Holding Back: Anti-Depressants in Treatment

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Introduction

Levy et al. (2018) suggested that a staggering number of patients avoid full-disclosure with their medical providers either through omission or outright deception. There are a variety of reasons for deceptive behavior. Patients cannot afford the economic costs of treatment. Other patients disagree with their healthcare provider and refuse to take the prescribed medication. Some patients turn to herbs, supplements, and home remedies. According to Gunn et al. (2020), even more dangerously, some clients mix their own cocktail of natural supplements combined with prescribed medications, which can prove to be deadly. Assessing mental health problems in patients with comorbidities also interferes with reporting and diagnosis.

Some medications actually cause depression, which can lead to treatment resistance mental health conditions, which are not alleviated by antidepressants or psychotherapy (Preston et al., 2021). Fava and Davidson (1996) reported that major depression is treatment resistant 34 to 46 percent of the time. Selective serotonin reuptake inhibitors (SSRIs) are the vehicle to navigate recent psychopharmacological research, explore possible drug interactions, consider supplemental treatment routes, and direct patients to more productive outcomes.

Antidepressant Medications: A Brief History

Pereira and Hiroaki-Sato (2018) contend that antidepressant (ADP) treatments were basically ineffective until the 1930s. After WWII, the pharmacologic revolution drove improved ADP treatment. During the 1950s, Imipramine and iproniazid (later monoamine oxidase inhibitor (MAOI)) were synthesized. These medications dominated treatment during the 1960s and into the 1970s, with a strong focus on monoamines and major depressive disorder (Lewis, 1986). In 1967, researchers postulated that serotonin (5-hydroxytryptamine or 5-HT) deficits in

intrasynaptic brain regions caused depression (Lapin & Oxenkrug, 1969). Mohammad-Zadeh et al. (2008) suggested that serotonin is a hormone and neurotransmitter and regulates appetite and body temperature, sleep patterns, and sexual behaviors. In terms of anxiety and stress, 5-HT promotes patience, modulates stress, and decreases anxiety (McDannald, 2015). Serotonin's role in positive mood regulation has been well-regarded (Cowen & Browning, 2015).

Primary takeaways from the advent of ADP treatment to the discovery and reign of the selective serotonin reuptake inhibitor, Prozac are threefold. First, primary discoveries were made through the exploration of other medications (Ban, 2006). It seems like a lot of ADP medications have been discovered through serendipity. Second, the development of advanced ADP medications occurred after major wars. To this day, PTSD is a tremendous cause of depression for veterans (Hobfoll, 2016). Third, in 1965, a major breakthrough occurred when researchers hypothesized there was a functional shortage of the catecholamine neurotransmitter, dopamine and norepinephrine, which contributed to the causes for depression (Maas, 1975). For the first time, monoaminergic theories led to breakthroughs in ADPs.

Review of SSRIs in Treatment

Selective Serotonin Reuptake Inhibitors (SSRIs)

After determining that fluoxetine hydrochloride was the most potent serotonin selective uptake inhibitor, and had the advantage of fewer side effects, Prozac took center stage. According to Lopez-Munoz and Alamo (2009), Prozac's popularity grew so much, that in 1994, it took second place as the most commonly prescribed medication worldwide. In fact, Wenatchee, Washington became the "Prozac capital of the world," when a local psychologist in town infamously prescribed Prozac to 700 of his patients (Roberts, 1995). The medication boomed worldwide in popularity (Slingsby, 2002). Other SSRIs emerged during this era,

including venlafaxine, reboxetine, nefazodone, and mirtazapine. Currently, SSRIs are the most prevalent treatment for depression, and in addition to treatment for depression disorders, there are off-label uses that include fibromyalgia, autism, and menopausal related symptoms (Chu & Wadhwa, 2022).

Mechanism of Action

There are two main subclasses of neurotransmitter transporters. Some are presynaptic, and other are on the glial membrane (Stahl et al., 2021). SSRIs impede the presynaptic reuptake of serotonin at the transporter (SERT). By blocking the uptake, serotonin is increased at the postsynaptic membrane in the serotonergic synapse (Chu & Wadhwa, 2022). Transporters act as a receptor, which fixes to the neurotransmitter before transmission occurs. The molecule from the SSRI medication enters the reuptake cycle and obstructs reuptake (Preston et al., 2021). When the SERT is inhibited, more 5-HT remains at the synaptic cleft, which stimulates the postsynaptic receptor for a longer time (Feighner, 1999; Preskorn, 1997; Xue et al., 2016). Basically, by stopping the reuptake process, serotonin activity increases. Also, SSRIs have little impact on dopamine or norepinephrine, and patients have fewer side effects than MAOIs or TCAs because there are fewer impacts on histaminergic, cholinergic, or adrenergic receptors (Chu & Wadhwa, 2022). Anecdotally, to better understand this process, when serotonin is pinned at the synaptic cleft, then serotonin activity increases, which improves depressed mood and decreases anxiety. Anecdotally, having experienced SSRIs, there was an immediate positive result, and an improved feeling of well-being.

Natural Remedies and Wellness Supplements

There is evidence from peer-reviewed articles to suggest that there could be a place for natural remedies, nutritional supplements, and wellness products in augmenting a

pharmacological approach. Vitamin D reportedly reduces depression in postmenopausal women. After observing a group of 81,189 women from ages fifty to seventy-nine, researchers found that vitamin D was helpful in preventing depression, treating depression, or both (Bertone-Johnson et al., 2011). Other researchers evaluated depression and anxiety in cancer patients, and identified herbs that would were both helpful in treating depression and also did not negatively interact with cancer treatments. According to Yeung et al. (2018), these herbs included passionflower, saffron, lavender, chamomile, and black cohosh. The strongest evidence for treating depression comes from polyunsaturated fatty acids (PUFAs) which targets inflammation and serves as an additional supplement to SSRIs. Vitamin D decreases depression, with small to moderate improvements in depression symptoms from omega-3, folate-based supplements, and N-acetyl cysteine (Nac) (Firth et al., 2019). Additional research has shown promise in decreasing symptoms with prebiotics. Other dietary supplements, including PUFAs, vitamin D, vitamin B-12, magnesium, omega-3 fish oil, zinc, and curcumin suggest that depressed patients experience moderate relief from symptoms, especially when these supplements are used (Al-Karawi et al., 2015; Hoffman et al., 2019; Kamezi et al., 2019; McNamara et al., 2016; NIH, 2020; Syed et al., 2013; Thurfah et al., 2022; Wang et al., 2018). While there is evidence suggesting that these supplements may work, clinicians should approach with caution, especially for products that are touted as cure-alls or that are not advised by a medical practitioner. In this situation, the psychologist should recommend ongoing support from a doctor. Psychologists have ethical binds.

St. John's Wort and Tryptophan

St. John's wort is taken for some mental health disorders, and is specifically identified as a non-specific serotonin reuptake blocker (Coppock & Dziwenka, 2016). St. John's wort shows

some positive efficacy in treating depression (Borrelli & Izzo, 2009). Adverse effects include anxiety, agitation, headache, itching, skin rash, and increased anxiety (Knüppel & Linde, 2004). Tryptophan and 5-Hydroxytryptophan (5-HTP) are functionally and structurally similar to serotonin. Tryptophan and 5-HTP increases risk of serotonin syndrome and could cause death in some circumstances (Turner et al., 2006; Van Woert & Sethy, 1975).

Natural Wellness

There are natural wellness supports for depression. One study suggested that exercise improved a depressed mood (Rethorst, 2019). Go for a walk. Get into a habit of healthy eating, and eat foods that contain omega-3 fatty acids, folic acid, and vitamin D (Thurfah et al., 2022). Get outside. Get some sun. Sleep well. Sleep hygiene is important. Given the relationship between the serotoninergic system with sleep, it makes sense that improved sleep could decrease depression (Rosenzweig, 2022). Acupuncture also showed promise in treating women with depression and anxiety (Tu et al., 2021). Finally, decreasing hazardous alcohol consumption decreases depressed symptoms, particularly in groups that participate in abusive drinking (Strid et al., 2019). Over-the-counter dietary supplements such as Natrol (melatonin), glutamine (α-amino acid), and malic acid are used to reduce weight and are supplemented to decrease depression caused from weight gain (Patel & Marzella, 2017).

Other Adverse Medications

Aside from the wellness products mentioned previously, patients who are taking SSRIs should also be cautioned against using some over-the-counter-cold remedies, especially those that contain dextromethorphan. Dy et al. (2017) described a situation in which a 63-year-old woman was hospitalized after combining escitalopram with a cold medication. The adverse

effects were nearly lethal. She did not know about the ill-effects of cold medication used in conjunction with her prescribed SSRI.

What is Serotonin Syndrome?

Serotonin syndrome (SS) is an adverse side effect of using SSRIs, especially when combined with other serotonergic agents (Boyer & Shannon, 2005), such as those in dietary supplements. This interaction could be the result of a very problematic possible drug or supplement interaction. SS typically occurs from a post-exposure to serotonin agonists (Talton, 2020). SS is potentially life threatening (Simon & Keenaghan, 2022). SS has been observed in all age groups, so it is very important for caregivers to understand the dangers of this disorder when caring for a vulnerable person (Boyer & Shannon, 2005). Mental states during SS include agitation, confusion, restlessness, and a heightened startle reflex (Ganetsky & Brush, 2005). Physical symptoms could include hyperthermia, tachycardia, hypertension, diarrhea, and vomiting (Prakash et al., 2020). There are other symptoms, as well, that would need to be evaluated and ruled out, such as neuroleptic malignant syndrome (NMS) (Iyer & Shah, 2011).

Ethical and Cultural Decision Making

Psychologists are bound to a code of ethics to establish compassionate and intelligent care. Part of the ethical conduct ensures that psychologists maintain therapeutic boundaries, seek consultant from others, work in collaboration with primary care physicians, and safeguard patients in high-risk situations (Hsin & Torous, 2016). First, psychologists have an ethical duty to “do no harm” (APA, 2016). They also have a duty of confidentiality, autonomy, and to practice in terms of their scope of practice and scope of competence (Smith, 2003). If a client is engaging in risky behavior by mixing prescribed medications with supplemental treatments, then the psychologist has an ethical duty to truthfully disclose the risks, especially if that is in their

scope of competence. If failure to inform would be a risk to the client (Hsin & Torous, 2016), then the psychologist should also seek additional clinical support and encourage the client to have a direct discussion with their PCP to ensure that the psychologist is recognizing their professional limits of practice and maintaining the appropriate boundaries with the client (Hsin & Torous, 2016). Depending on the type of treatment, there are considerations that pertain to ethics, health and safety, confidentiality, and culturally diverse philosophical differences. Tabish (2008) described complementary practices that are used in Eastern cultures and medicine that should also be considered when treating clients. If health and safety is a risk, then this merits a different response than philosophical differences. To be sure, this situation requires extra training by the psychologist, and a collaborative partnership with a PCP. Anecdotally, if the client is competent to make his or her own decisions, then it is best to provide informed consent so that the client understands any associated risks, and monitor the client's well-being and mental state to ensure there are no adverse impacts. Certainly, if the client is demonstrating adverse effects from a sideline treatment, and is observably showing losses in capacity, as a Mandated Reporter then psychologists have a duty of care to ensure safety (APA, 2016).

"Safer" Alternatives

Reviewing safest, best practice, there are safer alternatives that psychologists could recommend to augment medication. First, research indicates that yoga is helpful in addressing depression and anxiety (Butterfield et al., 2017; Chang et al., 2022; O'Dea et al., 2022). Second, practicing meditation or mindfulness might also be positive suggestions (Haller et al., 2019; Lorenc et al., 2018; Moir et al., 2019). Third, recommending proper nutrition, sleep hygiene, and exercise in general would be positive, safe alternatives to herbal remedies that a psychologist could feel more confident in recommending depending on the overall health of the client and

other potential comorbidities (Thompson-Casey et al., 2022). As always, seek support and engage honestly and ethically.

Conclusion

This paper discussed current evidence-based research from the field of psychopharmacology, and reviewed the SSRI class of medications in treating depression. The mechanism of action was identified and described. Potential home remedies or supplements were explored from both a wellness perspective and in terms of contraindicators and adverse side effects. Specific, Serotonin Syndrome was evaluated. Ethical considerations were explored. Finally, benign alternatives were suggested.

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