

THE EFFECTS OF L-ARGININE AND YOHIMBINE ON SEXUAL AROUSAL IN POSTMENOPAUSAL WOMEN WITH FSAD

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The present study was designed to determine the effects of oral administration of the nitric oxide-precursor L-arginine, in combination with the α_2 blocker yohimbine, on subjective and physiological (vaginal photoplethysmography) responses to erotic stimuli in postmenopausal women with Female Sexual Arousal Disorder (FSAD). Oral administration of arginine glutamate (6 g) plus yohimbine hydrochloride (6 mg), but not yohimbine alone (6 mg), has previously been shown to be effective in improving penile blood flow and erectile ability in males with erectile dysfunction (Padma Nathan, 2000 and Lebret et al., 2000). The present study was a randomized, double-blind, placebo-controlled, three-way crossover clinical trial comparing the effects of the combination of L-arginine glutamate (6 g) and yohimbine HCl (6 mg) with yohimbine alone (6mg) alone and placebo. Patients were 23 post-menopausal women who met DSM IV criteria for FSAD. At each of the three treatment sessions, patients received a double blind oral dose of the test drug, followed by three psychophysiological assessments at approximately 30, 60, and 90 minutes post-drug administration. Physiological sexual arousal was measured as changes in vaginal pulse amplitude responses between a neutral (non-sexual) and sexual film. Subjective sexual arousal was using a self-report questionnaire.

Results showed that the combined oral administration of arginine glutamate and yohimbine induced a rapid and significant increase in vaginal pulse amplitude response to the erotic film at 60 minutes post drug administration compared with placebo. Pulse amplitude responses at 30 and 90 minutes post drug administration were increased compared to placebo, but did not reach significance. There were no significant differences in vaginal pulse amplitude responses between yohimbine alone and placebo at any of the test times. There were no significant increases in subjective measures of sexual arousal in any of the experimental conditions. This latter finding could be either due to a lack of sensitivity of the questionnaire, or because the erotic stimulus-induced drug increase in vaginal pulse amplitude may not have been sufficient to induce subjective arousal under the conditions of this study. The physiological results are consistent with pharmacokinetic data which indicate that arginine glutamate and yohimbine (administered orally) attain peak plasma concentrations at about 40 minutes (Worcel et al., personal communication). The findings are also consistent with those of Meston et al. (1997), which showed that clonidine, an α_2 adrenergic agonist, has an opposite effect to the one reported here for arginine glutamate and yohimbine. In that placebo-controlled trial performed in sexually functional women, it was shown that clonidine inhibits vaginal pulse amplitude and subjective responses to erotic stimuli. Simonsen et al. (1997) showed that the release of nitric oxide (NO) from non-adrenergic-non-cholinergic (NANC) penile nerves in the rat is inhibited by stimulation of prejunctional α_2 receptors induced by clonidine. This suggests that the α_2 antagonist yohimbine could also augment NO release by blocking norepinephrine retro-control on NANC nerves and further increase the effects of the NO precursor arginine in the arginine glutamate and yohimbine oral combination. In conclusion, oral administration of arginine glutamate and yohimbine significantly increases physiological sexual arousal in post-menopausal women with FSAD. The mechanism responsible is most probably an increase in NO release from NANC vaginal nerves which enhances the effect of their stimulation by erotic stimuli.

References

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