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Case Report

Dopaminergic drug Combination for Stomatodynia Eliminates Tardive Dyskinesia Resulting from Higher Dosages of Dextroamphetamine

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Abstract

There are many inflammatory conditions under the umbrella of the common, but relatively unknown, pathological condition known as the increased cellular permeability syndrome. According to the tenets of the syndrome, many chronic inflammatory disorders are related to the inability of certain tissues to preclude infiltration of unwanted irritants, which, in turn, causes inflammation and subsequently pain. The exact syndrome that manifests is related to the organ system involved with the increased cellular permeability defect. Though many of these conditions are treated with anti-inflammatory drugs including immunosuppressives (that leads to an increased risk of cancer and serious infection), despite different clinical presentations, all the various manifestations of this condition respond to dopaminergic drugs related to the effect of dopamine diminishing cellular permeability. One rare manifestation of this syndrome is stomatodynia. Two cases have been described whose condition responded to dopaminergic drugs (one patient dextroamphetamine and the other cabergoline). The case responding to dextroamphetamine had not only improvement in her stomatodynia but her frequent severe headaches. However, for years she had the rare complication from the dextroamphetamine of mild orofacial tardive dyskinesia. The tardive dyskinesia was abated by decreasing the dosage of dextroamphetamine but adding cabergoline which still ameliorated the marked discomfort of stomatodynia and headaches. Thus, the combination of these two dopaminergic drugs may help to treat some of the clinical manifestation of the increased cellular permeability syndrome without causing a side effect related to these drugs when used in higher dosages.

Keywords: burning mouth syndrome; stomatodynia; dopaminergic drugs; increased cellular permeability syndrome; headaches; tardive dyskinesia

Introduction

Increased cellular permeability with infiltration of unwanted irritants into various tissues may be the cause of a large variety of different disorders, especially, but not limited to pain related to the inflammation caused by the irritants [1-3]. Despite different organ systems, they all respond very well to drugs that release more dopamine from sympathetic nerve fibers or drugs that directly stimulate dopamine receptors [1-3]. Dopamine functions to decrease cellular permeability [3].

The two main dopaminergic drugs used to increase dopamine release from sympathetic nerve fibers with generally very good success are dextroamphetamine or cabergoline [2,3]. There has been much more experience with the use of dextroamphetamine than cabergoline or bromocriptine in treating these disorders as evidenced by published case reports.

One type of uncommon pain syndrome that has responded well to the use of dextroamphetamine has been stomatodynia, otherwise known as the burning mouth syndrome, where despite the pain, there are no identifiable lesions [4]. The previous case that we reported had unexplained stomatodynia involving especially her tongue, lips, and palate that was severe and had been present for 8 years [4]. She had complete resolution of the stomatodynia following treatment with dextroamphetamine, and it also totally eradicated her almost daily complaint of headaches. Her only side effect was mild tardive dyskinesia which she accepted and as she stated was a "good trade." She required 18.8mg dextroamphetamine

sulfate am and noon for complete remission of the stomatodynia. The complete remission lasted 15 years. On occasion, related to a shortage of amphetamines, she would temporarily have a respite in therapy. The stomatodynia and headaches would return immediately but would resolve again with resuming the medication. She never had any withdraw symptoms with sudden cessation. In the description of her case once again the present report will present a successful option that was tried to keep her stomatodynia and headaches ablated while also eradicating the tardive dyskinesia (TD) We were reasonably sure that the TD was a side effect of the dextroamphetamine sulfate since it would disappear during the times she was off the medication for short intervals [4].

Thus, the case reported here discusses a successful treatment option that allowed complete remission of the stomatodynia and headaches but without the mild tardive dyskinesia and that was reducing the dosage of dextroamphetamine but adding cabergoline.

Case Report

The patient at age 50 during her consult for renewal of medication (which was required every 3 months because dextroamphetamine is considered a schedule II drug) stated that her tardive dyskinesia was stable and had not progressed to any of the more serious forms of tardive dystonia syndrome. (This mild form of TD is known as the orofacial dyskinesia phenotype).

However, she had heard about the possibility of medical therapy to add to her dextroamphetamine therapy to help TD.

We reviewed the literature and advised her that though there are various treatments for TD, they are generally reserved for more severe forms of TD and not only have not been very successful, but they also have side effects. The subject has been well reviewed by Testini and Factor [5].

As an alternate suggestion, we advised her that we have also seen success in a case with severe stomatodynia with the dopaminergic drug cabergoline [4]. We advised her that she may obtain a similar benefit with the reduction of dextroamphetamine to 9.4mg twice daily and try cabergoline 2.5g twice per week. That reduction has provided her with the same degree of relief as from the higher dosage of dextroamphetamines. If she noticed the return of symptoms in a much milder form, she was advised to increase the dosage of dextroamphetamine to 18.8mg and 9.4mg or increase the dosage of cabergoline. Because she maintained complete remission of the stomatodynia and headaches with little or no TD over 4 months she has chosen to maintain the same dosage of both drugs, i.e., 9.4mg twice daily and 0.25g cabergoline two times per week.

Discussion

This patient has the idiopathic form of stomatodynia because of the absence type of any known local or systemic cause and the absence of identifiable lesions. This condition is not common with a prevalence in the United States of only about one in 1,000 people [6]. Though a rare syndrome, we report a much more effective therapy to treat this disorder than the most commonly recommended treatments, e.g., psychotherapy and antidepressants [7].

In contrast, the increased cellular permeability syndrome, of which stomatodynia is only one of its many manifestations, is very common [2,3]. Even though one of the first case reports of this syndrome was published over 40 years ago, most clinicians are unaware of this syndrome and its various modes of presentation and how well all of the conditions respo0nd to dopaminergic drugs [2,3]. Headaches are a common disorder and there are many anecdotal reports of marked improvement of various types of headaches that were refractory to conventional therapy [2,9-16]. Thus, one of the main objectives is to familiarize healthcare workers with this condition of the increased cellular permeability syndrome and the treatment with dopaminergic drugs that are generally safer, less expensive, and more effective than the standard therapies available [2,3, 17].

Unfortunately, for unknown reasons, dextroamphetamine is a class II drug, and thus has restrictions. Thus, many physicians are reluctant to prescribe this therapy even if the benefits are known to that physician. As mentioned, cabergoline, another dopaminergic drug, has also been found effective in treating not only stomatodynia (burning mouth syndrome), but also headaches [4, 17]. Other conditions treated by cabergoline other than galactorrhea and hyperprolactinemia (the on-label approval for its use) includes pelvic pain and carpal tunnel syndrome and fibromyalgia [18, 19].

Tardive dystonia and dyskinesia (TD) are found to be a side effect after long-term treatment with antipsychotic medication. It may be seen in about 20% of schizophrenic patients treated with neuroleptics [20-22]. Though a popular theory of etiology links TD to increased dopaminergic binding sensitivity, there are data suggesting that this theory is an oversimplification (23,24). We would tend to agree that the dopaminergic therapy does not seem to explain the mechanism of why it is such a common experience with certain antipsychotic drugs. At least with dextroamphetamine, which releases more dopamine from sympathetic nerve fibers, we have only observed TD is one male patient despite treating thousands of patients with the drug. However, if the TD is very mild, it may have been underreported. Related to reluctance for physicians to prescribe amphetamines in the first place, and thus they may be apprehensive of using higher dosages if necessary, or if side effects occur with somewhat higher dosages, one may be able to obtain the same beneficial outcome by adding cabergoline and keeping the dextroamphetamine dosage lower.

We have a far greater experience with dextroamphetamine than cabergoline. So far, our opinion is that dextroamphetamine is more effective and better tolerated than cabergoline. Generally, higher dosages of cabergoline are needed e.g., 0.5mg 2 or 3 times per week to improve certain conditions related to increased cellular permeability. Some people with very serious life- threatening disorders refractory to all other therapies do tolerate high dosages of dextroamphetamine which may be needed to improve the condition [25,26].

As mentioned, this burning mouth syndrome (stomatodynia) is an oral pharyngeal problem without any lesions and is uncommon. There is a common problem involving the oral pharyngeal mucosa that is associated with lesions in the form of ulcers known as recurrent aphthous stomatitis (RAS) presenting in about 25% of the population [27]. Long-term very symptomatic RAS has been reported to also respond very well and quickly with dopaminergic drugs [28]. Unfortunately, most dentists are not aware of this type of treatment and treat with far less effective measures. It is hoped that those medical professionals treating mouth disorders will consider treating with dopaminergic drugs for other chronic mouth conditions and report their results whether positive or negative.

Conclusion

At least considering the side effect of TD, by reducing the dosage of dextroamphetamine and adding cabergoline we demonstrated that we could continue with marked amelioration of stomatodynia and headaches while markedly reducing or eliminating the side effect of TD, by reducing the dosage of dextroamphetamine and adding cabergoline we demonstrated that we could continue with marked amelioration of stomatodynia and headaches while markedly reducing or eliminating the effect of TD.

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