Clinical note

Inés García-Martín[1]
Eva Mª Miranda-Vicario[1]
César A. Soutullo[1]

Duloxetine in the treatment of adolescents with somatoform disorders: a report of two cases

[1]Departamento de Psiquiatría y Psicología Médica
Unidad de Psiquiatría Infantil y Adolescente
Clínica Universidad de Navarra

Background. Our goal was to evaluate the effectiveness, safety and tolerability of duloxetine in the treatment of children and adolescents with somatoform disorder.

Results. We describe two cases, those of an 11-year old girl and a 17-year old boy, evaluated in our Department after being studied by a Pediatrician and Neuropediatrician due to complex physical symptoms. The evaluations to rule out medical causes were normal. We diagnosed somatoform disorder. The pharmacological treatments with antidepressants, benzodiazepines, stimulants and mood stabilizers only produced brief and partial improvement. After switching the treatment to duloxetine (30 and 60 mg/day, respectively) both patients experienced a gradual improvement that was maintained at 7 and 14 months.

Conclusion. Duloxetine may be effective and well tolerated in the treatment of adolescents with somatoform disorder. Controlled trials are need.

Key Words: Duloxetine, Childhood, Adolescence, Somatoform disorder

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Duloxetina en el tratamiento de adolescentes con trastornos somatomorfos: un informe de dos casos

Introducción. Nuestro objetivo fue evaluar la eficacia, seguridad y tolerabilidad de duloxetina en el tratamiento de adolescentes con trastorno somatomorfo.

Resultado. Describimos dos casos (chica 11 años y varón 17 años) evaluados en nuestro Departamento después de ser valorados por Pediatra y Neuropediatría por síntomas físicos complejos. Las evaluaciones para descartar causas médicas fueron normales. Realizamos un diagnóstico de trastorno somatomorfo. El tratamiento farmacológico con antidepresivos, benzodiacepinas, estimulantes y estabilizadores del humor sólo produjo una mejoría breve y parcial. Tras cambiar el tratamiento a duloxetina (30 y 60 mg/día respectivamente) los pacientes experimentaron una mejoría gradual y se mantuvo 7 y 14 meses.

Conclusión. La duloxetina puede ser eficaz y bien tolerada en adolescentes con trastorno somatomorfo. Son necesarios ensayos controlados.

Palabras clave: Duloxetina, Infancia, Adolescencia, Trastorno Somatomorfo

BACKGROUNDS

Somatomorphic disorders are characterized by multiple physical symptoms (gastrointestinal, sexual, pseudoneurological, painful) [1, 2] as well as recurrent ones that cannot be explained by a medical problem or by the effect of a substance. They are not intentionally produced or feigned and they are believed to be associated to psychological factors. These symptoms usually lead to multiple medical visits and complementary studies. In children, these symptoms cause familial, or social deterioration or low scholastic performance.[3, 4]

These disorders generally begin prior to 30 years of age, with greater prevalence in adolescence (10-25%) and in girls.[5] Some authors have suggested that the selective serotonin reuptake inhibitors (SSRIs) in children and adolescents with somatomorphic disorder may be effective.[3, 5] Citalopram has been used in pediatric patients with recurrent abdominal pain with comorbid internalizing disorders.[6]

Correspondence:
César A. Soutullo
Departamento de Psiquiatría y Psicología Médica,
Clínica Universidad de Navarra.
Apartado 4209
31008-Pamplona, SPAIN
Fax: 34 (948) 29 65 00.
Tel.: 34 (948) 29 64 35
E-mail: csoutullo@unav.es

In a review, Stewart indicated that due to a dual action mechanism, duloxetine and venlafaxine may be useful in the treatment of both physical and depressive symptoms.[7] In several controlled trials, it has been demonstrated that duloxetine is safe and effective for adults with depression and painful physical symptoms[8-12] and in the symptoms of fibromyalgia in patients with or without major depressive disorder, especially in women.[13]

There are little data available on the use of duloxetine in children and adolescents.[14] We have only found two articles: one on the use of duloxetine in one boy with depression, pain and dissociative symptoms[15] and another on the treatment of chronic pain in children and comorbid major depression,[16] in which duloxetine was effective and well tolerated. We describe two cases of adolescents with somatomorphic disorder previously treated with other pharmacological agents who demonstrated significant clinical improvement with the treatment with duloxetine.

CLINICAL CASES

Patient 1

The case of an eight-year three month old girl who was operated on for gastroesophageal reflux with a Nissen fundoplication is presented. Since then, intermittent epigastric pain has persisted. It was accompanied by a daily sensation of lack of air, sweating, and skin paleness that spontaneously stopped. She complained of headache between the episodes. These episodes did not appear during sleep. She missed many classes due to the frequent appointments with the physicians.

In her medical history, she also had appendicitis, chronic constipation (with several admissions due to pseudo-obstruction), traumatic epiphysiolysis and tenosynovitis in her right leg (with chronic pain), eosinophilic esophagitis and a wound on her right hand that required minor surgery (complicated by chronic pain of the wrist). Medical evaluations were normal (laboratory, gastroscopy with biopsy, measurement of pH, ECG and EEG). Treatment with omeprazole, ranitidine, sucralfate and domperidone did not help.

She was first evaluated in our units in January 2005 (11 years) after having been referred by her pediatrician after being diagnosed of somatomorphic disorder. Treatment with sertralin reduced the frequency of the episodes from one time/day to one time/month and its intensity also decreased. However, complete remission was not obtained. In March 2007, she suffered daily episodes of pain and was admitted in June 2007 (2.5 years after the initial evaluation). Treatment was initiated with duloxetine 30 mg/day and clonazepam 1 mg/day. The patient showed gradual improvement, which was evident at 10 days of the initiation of treatment. She was discharged 14 days later and followed up as an outpatient. In visits to the outpatient clinic three and five months after discharge, she remains stable. She is capable of going to school and is not concerned by her pain. (Figure 1).

Patient 2

The case of a 10-year old boy who shortly after the death of his maternal grandmother presented weakness in his hand and hip pain is reported. The different tests to rule out medical causes were normal (laboratory, bone scintigraphy and neuromuscular studies).

In October 2002 (13 years), he was referred by Neuropediatrics for evaluation by Psychiatry. His symptoms had worsened in the previous month, after the death of this paternal grandmother. He had daily episodes of general weakness with frequent falls (without losing consciousness), muscular pseudoparalysis, spinal pain and headaches. He was diagnosed of Somatization Disorder and treatment was initiated with sertraline up to 150 mg/day and clonazepam up to 3.5 mg/day and psychotherapy with good evolution.

However, in December 2002, he presented dissociation and depersonalization episodes. In order to increase the antidepressant effect, 30 mg/day of methylphenidate was added, with improvement of his physical symptoms. However, he became irritable, so that the methylphenidate was discontinued and up to 200 mg/day of quetiapine was added. His irritability and dissociative episodes improved, but he continued with syncopes that slowly improved and he was asymptomatic from February 2003 to January 2005.

During his exams in 2005 (January and March 2005), his began to suffer physical symptoms again (he could not move his legs) in spite of the pharmacological adjustments. In July 2005, he became irritable again and up to 100 mg/day of lamotrigine was added. The patient remained stable until October 2005, when his somatic symptoms deteriorated and 4 mg/day of reboxetine was initiated. Anxiety and psychosomatic symptoms persisted and up to 20 mg/day of aripiprazole was begun. His somatic symptoms improved, but with mild sedation that limited his academic performance. The doses of lamotrigine, aripiprazole and sertraline were slowly reduced, until their interruption in January 2006. During this period, he had occasional irritability, so that 50 mg/ of quetiapine was added and up to 50 mg/day of methylphenidate for sedation that had to be suspended due to insomnia and euphoria. In May 2006, lamotrigine was switched to valproate. With this medication, the patient remained stable until November 2006, when his work as administrative assistant ended and his somatic symptoms returned.

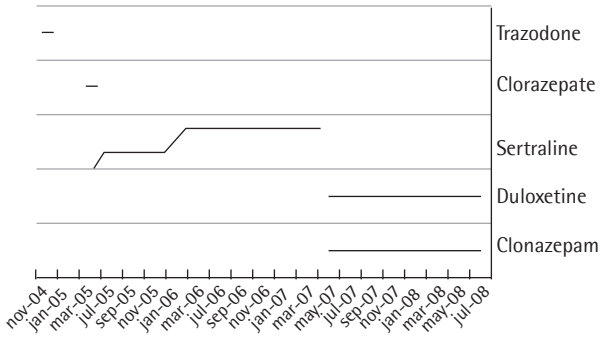

Figure 1 Medications used in Case 1 (November 2004 - August 2008)

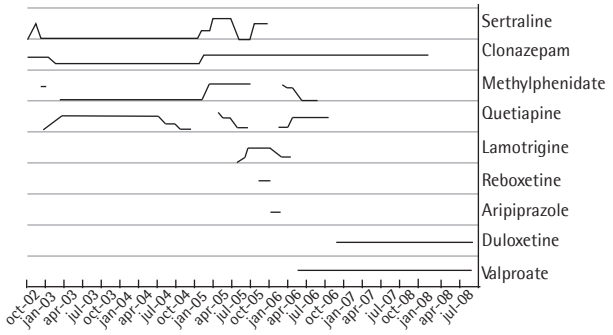

Figure 2 Medications used in Case 2 (October 2002 - July 2008)

At this point, we added treatment with duloxetine of up to 60 mg/day to his treatment with valproate 1250 mg/day and quetiapine 100 mg/day. He showed marked response in three weeks that was maintained until July 2008 (14 months). (Figure 2).

DISCUSSION

There is no clear biological explanation for the pain disorder. The neurobiological components of the pain imply complex interactions between ascending and descending pain pathways in the central and peripheral nervous system. Endorphins and biogenic amines, such as serotonin and norepinephrine, have modulation functions in the descending analgesic pathways. Antidepressants have been useful in the production of analgesias because they increase the concentration of biogenic amines in this descending pathways.[12, 17] In these 2 cases, duloxetine was initiated because of its potential beneficial dual action effect in the serotoninergic and norepinephrinergic pathway. Within 3 weeks after beginning treatment with duloxetine, the patients showed marked improvement and response was maintained over time.

In these cases, we can make the following two observations:

The dual action blockage of the serotoninergic and norepinephrinergic system with duloxetine has been found to be more useful in the treatment of pediatric chronic treatment and comorbid major depression[8] than blockage of serotonin alone. These two cases support this hypothesis.

The patients tolerated duloxetine well, similarly to that reported in adults, where duloxetine was, in general, safe and well tolerated in the clinical trials.[8]

This preliminary observation has several methodological limitations. Principally, these are non-blinded observations, without a control group or use of placebo. These findings should therefore be considered provisional, while waiting for them to be supported by controlled trials. However, this retrospective report suggests that duloxetine may be effective and well tolerated in the treatment of adolescents with somatomorphic disorders.

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