Autismo pode se beneficiar com naltrexone em baixas doses

Treatment of a serious autistic disorder in a child with Naltrexone in an oral suspension form
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CLINICAL BACKGROUND: Autism is a developmental disorder that is usually diagnosed in early childhood. According to ICD-10 criteria, autism can be characterized by delays in language skills, by impaired social interaction, verbal or non-verbal communication and by repetitive, stereotyped or severely restricted activities and interests. The causes of autism are not yet elucidated, but both genetics and environment seem to play a role in 10 to 25% of autism cases. Several biochemical abnormalities, such as impairment of serotoninergic, catecholergic, dopaminergic, and opioid systems have been reported. Autism therapies are designed to treat symptoms, and medication can be associated with psychoeducational and environmental interventions. Generally, the medications that are currently used are not intended for autism, and must be used with caution and selected according to the type and intensity of symptoms. The most common medication consists of psychotropic therapies by administration of dopaminergic and/or serotoninergic receptor antagonists (haloperidol, risperidone, clonipramine). Several drugs, such as anxiolytics (buspirone), mood stabilisers (lithium, sodium valproate), vitamins (vitamins B6, B12) or opioid antagonists (naltrexone) can be prescribed, in second intention, in cases of severe behavioural disorders. The prescription of opioid antagonists is based on the possible implication of an opioid system disorder observed in some cases. Nevertheless, several clinical studies reveal its variable effectiveness. Naltrexone is a competitive antagonist of opioid receptors OPRM1, OPRD1 and OPRK1. In France, this drug is prescribed for treating opioid and alcohol dependence. Moreover, several studies describe naltrexone as a possible treatment of autistic children in cases of developmental disorder and hyperactivity.

CLINICAL CASE: In the Child and Adolescent Psychopathology Department of Sainte-Anne’s Hospital, autistic children benefit from a multidisciplinary treatment program that sometimes includes the administration of psychotropic medication. One of these children presented with a severe autistic disorder according to the Childhood Autism Rating Scale (CARS). Considering ICD-10 criteria, he benefited from a multidisciplinary program, associating cognitive psychotherapy, psychomotor rehabilitation, speech therapy and educational intervention. However, persistent sleep disorder and motor instability led to successive prescriptions of several different psychotropic drugs. Initial treatment by thioridazine (10mg per day) followed by propenaizinc (2.5mg per day) improved sleep, but was not efficient in reducing self-mutilating behaviour. A new treatment by risperdone (from 0.5mg to 1.5mg per day) was therefore chosen; however it lost its efficacy after five months. Finally, an anxiolytic (cyamemazine) and a thymoregulator (sodium valproate) were successively tried without yielding any clinical improvement. Owing to the persistence of communication difficulties, major instability, self-mutilating behaviour and heteroaggressiveness, treatment with naltrexone was subsequently chosen with parental consent. In France, naltrexone hydrochloride is only available in tablet form (Nalorex 50mg and Revia 50mg), which is not adapted to children at the efficient dose. Consequently, an suspension form marketed in Spain (Antaxone 50mg) was imported, having obtained the Assaps’ (the French drug administration) authorisation for its temporary use. The Conners and Nisonger scales were used as outcome measures of behavioural symptom change. The Conners scale is used to assess attention deficit and hyperactivity, whereas the Nisonger scale analyses social skills and behaviour disorders in children and adolescents with mental retardation. The onset of treatment, at a dose of 1mg/kg/day, led to a transitory increase in negative behaviour. However, a dose of 0.75mg/kg per day subsequently led to significant improvements, as shown by outcome measurements. Self-mutilating behaviour disappeared completely. Certain side effects were observed, namely transitory sedation at the beginning of treatment and moderate constipation. CONCLUSION: This clinical case confirms that treatment of a serious autistic disorder in children using Naltrexone in oral suspension form is a potentially interesting therapeutic alternative for treating behavioural symptoms resistant to classical drug therapy.

Brief report: six months continuation treatment in naltrexone-responsive children with autism: an open-label case-control design.
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PMD: 10382138

Anxiolytics, adrenergic agents, and naltrexone.
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OBJECTIVE: To review extant data on the efficacy and safety of anxiolytic medications (benzodiazepines, buspirone, and other serotonin 1A agonists), adrenergic agents (beta-blockers and alpha 2-adrenergic agonists clonidine and guanfacine), and the opiate antagonist naltrexone that have been used to treat various psychopathologies in children and adolescents. To identify critical gaps in our current knowledge about these agents and needs for further research. METHOD: All available controlled trials of these medications in children and adolescents published in English through 1997 were reviewed. In addition, selected uncontrolled studies are included. RESULTS: The major finding, that there are virtually no controlled data that support the efficacy of most of these drugs for the treatment of psychiatric disorders in children and adolescents, is both surprising and unfortunate. For some drugs, e.g., buspirone and guanfacine, this is because no controlled studies have been carried out in children and/or adolescents. For other drugs, e.g., clonidine and naltrexone, most of the placebo-controlled studies have failed to demonstrate efficacy. CONCLUSIONS: The strongest recommendations for controlled studies of safety and efficacy in children and adolescents can be given for the following drugs: benzodiazepines for acute anxiety; buspirone and guanfacine (and newer serotonin 1A agonists as they become available) for anxiety and depression; beta-blockers for aggressive dyscontrol; guanfacine for attention-deficit/hyperactivity disorder; and naltrexone for hyperactivity, inattention, and aggression in autistic disorder.
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Naltrexone open trial with a 5-year-old-boy. A social rebound reaction.
The neurobiological rationale for an opiate antagonist pharmacotherapy of autism is presented. Naltrexone efficacy in decreasing autistic behaviour and in increasing social-affiliative behaviour was explored in a 5-year-old autistic boy. Naltrexone (0.5 mg/kg 3 times per week) was effective in immediately decreasing gross motor activity and stereotyped behaviour and caused a delayed increase of crying, smiling and rough-and-tumble play. This single case presents preliminary evidence that a therapeutically valuable rebound reaction is possible and that the human opioid system modulates social-affective processes. The possibility of psychological factors being instrumental in achieving this effect is discussed as being suitable for future clinical trials.

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Naltrexone in young autistic children: replication study and learning measures.
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OBJECTIVE: This study expanded upon previous work on naltrexone efficacy and safety in young autistic children and assessed performance on learning measures. METHOD: Eleven children with autistic disorder, aged 3.0 to 8.3 years, were studied in home, school, and outpatient laboratory, bringing to 24 the combined study sample. Naltrexone, 1.0 mg/kg, was given daily in a randomized, double-blind, crossover design. Dependent measures were parent and teacher Clinical Global Impressions (CGI) and Naltrexone Side Effects Rating Scale (SE), Conners Parent Impulsivity/Hyperactivity Factor, Teacher Hyperactivity Factor, laboratory CGI, and analysis of videotaped behavior. Learning measures were the Early Intervention Developmental Profile-Language and paired-associate learning. RESULTS: Comparisons between naltrexone and baseline, but not naltrexone and placebo, on parent and teacher ratings showed statistical significance. Three of 11 subjects improved in two or more settings. Side effects were mild. Administering naltrexone was a challenge. The combined study sample showed improvement on all parent measures and on Teacher CGI and SE-Restlessness compared with baseline and placebo. Eleven of the 24 children improved in two or more settings. Scores on learning measures did not change across conditions. CONCLUSIONS: Naltrexone was associated with modest improvement of behavior in 11 of 24 children, but learning did not improve.

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