Brief Report:
Phantom Limb Pain: Sub-Hallucinogenic Treatment With Lysergic Acid Diethylamide (LSD-25)

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SYNOPSIS

Oral treatment of phantom limb pain in five males and two females ranging in age from 25 to 78 years with subhallucinogenic doses of lysergic acid diethylamide (LSD-25) resulted in improvement in pain in five patients and reduction in use of analgesics. In two of the five patients improvement was striking and in the other three, pain and analgesic use were reduced moderately. LSD treatment was ineffective in two patients. Intravenous infusion or bolus injection of LSD-25, 10ng/ml at 0.5 ml/min. resulted in facilitation of 5-HT venospasm. The findings suggest that LSD-25 facilitation of 5-HT activity occurs centrally consistent with the hypothesis of the central nature of phantom limb pain.

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THE MECHANISM OF PHANTOM LIMB pain is obscure. Many theories of a central process responsible for this entity, including that of central biasing have been proposed. Briefly, the central biasing concept suggests that the brain stem reticular formation tonically inhibits or biases transmission of the somatic projection system at all synaptic levels. When a large proportion of sensory fibers is destroyed by amputation of a limb, the input to the reticular formation is reduced and its inhibitory influence decreased.

Serotonin (5-HT) is thought to be the most important neurotransmitter in central modulation of pain. Evidence from animal studies suggests that 5-HT modulates pain centrally under normal conditions and deficient 5-HT increases sensitivity to painful stimuli.

Lysergic acid diethylamide (LSD-25) and other lysergic derivatives antagonize or potentiate, depending upon the dose, 5-HT in animals is similar to that in humans. LSD-25 increases brain concentration of 5-HT by reducing its turnover and altering its uptake and retention. Moreover, it produces improvement in migraine and other vascular headaches, regarded by some to result from defective central pain modulation, in non-hallucinogenic doses. The present study, suggested by the preceding observations, is aimed at documenting the therapeutic efficacy of LSD-25 in non-hallucinogenic doses in patients with phantom limb pain.

METHODS

Five males and two females ranging in age from 25 to 78 years were studied. All patients were volunteers, and suffered from typical phantom limb pain. Three were hospitalized, and four were outpatients. Before LSD-25 treatment, placebo was administered for a week.

LSD-25 was given in a single oral dose 25 μg per day for the first week, and 50 μg per day for the other two weeks. After the three weeks of LSD-25 treatment, placebo was again administered for four weeks. The patients took the drug at 9:00 in the morning, and were questioned every day about their sensations. During the eight weeks of observation, the daily use of analgesics was also measured.

RESULTS

Psychic reactions were rare, transient, and mild. In four, perceptive distortion during the first two days of treatment with 50 μg of LSD-25 was noted; however, this reaction disappeared with continued treatment. In five patients, LSD-25 produced improvement in pain, and reduction in use of analgesics. In two of five patients, the therapeutic effect was striking, and the consumption of analgesics gradually decreased until they were no longer

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required (Fig 1). In the other three patients, the pain was decreased to a moderate intensity, and analgesic use was reduced by 50%. In two patients, LSD treatment was ineffective, and analgesic use remained unchanged.

DISCUSSION

The small doses of LSD-25 (25-50 µg/day) which were effective in ameliorating phantom limb pain suggests a central site of action and facilitatory effect on 5-HT. The plasma level of LSD-25 reached a maximum of 10 ng/ml immediately after intravenous administration and was 5 ng/ml at one hour after injection, concentrations which would not produce an antiserotonin effect peripherally. It has been shown that similar doses enhance 5-HT vasoconstriction, a finding obtained by using the vasoconstriction test. When LSD-25 (10 ng/ml) was infused intravenously at the rate of 0.5 ml/min. (Fig 2), or injected in a bolus, facilitation of 5-HT antagonism and adrenergic facilitation while lower doses induce 5-HT facilitation and hallucinations. Our findings indicate that the analgesic properties of LSD-25 in phantom limb pain and migraine result from central potentiation of 5-HT activity in pathways involved in central pain regulation.

REFERENCES


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