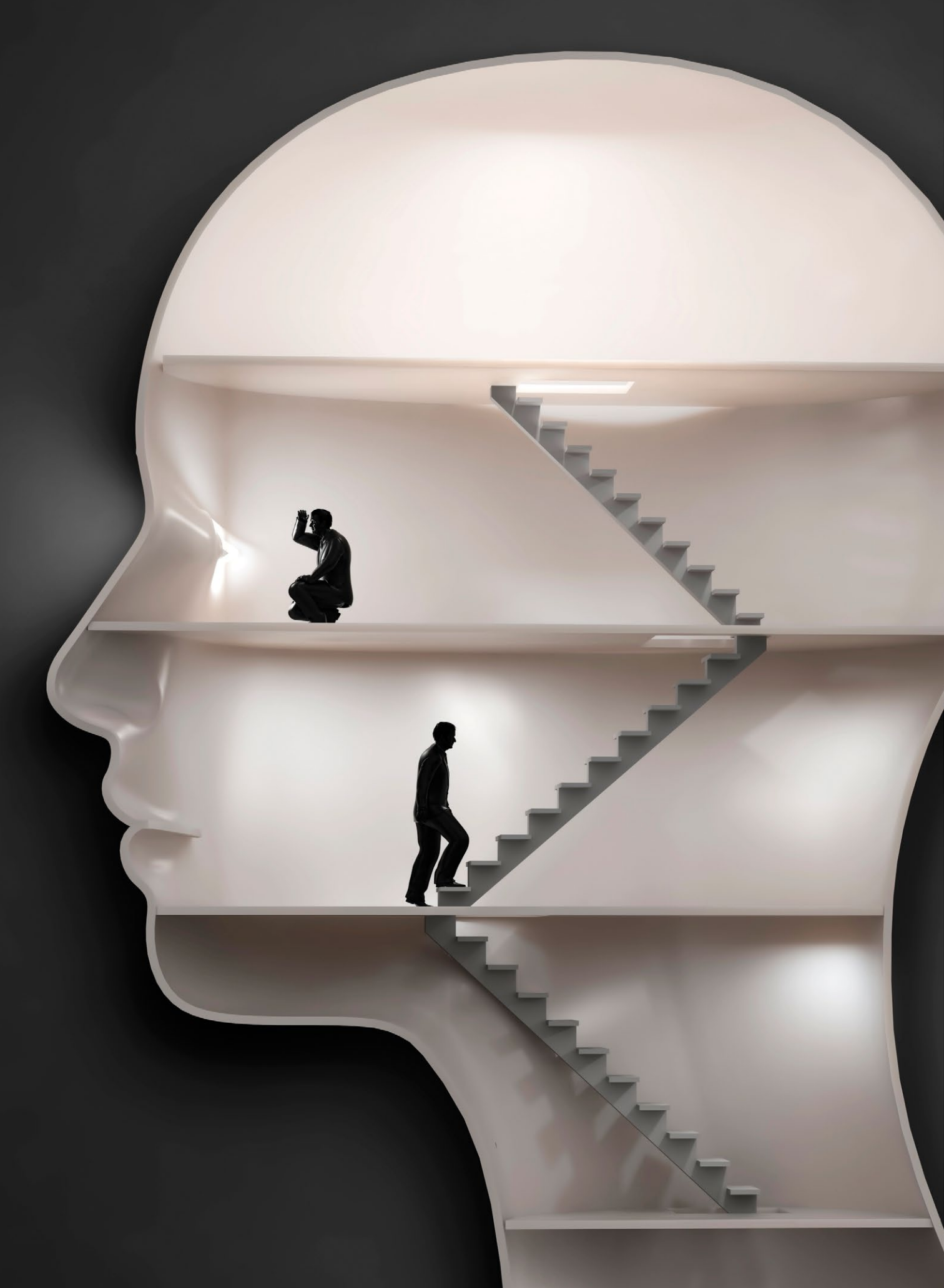

Interventional psychiatry (Part 1)

For some patients, IV medications, blocks, and injections could be effective treatments

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Advances in the understanding of neurobiological and neuropsychiatric pathophysiology have opened new avenues of treatment for psychiatric patients. Historically, with a few exceptions, most psychiatric medications have been administered orally. However, many of the newer treatments require some form of specialized administration because they cannot be taken orally due to their chemical property (such as aducanumab); because there is the need to produce stable blood levels of the medication (such as brexanolone); because oral administration greatly diminished efficacy (such as oral vs IV magnesium or scopolamine), or because the treatment is focused on specific brain structures. This need for specialized administration has created a subspecialty called interventional psychiatry.

Part 1 of this 2-part article provides an overview of 1 type of interventional psychiatry: parenterally administered medications, including those administered via IV. We also describe 3 other interventional approaches to treatment: stellate ganglion blocks, glabellar botulinum toxin (BT) injections, and trigger point injections. In Part 2 we will review interventional approaches that involve neuromodulation.

Parenteral medications in psychiatry

In general, IV and IM medications can be more potent that oral medications due to their overall faster onset of action and higher blood concentrations. These more invasive forms of administration can have significant limitations, such as a risk of infection at the injection site, the need to be administered in a medical setting, additional time, and patient discomfort.

continued

ANDRZEJ WOJCICKI

Interventional psychiatry

Clinical Point

Though most IV treatments are not FDA-approved for psychiatric indications, some, such as ketamine, are part of clinical practice

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Table 1 (*page 27*) lists short-acting injectable medications used in psychiatry, and *Table 2* (*page 28*) lists long-acting injectable medications. Parenteral administration of antipsychotics is performed to alleviate acute agitation or for chronic symptom control. These medications generally are not considered interventional treatments, but could be classified as such due to their invasive nature.[1] Furthermore, inhalable loxapine—which is indicated for managing acute agitation—requires a Risk Evaluation and Mitigation Strategy program consisting of 2 hours observation and monitoring of respiratory status.[2,3] Other indications for parenteral treatments include IM naltrexone extended release[4] and subcutaneous injections of buprenorphine extended release[5] and risperidone.[6]

IV administration

Most IV treatments described in this article are not FDA-approved for psychiatric treatment. Despite this, many interventional psychiatric treatments are part of clinical practice. IV infusion of ketamine is the most widely known and most researched of these. *Table 3* (*page 29*) lists other IV treatments that could be used as psychiatric treatment.

Ketamine

Since the early 1960s, ketamine has been used as a surgical anesthetic for animals. In the United States, it was approved for human surgical anesthesia in 1970. It was widely used during the Vietnam War due to its lack of inhibition of respiratory drive; medical staff first noticed an improvement in depressive symptoms and the resolution of suicidal ideation in patients who received ketamine. This led to further research on ketamine, particularly to determine its application in treatment-resistant depression (TRD) and other conditions.[7] IV ketamine administration is most widely researched, but IM injections, intranasal sprays, and lozenges are also available. The dissociative properties of ketamine have led to its recreational use.[8]

Hypotheses for the mechanism of action of ketamine as an antidepressant include direct synaptic or extrasynaptic (GluN2B-selective), *N*-methyl-D-aspartate receptor (NMDAR) inhibition, selectively greater inhibition of NMDARs localized on GABAergic (gamma-aminobutyric acid) interneurons, and the role of alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid receptor activation. There are links between ketamine's antidepressant actions and downstream mechanisms regulating synaptic plasticity, including brain-derived neurotrophic factor, eukaryotic elongation factor 2, mammalian target of rapamycin, and glycogen synthase kinase-3. Multiple other ketamine-associated mechanisms also have been described.[9,10] Action on the mu-opioid receptor is also known, possibly contributing to both antidepressant and anesthetic properties of ketamine.[11] Rapid onset of ketamine antidepressant action is especially valuable.[12]

Ketamine is a schedule III medication with addictive properties. Delirium, panic attacks, hallucinations, nightmares, dysphoria, and paranoia may occur during and after use.[13] Premedication with benzodiazepines, most notably lorazepam, is occasionally used to minimize ketamine's adverse effects, but this generally is not recommended because doing so reduces ketamine's antidepressant effects.[14] Driving and operating heavy machinery is contraindicated after IV infusion. The usual protocol involves an IV infusion of ketamine 0.4 mg/kg to 1 mg/kg dosing over 1 hour. Doses between 0.4 mg/kg and 0.6 mg/kg are most common. Ketamine has a therapeutic window; doses >0.5 mg/kg are progressively less effective.[15] Unlike the recommendation after esketamine administration, after receiving ketamine, patients remain in the care of their treatment team for <2 hours.

Esketamine, the S enantiomer of ketamine, was FDA-approved for TRD as an intranasal formulation. Esketamine is more commonly used than IV ketamine because it is FDA-approved and typically covered by insurance, but it may not be as effective.[16] An economic analysis by Brendle et al[17] suggested insurance companies would lower costs if they covered ketamine infusions vs intranasal esketamine.

Aducanumab and lecanemab

The most recent FDA-approved interventional agents are aducanumab and

Table 1
Short-acting injectable medications used in psychiatry[a]

First-generation antipsychotics	Second-generation antipsychotics	Benzodiazepines
Droperidol	Aripiprazole	Diazepam
Fluphenazine hydrochloride	Olanzapine	Lorazepam
Haloperidol lactate	Ziprasidone	Midazolam

[a]Injectable loxapine is no longer available in the United States

lecanemab, which are indicated for treating Alzheimer disease.[18,19] Both are human monoclonal antibodies that bind selectively and with high affinity to amyloid beta plaque aggregates and promote their removal by Fc receptor–mediated phagocytosis.[20]

FDA approval of aducanumab and lecanemab was controversial. Initially, aducanumab's safety monitoring board performed a futility analysis that suggested aducanumab was unlikely to separate from placebo, and the research was stopped.[21] The manufacturer petitioned the FDA to consider the medication for accelerated approval on the basis of biomarker data showing that amyloid beta plaque aggregates become smaller. Current FDA approval is temporary to allow patients access to this potentially beneficial agent, but the manufacturer must supply clinical evidence that the reduction of amyloid beta plaques is associated with desirable changes in the course of Alzheimer disease, or risk losing the approval.

Lecanemab is also a human monoclonal antibody intended to remove amyloid beta plaques that was FDA-approved under the accelerated approval pathway.[22] Unlike aducanumab, lecanemab demonstrated a statistically significant (although clinically imperceptible) reduction in the rate of cognitive decline; it did not show cognitive improvement.[23] Lecanemab also significantly reduced amyloid beta plaques.[23]

Aducanumab and lecanemab are generally not covered by insurance and typically cost >$26,000 annually. Both are administered by IV infusion once a month. More monoclonal antibody medications for treating early Alzheimer disease are in the late stages of development, most notably donanebab.[24] Observations during clinical trials found that in the later stages of Alzheimer disease, forceful removal of plaques by the autoimmune process damages neurons, while in less dense deposits of early dementia such removal is not harmful to the cells and prevents amyloid buildup.

Brexanolone

Brexanolone is an aqueous formulation of allopregnanolone, a major metabolite of progesterone and a positive allosteric modulator of GABA-A receptors.[25] Its levels are maximal at the end of the third trimester of pregnancy and fall rapidly following delivery. Research showed a 3-day infusion was rapidly and significantly effective for treating postpartum depression[26] and brexanolone received FDA approval for this indication in March 2019.[27] However, various administrative, economic, insurance, and other hurdles make it difficult for patients to access this treatment. Despite its rapid onset of action (usually 48 hours), brexanolone takes an average of 15 days to go through the prior authorization process.[28] In addition to the need for prior authorization, the main impediment to the use of brexanolone is the 3-day infusion schedule, which greatly magnifies the cost but is partially circumvented by the availability of dedicated outpatient centers.

Magnesium

Magnesium is on the World Health Organization's Model List of Essential Medicines.[29] There has been extensive research on the use of magnesium sulfate for psychiatric indications, especially for depression.[30] Magnesium functions similarly to calcium channel blockers by competitively blocking intracellular calcium

Clinical Point

Aducanumab and lecanemab bind selectively and with high affinity to amyloid beta plaque aggregates to treat Alzheimer disease

Clinical Point

IV magnesium has a pronounced beneficial effect in many patients with anxiety

Table 2

Long-acting injectable medications used in psychiatry

Haloperidol decanoate
Fluphenazine decanoate
Risperidone microspheres
Risperidone
Aripiprazole
Aripiprazole lauroxil
Olanzapine
Paliperidone
Naltrexone
Buprenorphine

channels, decreasing calcium availability, and inhibiting smooth muscle contractility.[31] It also competes with calcium at the motor end plate, reducing excitation by inhibiting the release of acetylcholine.[32] This property is used for high-dose IV magnesium treatment of impending preterm labor in obstetrics. Magnesium sulfate is the drug of choice in treating eclamptic seizures and preventing seizures in severe preeclampsia or gestational hypertension with severe features.[33] It is also used to treat torsade de pointes, severe asthma exacerbations, constipation, and barium poisoning.[34] Beneficial use in asthma treatment[35] and the treatment of migraine[36] have also been reported.

IV magnesium in myocardial infarction may be harmful,[37] though outside of acute cardiac events, magnesium is found to be safe.[38]

Oral magnesium sulfate is a common over-the-counter anxiety remedy. As a general cell stabilizer (mediated by the reduction of intracellular calcium), magnesium is potentially beneficial outside of its muscle-relaxing properties, although muscle relaxing can benefit anxious patients. It is used to treat anxiety,[39] alcohol withdrawal,[40] and fear.[41] Low magnesium blood levels are found in patients with depression, schizophrenia,[42] and attention-deficit/hyperactivity disorder.[43] However, it is important to note that the therapeutic effect of magnesium when treating anxiety and headache is independent of preinfusion magnesium blood levels.[43]

The efficacy of oral magnesium is not robust. However, IV administration has a pronounced beneficial effect as an abortive and preventative treatment in many patients with anxiety.[44]

IV administration of magnesium can produce adverse effects, including flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, and cardiac and CNS depression. These complications are very rare and dose-dependent.[45] Magnesium is excreted by the kidneys, and dosing must be decreased in patients with kidney failure. The most common adverse effect is local burning along the vein upon infusion; small doses of IV lidocaine can remedy this. Hot flashes are also common.[45]

Various dosing strategies are available. In patients with anxiety, application dosing is based on the recommended preeclampsia IV dose of 4 g diluted in 250 mL of 5% dextrose. Much higher doses may be used in obstetrics. Unlike in obstetrics, for psychiatric indications, magnesium is administered over 60 to 90 minutes. Heart monitoring is recommended.

Scopolamine

Scopolamine is primarily used to relieve nausea, vomiting, and dizziness associated with motion sickness and recovery from anesthesia. It is also used in ophthalmology and in patients with excessive sweating. In off-label and experimental applications, scopolamine has been used in patients with TRD.[46]

Scopolamine is an anticholinergic medication. It is a nonselective antagonist at muscarinic receptors.[47] Tricyclic antidepressants (TCAs) possess strong anticholinergic function. Newer generations of antidepressants were designed specifically not to have this function because it was believed to be an unwanted and potentially dangerous adverse effect. However, data suggest that anticholinergic action is important in decreasing depressive symptoms. Several hypotheses of anticholinergic effects on depression have been published since the 1970s. They include the cholinergic-adrenergic hypothesis,[48] acetylcholine predominance relative to adrenergic action

hypothesis,[49] and insecticide poisoning observations.[50] Centrally acting physostigmine (but not peripherally acting neostigmine) was reported to control mania.[48,51] A genetic connection between the M2 acetylcholine receptor in patients with major depressive disorder (MDD) and alcohol use disorder is also suggestive.[52]

Multiple animal studies show direct improvement in mobility and a decrease in despair upon introducing anticholinergic substances.[53-55] The cholinergic theory of depression has been studied in several controlled clinical human studies.[56,57] Use of a short-acting anticholinergic glycopyrrolate during electroconvulsive therapy (ECT) may contribute to the procedure's efficacy.

Human research shows scopolamine has a higher efficacy as an antidepressant and anti-anxiety medication in women than in men,[58] possibly because estrogen increases the activity of choline acetyltransferase and release of acetylcholine.[59,60] M2 receptors mediate estrogen influence on the NMDAR, which may explain the anticholinergic effects of depression treatments in women.[61]

Another proposed mechanism of action of scopolamine is a potent inhibition of the NMDAR.[62] Rapid treatments of depression may be based on this mechanism. Examples of such treatments include IV ketamine and sleep deprivation.[63] IV scopolamine shows potency in treating MDD and bipolar depression. This treatment should be reserved for patients who do not respond to or are not candidates for other usual treatment modalities of MDD and for the most severe cases. Scopolamine is 30 times more potent than amitriptyline in anticholinergic effect and reportedly produces sustained improvement in MDD.[64]

Scopolamine has no black-box warnings. It has not been studied in pregnant women and is not recommended for use during pregnancy. Due to possible negative cardiovascular effects, a normal electrocardiogram is required before the start of treatment. Exercise caution in patients with glaucoma, benign prostatic enlargement, gastroparesis, unstable cardiovascular status, or severe renal impairment.

Treatment with scopolamine is not indicated for patients with myasthenia gravis, psychosis, or seizures. Patients must be off potassium for 3 days before beginning scopolamine treatment. Patients should consult with their cardiologist before having a scopolamine infusion. Adverse reactions may include psychosis, tachycardia, seizures, paralytic ileus, and glaucoma exacerbation. The most common adverse effects of scopolamine infusion treatment include drowsiness, dry mouth, blurred vision, lightheadedness, and dizziness. Due to possible drowsiness, operating motor vehicles or heavy machinery must be avoided on the day of treatment.[65] Overall, the adverse effects of scopolamine are preventable and manageable, and its antidepressant efficacy is noteworthy.[66]

Treatment typically consists of 3 consecutive infusions of 4 mcg/kg separated by 3 to 5 days.[56] It is possible to have a longer treatment course if the patient experiences only partial improvement. Repeated courses or maintenance treatment (similar to ECT maintenance) are utilized in some patients if indicated. Cardiac monitoring is mandatory.

Table 3

IV medications used in psychiatry

Medication	Suggested mechanism of action
Ketamine[a]	NMDA antagonism
Aducanumab	Monoclonal antibodies
Lecanemab	Monoclonal antibodies
Brexanolone	GABA-A modulation
Magnesium sulfate[a]	Calcium channel blockade
Scopolamine[a]	Anticholinergic
Clomipramine	Anticholinergic; norepinephrine and serotonin reuptake inhibition

[a]Not FDA-approved for psychiatric treatment

GABA: gamma-aminobutyric acid;
NMDA: *N*-methyl-D-aspartate

Clomipramine

Clomipramine, a TCA, acts as a preferential inhibitor of 5-hydroxytryptamine uptake and has proven effective in managing depression, TRD, and obsessive-compulsive disorder (OCD).[67] Although this medication has reported treatment benefits for patients with phobia, panic disorder,[15]

Clinical Point

IV scopolamine should be reserved for patients with major depressive disorder who do not respond to usual treatment modalities

Clinical Point

Patients with severe, treatment-resistant OCD may be candidates for IV clomipramine

chronic pain,[68] Tourette syndrome,[69] premature ejaculation, anorexia nervosa,[70] cataplexy,[49] and enuresis,[71] it is FDA-approved only for the treatment of OCD.[72] Clomipramine may also be beneficial for pain and headache, possibly because of its anti-inflammatory action.[73] The anticholinergic effects of clomipramine may add to its efficacy in depression.

The pathophysiology of MDD is connected to hyperactivity of the HPA axis and elevated cortisol levels. Higher clomipramine plasma levels show a linear correlation with lower cortisol secretion and levels, possibly aiding in the treatment of MDD and anxiety.[74] The higher the blood level, the more pronounced clomipramine's therapeutic effect across multiple domains.[75]

IV infusion of clomipramine produces the highest concentration in the shortest time, but overall, research does not necessarily support increased efficacy of IV over oral administration. There is evidence suggesting that subgroups of patients with severe, treatment-refractory OCD may benefit from IV agents and research suggests a faster onset of action.[76] Faster onset of symptom relief is the basis for IV clomipramine use. In patients with OCD, it can take several months for oral medications to produce therapeutic benefits; not all patients can tolerate this. In such scenarios, IV administration may be considered, though it is not appropriate for routine use until more research is available. Patients with treatment-resistant OCD who have exhausted other means of symptom relief may also be candidates for IV treatment.

The adverse effects of IV clomipramine are no different from oral use, though they may be more pronounced. A pretreatment cardiac exam is desirable because clomipramine, like other TCAs, may be cardiotoxic. The anticholinergic adverse effects of TCAs are well known to clinicians[77] and partially explained in the scopolamine section of this article. It is not advisable to combine clomipramine with other TCAs or serotonin reuptake inhibitors. Clomipramine also should not be combined with monoamine oxidase inhibitors, though such a combination was reported in medical literature.[78] Combination with antiarrhythmics such as lidocaine or opioids such as fentanyl or and tramadol is highly discouraged (fentanyl and tramadol also have serotonergic effects).[79]

Clomipramine for IV use is not commercially available and must be sterilely compounded. The usual course of treatment is a series of 3 infusions: 150 mg on Day 1, 200 mg on Day 2 or Day 3, and 250 mg on Day 3, Day 4, or Day 5, depending on tolerability. A protocol with a 50 mg/d starting dose and titration up to a maximum dose of 225 mg/d over 5 to 7 days has been suggested for inpatient settings.[67] Titration to 250 mg is more common.[80]

A longer series may be performed, but this increases the likelihood of adverse effects. Booster and maintenance treatments are also completed when required. Cardiac monitoring is mandatory.

Vortioxetine and citalopram

IV treatment of depression with vortioxetine and citalopram has been explored but has not yet taken hold in clinical psychiatry.[81,82]

Injections and blocks

Three interventional approaches to treatment that possess psychotherapeutic potential include stellate ganglion blocks (SGBs), glabellar BT injections, and trigger point injections (TPIs). None of these are FDA-approved for psychiatric treatment.

Stellate ganglion blocks

The sympathetic nervous system is involved in autonomic hyperarousal and is at the core of posttraumatic symptomatology.[83] Insomnia, anxiety, irritability, hypervigilance, and other excitatory CNS events are connected to the sympathetic nervous system and amygdala activation is commonly observed in those exposed to extreme stress or traumatic events.[84]

SGBs were first performed 100 years ago and reported to have beneficial psychiatric effects at the end of the 1940s. In 1998 in Finland, improvement of posttraumatic stress disorder (PTSD) symptoms was observed accidentally via thoracic level spine blocks.[85] In 2006, cervical level sympathetic blocks were shown to be effective

for PTSD symptom control.[86] By the end of 2010, Veterans Administration hospitals adopted SGBs to treat veterans with PTSD.[87,88] The first multisite, randomized clinical trial of SGB for PTSD confirmed multiple previous reports of treatment efficacy. Specifically, 2 SGB treatments 2 weeks apart effectively reduced total symptom severity scores over 8 weeks.[87]

Since the stellate ganglion is connected to the amygdala, SGB has also been assessed for treating anxiety and depression.[89,90] Outside of PTSD, SGBs are used to treat complex regional pain syndrome,[91] phantom limb pain, trigeminal neuralgia,[92] intractable angina,[93] and postherpetic neuralgia in the head, neck, upper chest, or arms.[94]

The procedure consists of an injection of a local anesthetic through a 25-gauge needle into the stellate sympathetic ganglion at the C6 or C7 vertebral levels. An injection into C6 is considered safer because of specific cervical spine anatomy. Ideally, fluoroscopic guidance or ultrasound is used to guide needle insertion.[95]

A severe drop in blood pressure may be associated with SGBs and is mitigated by IV hydration. Other adverse effects include red eyes, drooping of the eyelids, nasal congestion, hoarseness, difficulty swallowing, a sensation of a "lump" in the throat, and a sensation of warmth or tingling in the arm or hand. Bilateral SGB is contraindicated due to the danger of respiratory arrest.[96]

Glabellar BT injections

OnabotulinumtoxinA (BT) injection was first approved for therapeutic use in 1989 for eye muscle disorders such as strabismus[97] and blepharospasm.[98] It was later approved for several other indications, including cosmetic use, hyperhidrosis, migraine prevention, neurogenic bladder disorder, overactive bladder, urinary incontinence, and spasticity.[99-104] BT is used off-label for achalasia and sialorrhea.[105,106] Its mechanism of action is primarily attributed to muscle paralysis by blocking presynaptic acetylcholine release into neuromuscular junctions.[107]

Facial BT injections are usually administered for cosmetic purposes, but smoothing forehead wrinkles and frown lines (the glabellar region of the face) both have antidepressant effects.[108] BT injections into the glabellar region also demonstrate antidepressant effects, particularly in patients with comorbid migraines and MDD.[109] Early case observations supported the independent benefit of the toxin on MDD when the toxin was injected into the glabellar region.[110,111] The most frequent protocol involves injections in the procerus and corrugator muscles.

The facial feedback/emotional proprioception hypothesis has dominated thinking about the mood-improving effects of BT. The theory is that blocking muscular expression of sadness (especially in the face) interrupts the experience of sadness; therefore, depression subsides.[112,113] However, BT injections in the muscles involved in the smile and an expression of positive emotions (lateral part of the musculus orbicularis oculi) have been associated with increased MDD scores.[114] Thus, the mechanism clearly involves more than the cosmetic effect, since facial muscle injections in rats also have antidepressant effects.[115]

The use of progressive muscle relaxation is well-established in psychiatric treatment. The investigated conditions of increased muscle tone, especially torticollis and blepharospasm, are associated with MDD, and it may be speculated that proprioceptive feedback from the affected muscles may be causally involved in this association.[116-118] Activity of the corrugator muscle has been positively associated with increased amygdala activity.[119] This suggests a potential similar mechanism to that hypothesized for SGB.

Alternatively, BT is commonly used to treat chronic conditions that may contribute to depression; its success in relieving the underlying problem may indirectly relieve MDD. Thus, in a postmarketing safety evaluation of BT, MDD was demonstrated 40% to 88% less often by patients treated with BT for 6 of the 8 conditions and injection sites, such as in spasms and spasticity of arms and legs, torticollis and neck pain, and axilla and palm injections for hyperhidrosis. In a parotid and submandibular glands BT injection subcohort, no patients experienced depressive symptoms.[120]

Medicinal BT is generally considered safe. The most common adverse effects are

Clinical Point

Facial glabellar botulinum toxin injections can have antidepressant effects

Related Resources

- Dokucu ME, Janicak PG. Nontraditional therapies for treatment-resistant depression. Current Psychiatry. 2021; 20(9):38-43,49. doi:10.12788/cp.0166
- Kim J, Khoury R, Grossberg GT. Botulinum toxin: emerging psychiatric indications. Current Psychiatry. 2018;17(12):8-18.

Drug Brand Names

Aducanumab • Aduhelm
Aripiprazole • Abilify
Aripiprazole lauroxil • Aristada
Brexanolone • Zulresso
Buprenorphine • Sublocade
Citalopram • Celexa
Clomipramine • Anafranil
Diazepam • Valium
Droperidol • Inapsine
Esketamine • Spravato
Fentanyl • Actiq
Fluphenazine decanoate • Modecate
Fluphenazine hydrochloride • Prolixin
Haloperidol decanoate • Haldol decanoate
Haloperidol lactate • Haldol
Ketamine • Ketalar
Lecanemab • Leqembi
Lidocaine • Xylocaine
Lorazepam • Ativan
Loxapine inhaled • Adasuve
Naltrexone • Vivitrol
Magnesium sulfate • Sulfamag
Midazolam • Versed
Olanzapine • Zyprexa
OnabotulinumtoxinA injection • Botox
Paliperidone • Invega Hafyera, Invega Sustenna, Invega Trinza
Rapamycin • Rapamune, Sirolimus
Risperidone • Perseris
Risperidone microspheres • Risperdal Consta, Rykindo
Scopolamine • Hyoscine
Tramadol • Conzip
Vortioxetine • Trintellix
Ziprasidone • Geodon

Clinical Point

Botulinum toxin is used to treat chronic conditions that may contribute to depression, such as spasticity and bladder disorders

hypersensitivity, injection site reactions, and other adverse effects specific to the injection site.[121] Additionally, the cosmetic effects are transient, given the nature of the medication.

Trigger point injections

TPIs in the neck and shoulders are frequently used to treat tension headaches and various referred pain locations in the face and arms. Tension and depression frequently overlap in clinical practice.[122] Relieving muscle tension (with resulting trigger points) improves muscle function and mood.

The higher the number of active trigger points (TPs), the greater the physical burden of headache and the higher the anxiety level. Gender differences in TP prevalence and TPI efficacy have been described in the literature. For example, the number of active TPs seems directly associated with anxiety levels in women but not in men.[123] Although TPs appear to be more closely associated with anxiety than depression,[124] depression associated with muscle tension does improve with TPIs. European studies have demonstrated a decrease in scores on the Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale following TPI treatment.[125] The effect may be indirect, as when a patient's pain is relieved, sleep and other psychiatric symptoms improve.[126]

A randomized controlled trial by Castro Sánchez et al[127] demonstrated that dry needling therapy in patients with fibromyalgia syndrome (FMS) showed improvements in pain pressure thresholds, body pain, vitality, and social function, as well as total FMS symptoms, quality of sleep, anxiety, hospital anxiety and depression, general pain intensity, and fatigue.

Myofascial pain syndrome, catastrophizing, and muscle tension are common in patients with depression, anxiety, and somatization. Local TPI therapy aimed at inactivating pain generators is supported by moderate quality evidence. All manner of therapies have been described, including injection of saline, corticosteroids, local anesthetic agents, and dry needling. BT injections in chronic TPs are also practiced, though no specific injection therapy has been reliably shown to be more advantageous than another. The benefits of TPIs may be derived from the needle itself rather than from any specific substance injected. Stimulation of a local twitch response with direct needling of the TP appears of importance. There is no established consensus regarding the number of injection points, frequency of administration, and volume or type of injectate.[128]

Bottom Line

Interventional treatment modalities that may have a role in psychiatric treatment include IV administration of ketamine, aducanumab, lecanemab, brexanolone, magnesium, scopolamine, and clomipramine. Other interventional approaches include stellate ganglion blocks, glabellar botulinum toxin injections, and trigger point injections.

Adverse effects of TPIs relate to the nature of the invasive therapy, with the risk of tissue damage and bleeding. Pneumothorax risk is present with needle insertion at the neck and thorax.[129] Patients with diabetes may experience variations in blood sugar control if steroids are used.

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Clinical Point

Relieving muscle tension with trigger point injections can improve mood as well as muscle function

Interventional psychiatry

Clinical Point

Many newer treatments require some form of specialized administration because they cannot be taken orally

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Clinical Point

More invasive forms of administration can have significant limitations, such as a risk of infection at the injection site