The Turkish Journal of Pediatrics 1995; 37: 19-23

THE EFFECTS OF NALTREXONE IN AUSTISTIC CHILDREN: REPORT OF TWO CASES*

*Füsun Akkök PhD***

SUMMARY: Akkök F. (Department of Educational Sciences, Middle East Technical University, Ankara, Turkey). The effects of naltrexone in autistic children: report of two cases. Turk J Pediatr 1995; 37: 19-23.

This paper reports the observations associated with a brief course of administration of naltrexone (NTX) to two autistic children. One male and one female child, aged 5.3 and 4.4, respectively, completed the trial. The children were placed on NTX for two weeks for six administrations. The dose was 0.5 mg/kg. The Behavior Summarized Evaluation and Childhood Autism Scale were completed by the teacher and the social worker for baseline and post-experimentation observations. The patients' parents were asked to fill out the Parental Satisfaction Survey. Although the literature indicates that NTX is effective in some children, our observations confirm that NTX is effective in the two cases with different degrees of severity of disease. *Key words: Naltrexone, autism treatment.*

Autism is a disorder of childhood and of development. It affects all of mental development and is characterized by powerful cognitive and affective dysfunctions[1]. Repetitive stereotyped behavior patterns and a deviant development of cognitive, language, and communicative functions are observed in autistic children[2]. Deficiencies in information processing have been established in austim by means of psychophysiological studies[3,4]. Behavioral, emotional and cognitive symptoms of autism suggest that the central nervous system functioning is altered in this pervasive developmental disorder[5], and neurotransmitters appear to be involved in behavior disturbances. Recently, it has been suggested that autism is a disorder of primary socialization, Findings indicate that endogenous opioid systems of the brain are a critical part of the processes of primary socialization[6]. The idea that Naltrexone (NTX) is a medicine suitable for the treatment of autism follows from the realization that salient features of autism resemble dosing with opioid agonists, such as morphine, and observations leading to the suggestion that endogenous opioidergic systems were associated with primary socialization.

NTX as a medicine for autism has found support in the data from a number of trials, including double-blind, placebo-controlled trials. Several researchers[6-10] have found that NTX decreased motor stereotypes and increased productive

* From the Department of Educational Sciences, Middle East Technical University, Ankara.

** Associate Professor of Psychology, Department of Educational Sciences, Middle East Technical University.

This study was conducted at the Wildwood School, Albany, United States of America.

attention, social interactions and communicative intent. NTX, a drug that blocks the cells' uptake of natural opium-like substances, is a promising treatment for autistic withdrawal, self-injury and other symptoms. Several studies indicate that the dose of naltrexone needed for maximum control of self-injurious behavior tends to be high (about 1.5 mg/kg), while lower doses (about 0.5 mg/kg) appear to have a greater effect on social behaviors. Their speculation is that the different receptors of brain cells may be affected by the differing dosages[10]. However, these studies have also indicated that only some children benefitted from the treatment.

Despite the growing data base supporting the idea that NTX is a medicine for the treatment of autism, a number of critical issues need attention. In order to gain some first-hand information to address these issues, the effects of NTX when given to two children were observed as preliminary data for further comprehensive studies. The purpose of this paper was to report the observations associated with a brief course of administration of NTX to two autistic children.

Material and Methods

Subjects

Two children with autism, one male and one female, aged 5.3 and 4.4 years, attending Wildwood School completed the trial. The children had previously taken no medication. Their parents volunteered for the study.

A, a 4.4-year-old girl who lived with her parents and one sibling, had autistic symptoms. She had been attending the Wildwood School for a year at the time of the study.

B, a 5.3-year-old boy, lived with his parents and two older siblings. He had been attending this school for two years.

Design and Medication

Following the baseline observations by the researchers, the teacher and the social worker filled out the Behavior Summarized Evaluation (BSE) and the Chlidhood Autism Rating Scale (CARS). The children were placed on NTX for two weeks for six administrations. The dose was 0.5 mg/kg. Medication was given by the school nurse in a single morning dose at 9 A.M. The parents, teacher, social worker and researchers were blind. The parents were asked to make detailed observations, keep a diary and record their interactions with their child during the study. Parents have the most intense and close interactions with their children, and the home environment is the child's most natural environment. Therefore, observations by the parents are an important aspect of evaluating the effects of NTX. Both children were observed at school and at home by parents at two different time. One was two hours after the administration of medication and the other was 24 hours later. At the end of

the two week period, the teacher and the social worker completed the BSE and CARS. Both mothers and fathers field out a Parental Satisfaction Survey (PASS). Also, the researchers had a meeting with the parents, teacher and social worker to discuss their observations and evaluations in detail. No biochemical examinations were carried out during or after the experiment. Parents chose to use NTX therapy voluntarily through their personal physicians.

Results

The effects of NTX therapy on two cases are discussed below.

Case 1

A grew in the areas of language development and social interaction. She was previously ritualistic and hyperactive. With the NTX treatment, a showed improvement in her behaviors. According to the teacher's and social worker's observations, A started to have more appropriate play, become more aware of peers, and seek out people more frequently. Her verbalization increased. However, she continued to have temper tantrums, but they were shorter in duration.

According to her parents' observations and daily records, she began appropriate and imaginative play, specifically with her dollhouse, and was attending more to the stimuli around herself (i.e., looking outside, looking at hands a lot, looking at herself in the mirror, responding to the doorbell much more). Her curiosity increased. She became more cooperative and responsive to her parents' instructions. Her bed-time behavior improved significantly. Her mother observed that she was behaving and playing more happily. She had subtle improvements in her behavior. Her verbalization and vocalization increased, she started to use a different tone of voice when playing with dolls and repeated many words. Her imitation increased. The mother was delighted at A's spontaneous kisses. A tolerated a haircut, and was quiet and cooperative. She continued to have temper tantrums, but they were shorter in duration. There was no change in her appetite, thirst, anger or toilet training.

Case 2

With NTX treatment, B manifested self-stimulative behavior, hyperactivity and unrealistic fears. According to the educators' observations, his clinging increased dramatically. It became very hard to pull him off. His appetite decreased. He developed an overall general anxiety. His hyperactivity decreased and he had short periods of attending a toy.

His parents' observations were controversial. According to his mother's observations and PASS, he showed substantial improvement in smiling and eye contact. He also showed clear impovement in his activity level (a decrease in hyperactivity), curiosity, interest and attempts to communicate a number of word

sounds. He was rebelling more and showing more emotion. There was marginal change in his stereotyped behavior (teeth grinding), number of "good days" and his play and imitative behavior. However, there was no change in his play behavior and life habits, and he was irritable. His appetite decreased and he started to ask for sweet things. His father observed marginal improvement in his stereotyped behavior and activity level. However, he observed no change in expressions of motivation, social responsiveness, communicative and cognitive abilities and life habits.

The average CARS and BSE scores of the educators indicated no improvement in either child's behavior. PASS data are summarized in Fig. 1.

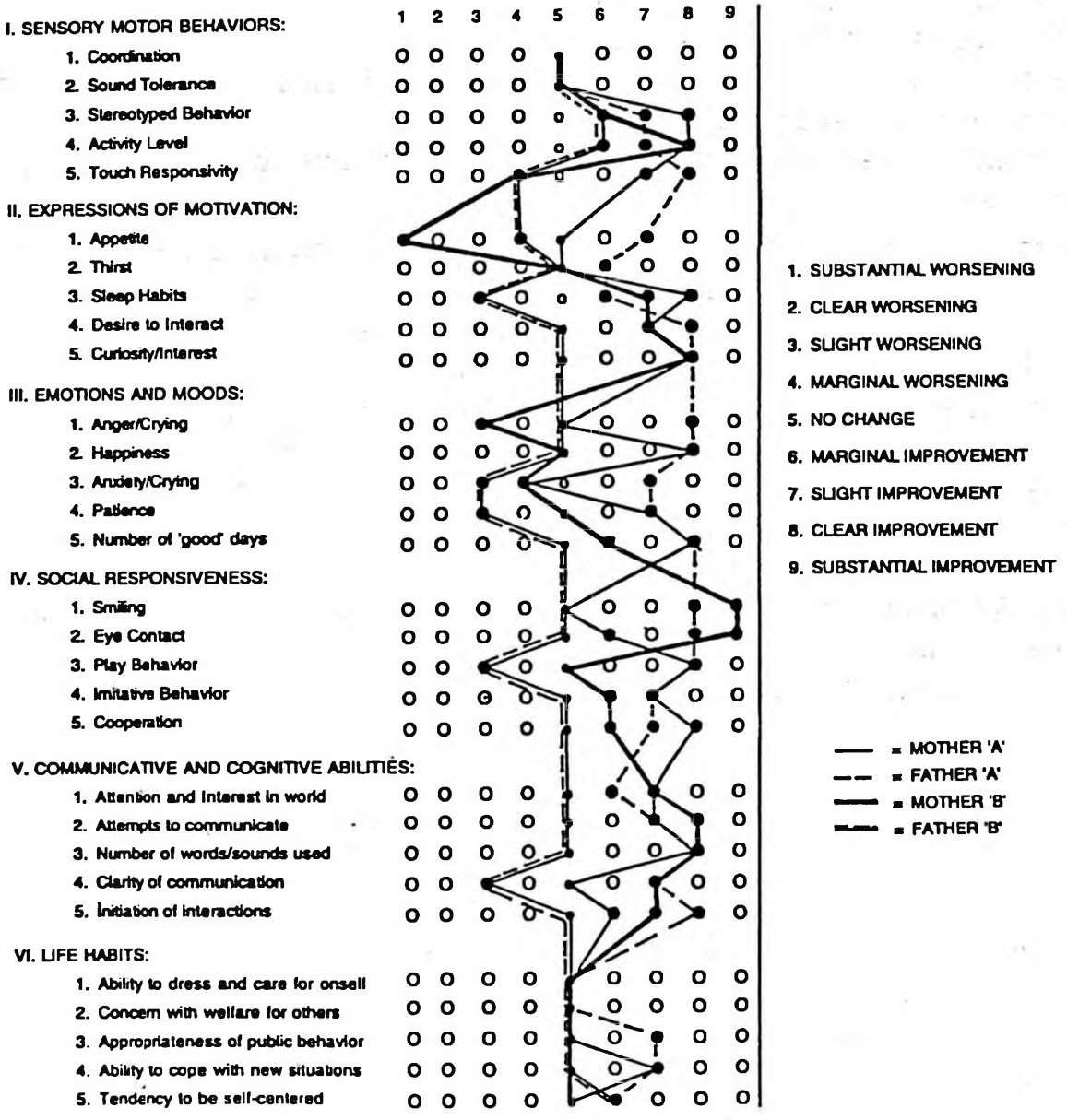

Fig. 1: Parental satisfaction survey (PASS) data.

Discussion

Our observations confirm some of the conclusions emerging from the limited available literature. The two children responded well to NTX, a potent, opiate antagonist, which has appeared to be a promising agent in several studies. Under NTX, autistic children appear less socially distant and more amenable to social interaction. They tend to engage in more creative object play, parallel play and social interactive play. However, NTX is effective among some children. Biochemical and neurometric predictors seem to differ in responders and nonresponders. In one study[10] it was detected that physiological changes accompany the behavioral changes in NTX-treated subjects. Levels of peptides that were abnormally elevated before treatment began are normalized by NTX administration. Further research should address these parameters to identify who will respond and who will not. Furthermore, the scales designed to diagnose autism, in contrast to other developmental disorders, do not appear to be sensitive to shifts in severity of the characteristic symptoms. To more fully assess NTX's effects, it seems necessary to devise new procedures that objectify professionals' and parents' judgments.

Further studies should address the effects of different dosages and the biochemical examinations to screen the responders and nonresponders to contribute to the effective use of NTX.

REFERENCES

1. Frith U. Autism. Explaining the Enigma. Worchester: Billing and Sons Ltd; 1989: 1-5.
2. Howlin P. An overview of social behavior in autism. In: Schopler E, Mesibova GB (eds). Social Behavior in Autism. New York: Plenum Press; 1991: 103-131.
3. Courchesne E, Lincoln AJ, Yeung-Courchesne R, Elmasian R, Grillon C. Pathophysiologic findings in nonretarded autism and receptive developmental language disorder. J Autism Dev Disord 1989; 19: 1-7.
4. van Engeland H, Roelofs JW, Verbaten MN, Slangen JL. Abnormal electrodermal reactivity to novel visual stimuli in autistic children. Psychiatry Res 1991; 38: 27-38.
5. Ornitz EM. Should autistic children be treated with haloperidol? Am J Psychiatry 1985; 142: 883-884.
6. Pankseep J, Lensing P, Leboyer M, Bouvard MP. Naltrexone and other potential new pharmacological treatments of autism. Brain Dysfunct (in press).
7. Herman BH. Effects of opioid receptor antagonists in the treatment of autism and self-injurious behavior. In: Ratey JJ (ed). Mental Retardation: Developing Pharmacotherapies. Washington, D.C: American Psychiatric Press; 1991: 107-131.
8. Leboyer M, Bouvard MP, Launay JM, et al. Brief report: a double-blind study of naltrexone in infantite autism. J Autism Dev Disord 1992; 22: 309-319.
9. Compbell M, Enderson LT, Small AM, Locascio JJ, Lynch NS, Choroco MC. Naltrexone in autistic children: a double-blind and placebo-controlled study. Psychopharmacol Bull 1990; 26: 130-134.
10. Panksepp J, Lensing P. Brief report: a synopsis of an open-trial of naltrexone treatment of autism brief report: a synopsis of an open-trial with four children. J Autism Dev Disord 1991; 21: 243-249.