



# RESPONSE OF CLUSTER HEADACHE TO SELF-ADMINISTRATION OF SEEDS CONTAINING LYSERGIC ACID AMIDE (LSA)



R. Andrew Sewell MD<sup>1</sup>, Kyle Reed<sup>2</sup>, Miles Cunningham MD PhD<sup>2</sup>  
<sup>1</sup>Yale University School of Medicine, New Haven, CT and VA Healthcare System, West Haven, CT  
<sup>2</sup>Neural Reconstruction Laboratory, McLean Hospital/Harvard Medical School, Belmont, MA

Fig 1: LSA-containing plants



- LSA is an ergoline alkaloid also known as *ergine* that is found in nature (unlike LSD) in three plants—two found in the United States and one in South America.
- **Hawaiian baby woodrose** is a perennial climbing vine that was native to the Indian subcontinent but now is present worldwide.
- **Morning glory** is a dicot climbing vine whose seeds contain LSA, and was originally used by Aztec priests in Mexico to commune with their gods.
- **Ololiuqui** was likewise used by native healers in shamanic healing ceremonies, and was the most common hallucinogenic drug used by the natives. It is still used by the Mazatecs, who live in the southern mountains of Mexico.
- The constituent LSA was identified in 1960 by Albert Hofmann, the inventor of DHEA, hydergine, methergine, and LSD. (Dr. Hofmann recently died at the age of 102). Its hallucinogenic properties were discovered later that decade, as poor people in Hawaii, Haiti and Puerto Rico consumed the seeds for a cheap buzz as an alternative to alcohol. Seven or 8 seeds will cause a 4 to 12 hour trip similar to LSD but lacking all the visuals, and characterized by severe nausea, flatulence, and vomiting.
- Because LSA is such an unpleasant trip, few recreational users take it twice, and as a result it is categorized in Schedule III, the same class as buprenorphine and anabolic steroids, rather than Schedule I as are the other psychedelics. The seeds are not controlled.

## Objective

This study was intended to explore whether lysergic acid amide (LSA), a naturally occurring and legal (to possess) analogue of LSD found in the seeds of the plants morning glory, Hawaiian baby woodrose, and ololiuqui (*Rivea corymbosa*) has therapeutic effects on cluster attacks, cluster periods, or remission periods.

## Background

Cluster headache is a rare syndrome of circadian-linked headaches that have accompanying autonomic signs such as ptosis, miosis, rhinorrhea, and a compulsion to pace about or bang the head. The intensity of these attacks is severe enough that patients have been known to commit suicide to escape the pain. Anecdotal evidence suggests that both lysergic acid diethylamide (LSD) and psilocybin may produce striking remissions in the disorder, often at sub-hallucinogenic doses. (Matharu *et al.*, 2005, Sewell *et al.*, 2006, Sempere *et al.*, 2006) Increasingly, patients have been using LSA to self-treat their disorder, because it is legal and more readily available than either LSD or psilocybin.

## Methods

367 patients in a pre-existing registry of cluster headache patients who have agreed to take part in clinical trials on cluster headache were surveyed to determine whether they were using LSA-containing seeds to self-medicate their cluster headache. 66 subjects either were currently or had done so. Those meeting inclusion criteria were interviewed to determine the effects of LSA on their cluster attack intensity and frequency, as well as cluster period and remission period length. We included all respondents who:

- 1) reported cluster headaches
- 2) had attempted to self-treat with LSA-containing seeds
- 3) Agreed to be contacted for evaluation by telephone or e-mail
- 4) Allowed us to obtain copies of their medical records.

## Outcome measures

- As **abortive** treatment: *effective* (causing termination of a cluster attack in less than 20 minutes) or *ineffective*.
- As **prophylactic** treatment: *effective* (causing total remission of the cluster period), *partially effective* (causing diminishment of cluster attack frequency or intensity), or *ineffective* (no change noted).
- For **remission extension**: *effective* (a delayed or missed cluster period), or *ineffective* (a subsequent cluster period at the expected time).
- The Hallucinogen Rating Scale (HRS) and Peak Experience Profile (PEP) were administered in order to quantify the strength of the subjective effects experienced.
- Subjects were also asked to send a 1g sample of the seeds that they had ingested for quantitative analysis of LSA content.

## Results

Seed analysis revealed wide and unpredictable variations in alkaloid content; consequently, the dosage self-administered by patients ranged from 0 mg to 2.8 mg.

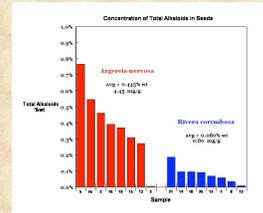


Fig 3: Concentration of total alkaloids in seeds. Seeds displayed a ten-fold variation in alkaloid content, and some contained no alkaloids at all.



Fig 6: Pain-free days following LSA self-administration (chronic cluster headache). Range: 2-120; mean: 25±37; median: 60 days.

38% reported the seeds effective as an acute abortive agent. Of those with episodic cluster headache, 43% reported termination of their cluster period, and a further 29% noted partial effect. All who ingested 0.5 mg or less of alkaloids were treatment non-responders.

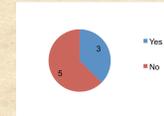


Fig 4: Was LSA effective in aborting an attack?

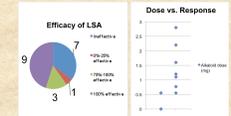
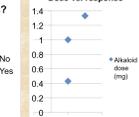


Fig 5: Was LSA effective in terminating a cluster period? 100% effective

Of the four subjects who ingested LSA-containing seeds during a remission period in order to extend the remission period, all four reported skipping their expected next cluster period. Two of them sent in seed samples, and had ingested 1.1 mg and 2.8 mg respectively.



Of those with chronic cluster headache, 56% reported pain-free periods ranging from 2 to 120 days (mean 25, SD 37). All of those who ingested 1 mg or less of alkaloids were treatment non-responders.

93% of subjects ingested LSA in a dose low enough to produce no psychoactive effects.

## Conclusions

Alkaloids in seeds known to contain LSA may be effective in aborting cluster attacks, terminating cluster periods, and extending remission periods, possibly through a mechanism unrelated to the seeds' hallucinogenic effects. No conventional medication either terminates cluster periods or extends remission periods. Clinicians should be aware of the increasing popularity of this method of self-treatment among their patients.

## References

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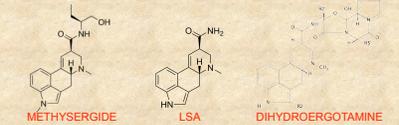


Fig 7: Comparison of chemical structure of LSA with methysergide and DHEA, both validated treatments for cluster headache.

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Fig 2: Path of seeds through study

1. Hawaiian baby woodrose seeds obtained via mail-order



2. Husks removed



3. Seeds ground with mortar and pestle in lemon juice



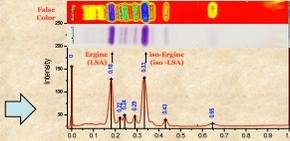
4. Seeds dried...



5. ...and placed in a teabag to make lysergic acid tea



4. Thin-layer chromatography (TLC) extraction of LSA



Silica Gel TLC of *Argyreia nervosa* Extract (10% Methanol/Chloroform); development with Ehrlich's reagent. LSA exists in tandem with an isomer that is inactive, and the two convert rapidly back and forth between one form and the other, equilibrating at a ratio of 4 LSA to 5 iso-LSA. The same is true of LSD.

## PATIENTS PREPARE THEIR OWN SEEDS



3. Seeds weighed, measured, and counted

