Treatment of Cluster Headache Symptoms using Synthetic Tryptamine N,N-Diallyl-5 Methoxytryptamine

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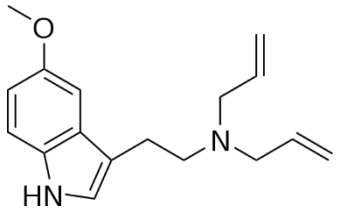


Fig. 1 – N,N-Diallyl-5 Methoxytryptamine molecule
IUPAC Name: N-allyl-N-[2-(5-methoxy -1H-indol-3-yl)ethyl] prop-2-en-1-amine
PubChem: CID 50878551

Abstract

Cluster headache patients (both chronic and episodic) have historically shown widely-varying therapeutic response to standard prophylactic treatments; however, some have responded positively to the self-administration of tryptamines and tryptamine-type compounds. The mechanism of action common to these substances indicates that cluster headache patients may respond to an agonist of the serotonin 2A receptor. N,N-dially-5-methoxytryptamine (commonly known as 5MeO-DALT) was selected for this case study based on its molecular structure, oral bioavailability, and relatively short-duration side effects. Varying dosages of 5MeO-DALT were taken by refractory cluster headache patients, and their results tracked to establish trends.

Administration of 5MeO-DALT at regular intervals resulted in significant reduction or elimination of cluster headache attacks. Based on its considerable efficacy and observed low risk of adverse side effects, 5MEO-DALT may be considered a viable treatment option for refractory cluster headache patients who are comfortable with self-administration of alternative treatments when used in a regimented self-treatment program under careful controls.

Introduction

Cluster headaches are a primary headache disorder affecting less than 1% of the population, classified as TACs (trigeminal autonomic cephalgias). Characterized by intense unilateral head pain, localized in the supraorbital or suborbital regions, cluster headache attacks have a very rapid onset (~5 minutes) and generally last from 30 to 90 minutes on average. During this time, the pain is frequently debilitating for the patient, and may be accompanied by parasympathetic symptoms including lacrimation, and a histamine-like reaction leading to sinus congestion and nasal discharge. Cluster headache patients may be classified as episodic, with periods of remission of at least 30 consecutive days; or as chronic, with no marked periods of remission. Sometimes referred to as "suicide headaches", the recurring pain of cluster headaches has caused some patients to take their own lives during or in anticipation of an attack.

Availability of reliable and safe medical treatments is a troublesome issue for the cluster headache patient community. At present, there are no pharmaceutical products developed specifically to treat cluster headache symptoms. The current state of the medical science in this area is divided between off-label applications of existing medications (including the calcium-channel blocker verapamil, the anticonvulsant topiramate, lithium, and a host of triptans, the most common being sumatriptan) and a growing number of "alternative" treatments generally consisting of non-pharmaceutical substances acting on 5HT receptors, including psilocybin, lysergic acid diethylamide (LSD), and d-lysergic acid amide (LSA).

Focusing primarily on alternative treatments, many cluster headache patients report partial or complete relief from self-administration of substances acting as agonists of the 5HT-2a receptor, including psilocybin-containing mushrooms, LSA extracted from plant materials, and lab-created LSD. This has led to cursory medical research into these hallucinogenic compounds, as well as one trial aimed at developing non-hallucinogenic forms of LSD for potential medical use.[i]

Because these treatments currently fall outside of accepted medical practice, cluster headache patients have turned to self-medication to relieve their symptoms. This presents two critical problems for the patient group: dosage control and availability of safe and reliable materials. In the case of psilocybin and LSA, the fungus/plant-derived options, the lay patient has no method for controlling dosage, and the net amount of ingested tryptamines can vary greatly from dose to dose. In the case of LSD, the ability to measure doses down to the microgram level is extremely difficult for most patients.

N,N-Diallyl-5 Methoxytryptamine (hereafter referred to as 5-MeO-DALT) is a synthetic tryptamine first formulated by Alexander Shulgin. Although never produced commercially, the compound was synthesized using Shulgin's formula, and propagated on the research chemical market beginning in June of 2004. 5-MeO-DALT shares many properties of common tryptamines, including potential agonist activity of the 5HT-2A receptors. Unlike many synthetic tryptamines, however, 5-MeO-DALT has the unique advantages of high oral bioavailability, extremely short-duration onset, and rapid elimination. It also has measurable efficacy at low doses.[ii] These traits combined make this compound a promising alternative treatment method for cluster headache patients.

In this study, 5-MeO-DALT was self-administered by two cluster headache patients who had proven to be refractory to most mainstream treatments. In patient A, dosages and durations were adjusted over a two-month period to establish a baseline for effective treatment and to gauge potential side effects. In Patient B, following an initial high dose, dosage was kept consistent with the effective dosage determined by Patient A, and duration was modified to establish consistent relief of symptoms. In both case studies, the patients were able to attain complete relief from cluster headache symptoms at a mean dosage of 15mg of 5-MeO-DALT administered at a five-day interval.

Materials and Methods*

***Author's Note:** The materials and methods used in this case study call into question multiple issues of legality, ethics, and methodology. Those will be addressed here:*

- *The current legal status of 5-MeO-DALT varies from country to country, ranging from complete legality to most-restricted status. In addressing legality, the author makes no representation of the country or legal jurisdiction in which this study took place.*

- *This study was not conducted with a control group, nor were any patients administered placebo. Because the author is not a licensed clinician, and due to the extremely painful nature of cluster headaches, the author did not consider it ethical to withhold treatment from a patient, nor to request a patient stop taking any previously-effective treatment for the purposes of this study.*

- *Reviewers will note in the methodology that this study uses an extremely small sample size, and does not feature any control group. The author acknowledges the shortcomings in methodology, and asserts that the results demonstrated will be reproducible in a clinical setting.*

Patients for this study were selected based on a confirmed diagnosis of cluster headaches, and having no other neurological or physical disorders other than those directly resulting from cluster headaches. Patients also had to meet criteria for frequency of cluster headache attack (minimum average of two attacks per day), and have a minimum amount of historical data showing frequency and severity of cluster headache attacks (minimum of three months of data).

5-MeO-DALT was sourced from an independent laboratory with full assays showing purity of >98%. Each individual dose was weighed on a calibrated milligram balance, and administered orally in a gelatin capsule. Patients then self-reported cluster headache activity* following each dose. Side effects were recorded anecdotally by each patient, and included herein as a general commentary on overall experience.

**NOTE: Cluster headache intensity was self-reported using the "kip" scale, a commonly-used but subjective measure of pain originally developed by cluster headache patient Bob Kipple, and commonly used throughout patient groups. The scale ranges from 0-10 in intensity, with 10 being the most severe pain, commonly resulting in hospitalization and thoughts of self-harm.*[iii]

Results

Patient A

Profile: Patient A (PA) is a 42-year-old male with a five year history of chronic cluster headaches. After diagnosis, PA has been primarily self-treated. Pharmaceutical treatments were limited to a 30-day trial of Cafergot (ergotamine tartrate and caffeine) with little to no effectiveness, and a 10-day taper of prednisone that provided short-term relief. PA has relied on alternative treatments for approximately four years, including self-administered LSA doses, a high-dose vitamin D3 regimen, and doses of licorice root tincture. Each alternative treatment has subsequently lost effectiveness over time, leading to frequent changes in treatment protocol. PA has relied on taurine/caffeine energy drinks as an abortive, and has never used any pharmaceutical abortive.

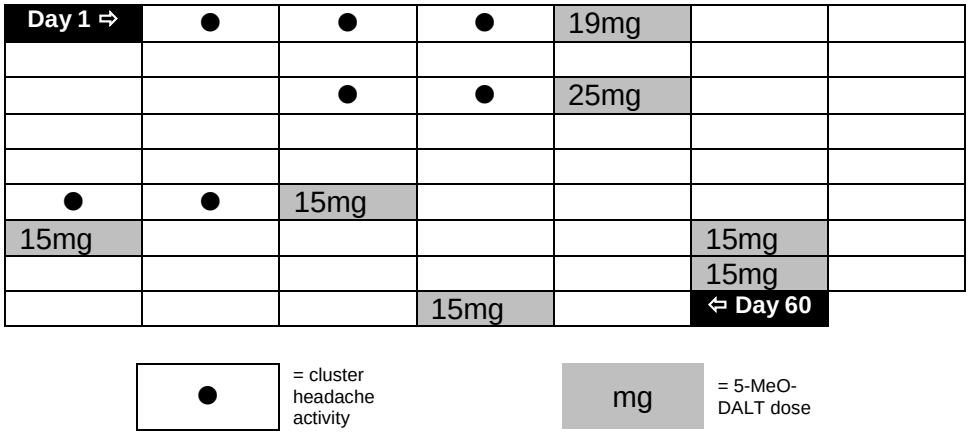
Patient A Cluster Headache Profile (Untreated):

Avg. CH per day:	2.8
CH timing:	Random / No pattern
Avg. CH intensity:	6.6 kip

Patient A was removed from his regular treatment protocol (LSA dosing and vitamin D3) for 18 days, then self-administered a dose of 19mg 5-MeO-DALT. This initial dosage was followed by a period of 11 days with no cluster headache symptoms. On day 12, symptoms began to return with low-intensity pressure and pain (3.0 kip). On day 14, full symptoms had returned with normal frequency and slightly lower intensity (5.0 kip). PA took a dose of 25mg 5-MeO-DALT on day 14, followed by a 16-day period with no cluster headache symptoms. Dosages were gradually adjusted downward and frequency of dosing increased (based on anecdotal evidence from regular users of tryptamines as primary cluster headache treatment.) At a final dosage of 15mg of 5-MeO-DALT spaced at intervals of five to seven days, all cluster headache symptoms were eliminated. Symptoms returned only after administration of 5-MeO-DALT was stopped for a period of 15 days.

Summary of Results, Patient A: After an initial adjustment period to determine correct dosage and intervals, Patient A was able to successfully eliminate all symptoms of cluster headaches and related activity by using doses of 15mg 5-MeO-DALT at five day intervals.

Fig. 2: 60-day timeline of 5-MeO-DALT administration and cluster headache activity for Patient A:



Patient B

Profile: Patient B (PB) is a 27-year-old female with an eight year history of episodic cluster headaches* beginning in 2006, increasing in frequency over an approximately four year period. PB has been treated primarily using pharmaceuticals in a clinical setting. Medications having no effect on PB's cluster headache symptoms included the muscle relaxant metaxalone, NSAIDS including naproxen, and the hybrid analgesic tramadol. Varying degrees of relief were obtained from orally-dissolving rizatriptan, the combination drug Fioricet, tapers of the steroid dexamethasone, and the anti-epilepsy drug topiramate. Each of these medications eventually lost effectiveness or produced undesirable side effects for PB and were discontinued. Alternative treatments used by PB include high-dose vitamin D3, licorice root tincture, LSA, and a single dose of psilocybin. Abortive treatments used by PB to stop cluster headache pain have included Maxalt MLT (rizatriptan) and taurine/caffeine energy drinks.

Patient B Cluster Headache Profile (Untreated):

Avg. CH per day:	3.6
CH timing:	Regular pattern at ~6-hour intervals
Avg. CH intensity:	9.0 kip

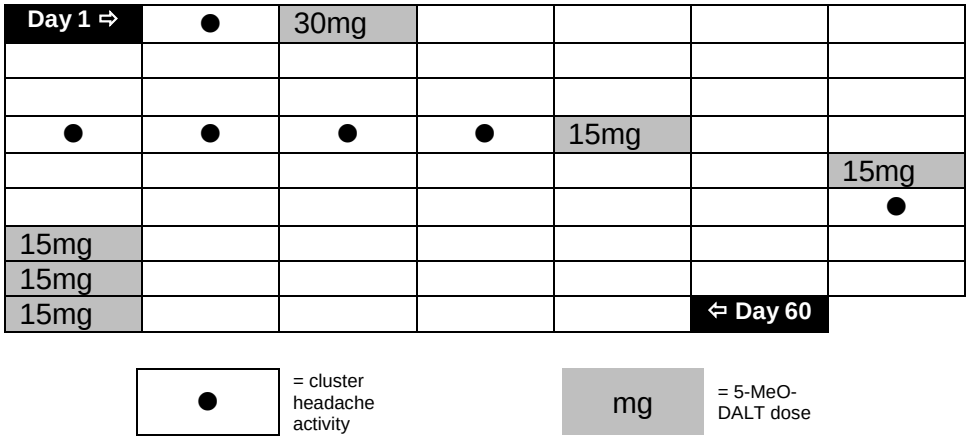
Patient B was self-administering LSA as her primary method of managing cluster headache symptoms, averaging approximately nine days of relief following each dose. An initial dose of 30mg of 5-MeO-DALT was substituted into the self-treatment schedule, resulting in 18 days with no cluster headache symptoms. PB experienced unpleasant side effects from the 30mg dosage,

and reduced it to 15mg for each subsequent dose. The second dose of 5-MeO-DALT resulted in no cluster headache symptoms. A third dose was taken after nine days, and mild cluster headache symptoms (1-2 kip) returned in approximately seven days. PB then began a treatment regimen of 15mg doses of 5-MeO-DALT at intervals ranging from 12 days down to five days, resulting in no cluster headache activity for the duration of treatment.

**Note: It is important to note the episodic nature of Patient B's cluster headaches in reviewing these results. Prior to this study, the length of PB's cycles had been increasing, and the cycle concurrent with this study was an extended one lasting longer than any previous cycles. While the results here indicate relief of cluster headache symptoms following regular dosing of 5-MeO-DALT, it remains a possibility that PB also experienced an end to her normal cycle.*

Summary of Results, Patient B: Patient B was transitioning treatments from one tryptamine (LSA) to another (5-MeO-DALT), and was able to achieve complete elimination of cluster headache symptoms with regular dosing.

Fig. 3: 60-day timeline of 5-MeO-DALT administration and cluster headache activity for Patient B:



Experience Notes: Both patients were asked to describe the physical effects of 5-MeO-DALT while dosing. Commonalities include marked drowsiness, intense relaxation, some feelings of spatial distortion, and very mild closed-eye visuals. In some cases, mild feelings of lightheadedness were reported. The total duration of these feelings was generally less than two hours for all doses, at which time the patients returned to baseline functioning.

The higher dose (30mg) experienced by PB resulted in a greater degree of spatial distortion, disorientation, and moderate dizziness. PB also felt a rapid drop in temperature at this dosage, leading to chills/shivering.

Discussion

Cluster headaches remain one of the most intractable medical conditions in the field of neurology, highlighted by the fact that there are currently no medications indicated primarily for treatment of this disorder. The current state of the medical science is divided; knowledgeable clinicians have achieved some degree of success using available medications in off-label applications; the most reliable medication currently available is the calcium-channel blocker verapamil, with the challenge being to find the lowest possible effective dosage due to potentially harmful or fatal side effects of this drug.[iv] Sumatriptan injections are effective in aborting cluster headache attacks within about 15 minutes once they have started, but require immediate administration and can cause marked side effects in some patients.[v] High-flow oxygen inhalation has also proven to be an effective abortive for cluster headache attacks, often resulting in relief within 15 minutes of the onset of attack.[vi] Unfortunately, these abortive treatments have the disadvantage of being reactive options, requiring the patient to endure the pain of cluster headache onset to signal the need for treatment. Based on the severity of the pain and its potential psychological impact on the patient, abortive treatments are generally considered a second line of defense to preventive therapies that can help reduce or eliminate attacks altogether.

The relative lack of reliable and safe pharmaceutical treatments has led to a large amount of "citizen science" in the cluster headache patient community. Aided by the internet and advent of social media, many cluster headache patients have discovered alternative treatments, instructions for self-administration, and informal support networks centered on the use of tryptamines and other alternative remedies. Among the most active and prevalent do-it-yourself treatment communities, psilocybin and LSD have a large following and anecdotally have proven to be effective alternative treatment methods. As a general guideline, cluster headache patients use approximately 2g of dried psilocybin mushroom material or a 25mcg dose of LSD at the onset of a cluster headache cycle (for episodic patients) or at regular intervals (for chronic patients) to achieve long-term relief of symptoms.[vii] Within the patient community, this line of treatment is colloquially referred to as "busting", a blanket term used to describe the use of any hallucinogenic substance to reduce cluster headache symptoms.

Accepting the theory that psychoactive tryptamines in low doses can have a positive therapeutic effect on cluster headache symptoms, there are challenges to this line of treatment for patients who suffer from this condition:

1. **Legality and morality.** The two most commonly-used substances, psilocybin and LSD, have been placed in the most restrictive drug categories in most countries. Cluster headache patients who choose this method of treatment must necessarily violate drug laws to obtain their treatment chemicals. Some of the other options, like LSA, are generally in less-restrictive (but still illegal) categories. Some cluster headache patients may also object to using these treatments on moral or religious grounds. Many are not interested in the potential psychedelic effects of these substances, and avoid them as a treatment option for fear of a "trip" experience.

2. **Access.** Setting aside legalities, these chemicals are also difficult to obtain for most cluster headache patients. They may form a relationship with people who sell drugs, or grow/produce their own. For some patients, neither option is viable.

3. **Dosage.** Patients who self-administer these treatments have little or no control over the dosage of the active chemical they are ingesting. The amount of psilocybin contained in 2g of dried mushrooms can vary widely based on potency and moisture content of the material. Similarly, the exact amount of LSD contained in a blotter or tab delivery method is impossible to measure, so the end user must rely on the accuracy of the lab equipment used to produce it. Even home extractions of LSA are variable and impossible to accurately measure.

While 5-MeO-DALT is subject to some of these same problems, it does provide an attractive option for cluster headache patients who wish to self-administer a tryptamine:

- Legally, 5-MeO-DALT remains uncontrolled in many countries, making access slightly easier for some patients. Because of its undecided legal status, it is commercially available on the research chemical market.

- For patients concerned about potential "trip" effects, 5-MeO-DALT has extremely mild physical effects, which are almost unnoticeable at the low doses required. It has a rapid onset of effects (~10 minutes), indicating that it is highly orally bioavailable. The subsidence of all effects after two hours would indicate a short half-life, reassuring patients who may be worried about long-term impairment.

- Because 5-MeO-DALT is a pure chemical (and not a plant/fungus compound or an extraction), accurately measuring dosage in its powdered freebase form is relatively easy for the patient. A quality milligram scale and gelatin capsules for ingestion will give the patient control over each dose to a degree they can't achieve with other tryptamines.

Any open discussion of 5-MeO-DALT will necessarily include its reputation as a grey-market "party drug", as it has found a small following in the pseudo-illicit research chemical community. This may understandably cause apprehension among patients seeking self-treatment options. This case study in no way seeks to position 5-MeO-DALT as a mainstream pharmaceutical solution for cluster headaches; instead, this substance should be viewed alongside its counterpart tryptamines already in use by this patient group. Like psilocybin, LSD, and LSA, the therapeutic dosage used here is a fraction of the substance's common recreational dose. A direct comparison of 5-MeO-DALT to these other tryptamines may help alleviate some of its stigma in the mind of the patient when making a decision about self-treatment of cluster headaches.

Conclusion

While 5-MeO-DALT does not represent a wholly new method of treatment for cluster headache patients, it offers another option for patients who choose to self-administer tryptamines as their chosen method of prevention. 5-MeO-DALT should be considered as a viable preventive treatment, given its advantages of access, dosage control, and extremely low risk of undesirable side effects as compared with other tryptamines.

The author and participants in this study in no way condone the use, procurement, or production of any illegal substances for the treatment of cluster headache symptoms.

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