analysis (BIA) questionnaires. The results of this study showed that the use of Withania somnifera resulted in the improvement of anxiety or stress scores, compared to placebo and psychotherapy[19].

In our study, a significant decrease was observed in the mean scores of the RCMA after six weeks. In the intervention and control group, it decreased from 21.21% to 8.29% and 20.21% to 15.43%, respectively. It indicates a decrease by 61% in the intervention group and 23.6% in the control group. In a double-blind study by Andria et al. on patients with anxiety, a decrease was observed regarding the RCMA scores after six weeks. The reduction rates were estimated at 85% and 50% within the Withania somnifera group and the placebo group, respectively[20].

Chandrasekhar et al. conducted a study titled “A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety among adults” in 2012. This study utilized the PSS and Depression Anxiety Stress Scale (DASS) questionnaires.

The results of this study showed that the scores in terms of anxiety and insomnia, stress, and PSS questionnaire in the group treated with Withania somnifera decreased by 69.7%, 64.2%, and 44% respectively[21].

Morgan et al. conducted a systematic review study in 2014. According to the results, a decrease was observed in terms of anxiety level within the groups treated with the root extract of Withania somnifera. Moreover, there was a significant reduction regarding the scores of Hamilton test, PSS, DASS, and anxiety within the intervention, compared to the placebo group[19]. In our study, the anxiety scores in the intervention group decreased by 51.73% after six weeks.

Furthermore, the results of this study showed a decrease in ADHD scores within both groups; however, this difference was not significant.

Katz et al. examined the combined effects of medicinal herbs, such as Paeoniae Alba, Withania somnifera, and Centella Asiatica on the symptoms of children with ADHD. The results showed the efficacy of these plants on the improvement of attention, impulse control, and cognitive symptoms among children after four months[22]. However, the obtained results were not in line with the findings in this study.

In some animal studies, the effects of Withania somnifera have been investigated on various diseases, including depression, anxiety, stress, and cancer[14,23].

Verma et al. conducted a review study (animal study) in 2011 on the pharmacological effects of Withania somnifera extract. The results showed anti-anxiety, anti-stress, and anti-aging effects of Withania somnifera extract[14].

In another review study, Mishra et al. investigated the effects of Withania somnifera on mice. The results showed that this plant played an effective role in the improvement of stress-induced fatigue[23].

According to the obtained results, it is recommended that further studies employ more sample sizes with longer follow-ups. In addition, more research is required to assess anxiety symptoms. Future studies are also suggested administering medicinal plants at a higher dose with the measurement of the serum levels.

CONCLUSION

The use of Withania somnifera root extract reduces the symptoms of physiological anxiety, sensitivity, social concerns, and an overall score of RCMA among children with ADHD and comorbid anxiety disorders. However, no significant effects were observed in terms of social acceptability and an overall score of ADHD.

Conflict of interest: There is no conflict of interest regarding the publication of this study.

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There is no financial for this study.

The trial was registered at the Iranian registry of clinical trials (www.irct.ir; registration number: IRCT201506215280N18

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