cally ill wife was having on his son, who was born in 1984.

The patient went into residential care in 1996. The patient's husband visited two or three times every week and he always took his wife out for a trip. These trips were difficult because of the patient's refusal to be strapped into the car or her wheelchair, which sometimes resulted in falls caused by violent choreic movements when he was unable to physically hold her in the chair because he was using his hands for some other purpose.

In 2001, he began to give his wife cannabis to smoke when he took her out on these regular trips. When he returned his wife to the nursing home after these visits the staff were aware of a significant difference in the patient. The cannabis appeared to improve her mood and she was calmer and more relaxed. Prior to the introduction of cannabis she was extremely impatient and would get angry if required to wait even a few minutes for a cigarette. After taking cannabis, she was able to wait a while without screaming and throwing things. The patient also willingly accepted the use of a car seat belt and wheelchair harness.

In December 2001, the local general practitioner prescribed a regimen of nabilone, a synthetic 9-keto cannabinoid, which the patient began taking, 1mg each day. The husband and the nursing home staff both reported improvements in behavior and reduction of chorea coinciding with the introduction of cannabis and maintained by daily taking nabilone.

Comment

This report has many limitations. It is a single case report and no measurements were taken at the time of the introduction of cannabis and nabilone. The information was obtained by interviewing the husband and staff from the care home in 2005. The symptoms of Huntington's disease do change over time and the movements are different in the later stages of the disease. However both the husband and the staff are sure that the introduction of cannabis was beneficial and greatly improved the patient's quality of life in her last years. There is need for further trials to establish the therapeutic use of cannabinoids in the symptomatic treatment of Huntington's disease.

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Essential Blepharospasm Responding to Haloperidol

SIR: Blepharospasm is a disorder of adulthood that is more common in women. It presents as a sudden involuntary bilateral eye closure that is often exacerbated by air pollution, wind, exposure to bright light, movement, and stress. However, to date it is not possible to correlate it with any psychopathology. If it presents as an isolated blepharospasm in adults, it is better termed as essential blepharospasm. It must be differentiated from Meige's syndrome which includes oromandibular dystonia along with blepharospasm.[1]

Below we describe a case of essential blepharospam that responded to low doses of haloperidol but not to other drugs.

Case Report

A 32-year-old married man presented with bilateral blepharospasms that lasted for 1 to 2 minutes. The spasms were provoked by light, embarrassment, and fatigue. The spasms would disappear in sleep. These complaints were of 5-month duration.

There was no history of any chronic physical illness including neurological illnesses such as parkinsonism, Wilson's disease, epilepsy, stroke, nor a history of ocular pathology (e.g., blepharitis, conjunctivitis or iritis), any psychiatric

disorder, or intake of any drug in recent past. Family history was unremarkable.

General physical examination, laboratory investigations, including venereal disease research, EEG, computed tomography (CT) scan, and ocular examination were normal. Mental status examination was also normal with the exception of preoccupation with symptoms. He was started on a regimen of trihexyphenidyl (10 to 12mg daily in divided doses) and 2mg of clonazepam (at night) for about 2 weeks. He did not show improvement and the distress due to the problem persisted. This therapy was gradually withdrawn over the next 2 weeks. He was then given trials of following treatments: tetrabenazine (50mg/day) for 3 weeks, then risperidone (6mg/day) for 2 weeks, then olanzapine (10mg/day) for 2 weeks, followed by a trial with the tablet quetiapine (150 to 200mg/day) for 3 weeks without any improvement. Since the patient was becoming more and more distressed due to symptoms and demanding the discontinuation of therapy, frequent changes became necessary. During all of these therapies, we used the method of tapering one medication while another was simultaneously initiating another drug method. Lastly, the patient was started on the tablet haloperidol, 1.5mg, twice daily for 1 week, and the dose was escalated up to 7.5mg daily in the third week. Improvement started after 4 days and he reported a marked decrease in frequency of spasms after 2 weeks. The spasms were totally controlled after about 6 weeks.

Comment

Two issues are important that need to be focused on in this discussion. The first issue addresses the underlying pathology of essential blepharospasm. It has been reported prominently in the elder age group and as more common in females.[1] Though it does not qualify the diagnosis of Meige syndrome, Domzal et al.[2] reported that blepharospam may be a syndrome of different origins and can be only a phase of Meige's syndrome.

A number of pathologies has been ascribed to this disorder, including upper brainstem lesion,[3] ganglioglioma of the lateral ventricle,[4] thalamic hypodensity, and caudate nucleus lesion.[2] Other causes can be peripheral facial palsy, herpes zoster infection of trigeminal nerve, brain infarcts, neuroleptics, Shy-Drager syndrome, progressive supranuclear palsy, and kernicterus. However, there are a lot of cases that are primary or idiopathic.[5]

In conclusion, this data indicates basal ganglia-thalamic involvement in these cases. According to the model proposed by Vitek,[6] dystonia occurs with the altered activity in the globus pallidus externa and internal globus pallidus through indirect and direct pathways. Increased activity in the internal globus pallidus leads to thalamic disinhibition and lowered globus pallidus externa neuronal activity causes enhanced activity in the subthalamic nucleus that further activates internal globus pallidus. Further evidence for this pathology has been provided by functional imaging in these cases that have shown the activation of subregion of putamen[7] and decrease in D2 binding in the putamen with [fluorine-18] spiperone.[8] Decreased D2-like binding in the striatum leads to decreased dopaminergic inhibition and increased activity in indirect pathways. Augmented subthalamic nucleus activity could also occur through the increased activity of cortico-subthalamic excitatory neurons. According to present model, the internal globus pallidus receives inhibitory stimuli from the striatum and excitatory impulses from the subthalamic nucleus simultaneously. It leads to reduction of mean discharge rate, alteration in receptive field properties, and changes in pattern of neuronal activity in the internal globus pallidus that is consistent with the development of dystonia.[6]

This model also explains why L-dopa and antipsychotics are effective in treatment of some dystonic conditions along with their dystonia inducing property. It is known that D2 receptors in the straitum are inhibitory in nature; that is, their activation leads to hyperpolarization of striatopallidal neurons that causes decreased GABA in globus pallidus externa that, in turn, activates the internal globus pallidus directly and inhibits the subthalamic nucleus. In this situation the internal globus pallidus gets excitatory impulses from globus pallidus externa directly with the reduced stimulation from the subthalamic nucleus. This will lead to increased GABA release in thalamus thus inhibiting it. This may be one mechanism causing dystonia to respond to L-dopa.

Based on the same principle, neuroleptics should increase the GABA in globus pallidus externa that leads to the disinhibition of the subthalamic nucleus as well as reduced excitation of the internal globus pallidus directly. In this situation, the internal globus pallidus will get excitatory impulses from the subthalamic nucleus with reduced stimulation from globus pallidus externa. This should also increase GABA in the thalamus, and relieve dystonia. However, they are known to induce dystonia.[9,10]

But the above model is simplistic that takes only the rate of firing of pallidal neurons in account. To explain it further we need to know the other properties of neurons that

are responsible for inducing dystonia as explained.

There are many reports that show that blepharoclonus/Meige syndrome responds to clonazepam,[11] clozapine,[12] trihexyphenidyl, perphenazine, fluphenazine[10] haloperidol, L-dopa with deprenyl, botulinum toxin A,[13] quetiapine.[14] This patient responded to haloperidol but did not improve with anticholinergics and atypical neuroleptics. This could be affected by a different receptor profile of typical and atypical neuroleptics. Conventional antipsychotics, like haloperidol, bind to D2 more efficiently than atypical drugs and 5HT2A binding of atypical drugs reverses the D2 blockade in nigrostriatal pathway. In addition, GABA concentration in the pallidum is also regulated by direct effect of D2 binding drugs in the pallidum where they can either decrease[15] or increase extracellular GABA,[16] thereby influencing thalamic activity.

In conclusion, to date we are not able to explain the pathophysiology of dystonia completely and further research is required to understand the differential effects of drugs.

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Using Pramipexole in Neuropsychiatry: A Cautionary Note

SIR: Recent reports have recommended using the D2/D3 agonist pramipexole as a treatment for various psychiatric disorders such as depression in Parkinson's disease, treatment-resistant depression and bipolar depression.[1–3] These reports have not adequately emphasized the psychiatric toxicity of pramipexole. While hallucinations have been described as side effects of pramipexole,[4] there are few reports of other psychotic symptoms such as delusions. A recent case report described delusional jealousy arising in the context of mania.[5] We report a case of acute nonaffective psychosis with delusional jealousy developing on pramipexole treatment of Holmes' tremor, remitting on stopping the drug, relapsing on rechallenge with a lower dose and gradually remitting with complete stoppage.

Case Report

"Mrs. A," a 37-year old Caucasian woman, had a subarachnoid hemorrhage 7 years ago from a basilar tip aneurysm following which she was left with a spastic hemiparesis in the right limbs, partial third nerve palsy, mild dysarthria and right-sided Holmes' tremor. She had been taking daily doses of frusemide, 20mg, mirtazapine, 45mg, tizanidine, 12mg, and amantadine, 300mg, for several years. Three months prior to the current admission, a daily regimen of pramipexole, 2.1mg, was added and the dose increased to 2.8mg daily after 2 months. Three to 4 weeks after the increase in dose, she started hearing a buzzing sound that she associated with a mobile phone and muffled sounds which she identified as the