

KETAMINE

Many patients have migraines with prolonged aura where triptans or ergotamine derivatives cannot help. Ketamine can inhibit this by blocking cortical spreading depression, which is thought to correlate with aura. Furthermore, ketamine has been shown to increase cerebral blood flow in humans.

GABAPENTIN

Originally an antiepileptic drug now used to treat neuropathic pain in diabetics, gabapentin reduces the release of inflammatory neuropeptides important in headache pain, such as calcitonin gene-related peptide and substance P.⁸

TIZANIDINE

Tizanidine is a centrally acting, pre-synaptic alpha 2 adrenergic agonist that inhibits the release of norepinephrine and acts as a central muscle relaxant. Studies showed the benefit in prevention of migraines as well as decreased frequency of headaches (22.83 days to 15.83 days per month).⁹

MAGNESIUM

Magnesium reduces inflammation, relaxes muscles and blood vessels, and modulates calcium ion channels within our cells, which trigger the release of neurotransmitters. Magnesium also decreases release of substance P, and may be more effective in migraines with auras, possibly because magnesium can prevent cortical spreading depression, which may correlate with aura.¹⁰

LIDOCAINE

Lidocaine is a potent local anesthetic agent that may also alleviate migraines. It is hypothesized to act by its membrane-stabilizing effect, which inhibits the release of vasoactive substances from platelets, thus inhibiting the sterile inflammatory response.¹²

CAFFEINE

Caffeine is similar in structure with adenosine, an inhibitor of neuronal activity. Activating adenosine receptors (A1 and A2A) leads to antinociception in neuropathic pain and inflammatory models.¹³

HORMONES AND MIGRAINES

When women have a drop in estrogen and progesterone during their menses, these hormone withdrawals alter the function of neurotransmitters relevant to migraine pathophysiology.¹⁴ The mechanism of estrogen withdrawal on migraines is unknown, but estrogen is theorized to have neuroexcitatory effects, which is counterintuitive since estrogen withdrawal seems to trigger migraines.¹⁴ Patients with menstrual migraines may benefit from progesterone therapy, which has antiestrogen properties. Additionally, progesterone plays a major role in calming down the stimulatory effect of estrogen.¹⁵