

# N-acetylcysteine for treatment of autism, a case report

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There are a limited number of Food and Drug Administration (FDA)-approved medications for the treatment of autism. Meanwhile, oxidative stress and neuroinflammation are supposed to play a causative role in autism. N-acetylcysteine may provide cystine, a precursor for glutathione (GSH), which is an important antioxidant factor in the brain. We here report a child with autism, whose symptoms were markedly decreased after taking oral N-acetylcysteine 800 mg/day, in three divided doses. His social interaction was significantly increased. The score of social impairment on a visual analog scale decreased from 10 to 6 in the two-month trial. The aggressive behaviors decreased from 10 to 3. This case suggests that N-acetylcysteine may decrease some symptoms of autism.

**Key words:** Autism, children, glutathione, oxidative stress, treatment

## INTRODUCTION

Autism is a neurodevelopmental disorder, with a complex pathophysiology. Its main characteristics are: Limited social interests, stereotypic behaviors, limited social communications, and impaired social interactions. Some studies suggest that neuroinflammation may play a casual role in autism.<sup>[1]</sup> There is no curative therapeutic intervention for autism.<sup>[2,3]</sup> In addition, more evidence must be provided for many of the suggested interventional approaches in children with autism. N-acetylcysteine (NAC) is a precursor to glutathione (g-glutamylcysteinylglycine, GSH). NAC is a relatively safe and available medication for children and adolescents.<sup>[4]</sup> Here, we report the case of a boy with autism, where his autistic behaviors decreased after taking NAC, for managing his nail-biting behavior.

## CASE REPORT

The patient is an eight-year-old boy who was referred to Hafez Hospital at Shiraz, Iran, in 2011. He was diagnosed with autism disorder according to the DSM-IV diagnostic criteria.<sup>[5]</sup> There was marked limited

verbal communication and skills, stereotypic behaviors, restricted interest, and a significant impairment in social relationships and interactions. He also displayed hyperactivity and inattentiveness in preschool. From two years ago, oral risperidone 2 mg/day and oral thioridazine 10 mg/day were administered, to control his hyperactivity and inattentiveness. No neurological or significant medical problems were found. His laboratory examination was unremarkable.

After a written informed consent form was provided by the parents, for participation of the child in a clinical trial (Irct registration number: IRCT201103023930N3), oral NAC 800 mg per day (Pharma Chimi, Iran) was added for management of his severe nail-biting behavior. There was a significant reduction in his nail-biting behavior. In addition, the parents noticed that there was a marked reduction in his autism symptoms 30 days after the onset of NAC administration. The visual analog scale showed that his social interaction was significantly increased and he responded to social interactions better than at the baseline. According to his parents' report, the score of social impairment on the visual analog scale decreased from 10 to 6 in the two-month trial. The parents also reported that his verbal skills and communications increased from 5 to 9 after using the visual analog scale. The aggressive behaviors decreased from 10 to 3. His aggression toward his sister also significantly decreased. The parents had not marked a complaint about their children's aggressive behavior on the last visit. In addition, his hyperactivity and limited interests were reduced after taking NAC. His preoccupation with a toy car was decreased and he was interested in playing with different

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toys. He had persuaded his parents to cut his hair every day before administration of NAC. They had to even cut his hair more than once a day. Now, his interest and persuasion to cut his hair was markedly decreased. Moreover, the severity and frequency of his blinking tic decreased. The parents did not report any side effect, except a mild abdominal pain. He had never experienced this type of significant improvement in the last few years, even after taking risperidone. They also reported that nothing worsened after the administration of NAC. He did not take any other antioxidant or glutathione prodrug during the period of study or for weeks before.

## DISCUSSION

To the best of the authors' knowledge, this is the first case report about the effect of NAC for treating autism. N-acetylcysteine (NAC) is a precursor of glutathione (GSH), which has antioxidant effects. NAC is administered for treating different psychiatric disorders.<sup>[6]</sup> Autism is a neurodevelopmental disorder. Its etiology and neurobiology are not exactly known. Oxidative stress is increased and detoxification is decreased in autism.<sup>[7]</sup>

Even as the level of oxidized GSH is increased in autism, the levels of reduced glutathione (GSH), methionine, and cysteine are decreased.<sup>[8,9]</sup> Methylation capacity is also decreased in autism.<sup>[10]</sup> Moreover, the transsulfuration abnormality is associated with autism symptoms.<sup>[11]</sup> Besides, improvement of the transmethylation/transsulfuration pathways is associated with the reduction of autism symptoms.<sup>[12]</sup> Cystine, glutamate, and glycine are required for the production of GSH. However, cystine has a rate-limiting role. A low cystine level decreases the production of GSH and may make cells prone to oxidative stress.

Oxidative stress plays a significant role in the pathophysiology of autism. Therefore, the demand for cystine is increased in autism. Hence, it is speculated that medications that increase the level of cystine may decrease some symptoms of autism.<sup>[13]</sup> Meanwhile, NAC plays a significant role in restoring GSH levels.<sup>[6]</sup>

Moreover, NAC can decrease inflammation through lowering oxidative stress.<sup>[6]</sup> This is an explanation for improvement of our patient. It is noticeable that there is a marked neuroinflammation in autism and the interventions directed to decrease neuroinflammation are suggested for treating autism.<sup>[14-16]</sup>

The effect of N-Acetylcysteine on the glutamate level is another explanation for the improvement of this patient. N-acetylcysteine decreases high glutamate levels.<sup>[17]</sup> The high levels of glutamate and the NMDA receptor is

proposed as a target for treating autism.<sup>[18]</sup> N-acetylcysteine may target the imbalance of oxidative stress in autism.<sup>[19,20,21]</sup>

It should be remembered that this was just a case without any control group. Moreover, biochemical assessment was not conducted. Therefore, these results cannot be generalized to other children with autism. However, this case report encourages conducting further long-term controlled clinical trials with a larger sample size, in order to investigate the possible role of NAC for managing autism.

## CONCLUSION

Although the anti-inflammatory and anti-oxidative roles of NAC are suggested for the reduction of symptoms, its exact mechanism is not clear. However, this case report suggests that NAC may play a potential role for treating autism.

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