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Review

Psychopharmacological Therapies in Dermatology

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Abstract

When patients with psychodermatologic disorders present in clinic, the dermatologist can refer them to psychiatrists or other mental health care professionals. However, it is often the case that these patients will refuse a psychiatric referral because they either do not believe they have a disorder of psychiatric nature or they feel there is societal stigma associated with psychiatric illness. Therefore, it is essential for dermatologists to understand the common classifications for psychodermatological cases and to know how to optimally treat these patients with pharmacotherapy. The intent of this article is to help guide physicians in understanding the classifications of psychodermatological cases and in managing these conditions with pharmacotherapies. In this article, two classifications for psychodermatological cases are presented, followed by a discussion of medical therapies used to treat the main categories of psychopathologies that are more frequently encountered in dermatology. These include depression, anxiety, delusions, and obsessive-compulsive disorder.

Key Words: psychopharmacology, psychodermatology, psychocutaneous medicine

Introduction

Many patients seen in dermatology clinics have psychiatric or psychosocial issues that may or may not be related to their skin conditions. In fact, Hughes et al. reported that 30-40% of dermatology outpatients had psychiatric symptoms [1]. Moreover, it has been documented that compared with general medicine inpatients, dermatology inpatients have a greater prevalence of psychiatric disorders [1]. The most troublesome of the psychodermatological disorders encountered is delusions of parasitosis, in which patients have no primary skin pathology, but present with skin manifestations related to manipulation of the skin. In addition, patients may experience depression or anxiety owing to perceived or real disfigurement from their skin disease. Furthermore, psychosocial issues, such as emotional stress, can exacerbate common skin disorders such as psoriasis, eczema, and acne.

When patients with psychodermatological disorders present in clinic, the dermatologist can refer them to psychiatrists or other mental health care professionals. However, it is often the case that these patients will refuse a psychiatric referral because they either do not believe they have a disorder of an underlying psychiatric nature or they feel there is societal stigma associated with psychiatric illness. Therefore, it is essential for dermatologists to understand the common classifications for psychodermatological cases and how to optimally treat these patients with pharmacotherapy. Although nonpharmacological treatments can be helpful for these patients, there is frequently limited training and available time for

dermatologists to feasibly incorporate non-pharmacologic treatment options in his or her practice. For those readers interested in learning about alternative therapies to medications, including psychotherapy, biofeedback, relaxation training, and hypnosis, we recommend a paper by Dr. Richard Fried titled "Nonpharmacological treatments in psychodermatology [2]."

Therefore, the intent of this article is to review and help guide physicians in understanding the classification and pharmacological management of psychodermatological cases. In this article, two classifications for psychodermatological cases are presented, followed by a discussion of medical therapies to treat the main categories of psychopathologies that are more frequently encountered in dermatology. These include depression, anxiety, delusions, and obsessive-compulsive disorder (OCD).

First Classification: Four Categories of Psychodermatological Disorders

To better guide dermatologists in choosing the most effective pharmacological therapy, it is helpful to categorize the psychodermatological disorders into four distinct groups. The four major categories are psychophysiological disorders, primary psychiatric disorders, secondary psychiatric disorders, and cutaneous sensory disorders.

Psychophysiological Disorders

Psychophysiological disorders are conditions in which actual skin disorders are worsened by psychological factors, most commonly stress. Psoriasis, eczema, lichen simplex chronicus, acne, hyperhidrosis, and rosacea are common conditions exacerbated by stress.

Primary Psychiatric Disorders

Primary psychiatric disorders are cases in which patients have a psychiatric condition but no primary skin disorder. Patients often present with a dermatological complaint, but lesions on the skin are self-induced. Primary psychiatric disorders include delusions of parasitosis, dermatitis artefacta, neurotic excoriations, and trichotillomania.

Secondary Psychiatric Disorders

Secondary psychiatric disorders refer to cases in which patients who have real skin problems. However, as a result of disfigurement, they have developed emotional problems, commonly depression and anxiety. These disorders include alopecia areata, cystic acne, and vitiligo.

Cutaneous Sensory Disorders

Cutaneous sensory disorders describe conditions in which patients have unpleasant cutaneous sensations. These may include crawling, biting, stinging, burning, pruritus, or any other uncomfortable sensation of the skin. These sensations occur in the absence of a visible primary skin disorder, diagnosable neurological disorder, or identifiable medical condition. These patients may or may not also have a psychiatric disorder.

Dermatological diseases effectively treated with psychotropic medications

In addition to the four main categories of psychodermatological disorders, there is also a situation in which psychotropic medications may be more effective in treating bona fide "traditional" dermatological conditions. For instance, doxepin is an antidepressant, but it is a more powerful antipruritic medication than traditional antihistamines such as hydroxyzine (Atarax ®) and diphenhydramine (Benadryl ®). Therefore, doxepin is frequently prescribed in dermatology clinics for pruritus secondary to psoriasis and eczema.

Understanding these classifications can help dermatologists determine how to optimally approach and treat their patients. For patients with psychophysiological disorders or secondary psychiatric disorders, patients may be more willing to discuss their psychological and social situation. However, for patients with primary psychiatric disorders, they are often very resistant to discussing their symptoms in terms of a psychiatric condition. For psychophysiological patients, a dual approach of using both dermatological and psychopharmacological treatments may be more effective than a singular approach because these patients have both a skin disease and an exacerbating psychological stressor. For a patient with

primary psychiatric disorder, dermatological treatments are often not effective. In cases of secondary psychiatric disorders, more aggressive dermatological therapy may be required in order to reduce the psychological stress of the patient. Psychological support may also be helpful.

Second Classification: Four Main Underlying Psychopathologic Conditions

Another way to categorize psychodermatological disorders is by the underlying psychopathological condition. They are depression, anxiety, psychosis (i.e. delusional disorder), and OCD. Specific psychotropic therapies are appropriate for each underlying psychopathology. Therefore, antidepressants are prescribed for depression, anxiolytics for anxiety, antipsychotics for psychosis, and anti-OCD agents for OCD.

Any of these psychopathologies can be found in the categories of psychodermatological disorders. The ultimate decision of the category of pscyhodermatological disorder and determination about the underlying psychopathology are made independently of one another.

Psychopharmacology in Dermatology:

Treatment of Depression

Dermatologists commonly encounter patients with depression. Patients with depression report difficulty feeling pleasure (i.e. anhedonia) or a depressed mood. In addition, they may report feelings of hopelessness, worthlessness, and extreme guilt. They may present with loss of appetite, changes in sleep pattern, decreased energy, weight changes, and difficulty concentrating. These symptoms may result in emotional distress, impairment of function, and significant occupational or social dysfunction.

SSRIs*:* The first line treatment for depression is administration of selective serotonin reuptake inhibitors (SSRIs). The mechanism of action is to selectively inhibit serotonin (5-HT) reuptake at the presynaptic membrane, leading to increased 5-HT at neuronal synapses. SSRIs include sertraline (Zoloft ®), paroxetine (Paxil ®), fluoxetine (Prozac ®), and citalopram (Celexa ®). Although fluvoxamine (Luvox ®) is an SSRI, it is not as easy to use because it can cause many adverse drug interactions with medications metabolized by cytochrome P450 (CYP450).

The *Physician's Desk Reference* or a similar reference of dosing guidelines for SSRIs should be consulted for dosing. The onset of clinical response to SSRIs is gradual because it begins at least two to three weeks after optimal dosage is reached. For complete therapeutic effect to be reached, it may take four to six weeks or longer. Partial responders may require a higher SSRI dose. If no improvement is observed after six to eight weeks, another SSRI might be considered or the patient should be switched to venlafaxine (Effexor ®) or buproprion (Wellbutrin ®). Paroxetine is initiated at a dose of 20 mg every morning and may be increased up to a maximum of 50 mg/day. Sertraline is started at 50 mg/day, up to a maximum of 200 mg/day. Citalopram is initiated at 20 mg/day up to a maximum of 40 mg/day. Escitalopram is started at 10 mg/day, up to a maximum of 20 mg/day. Furthermore, fluoxetine is started at 20 mg each morning, up to 80 mg/day. The most common side effects of SSRIs collectively include gastrointestinal effects such as diarrhea and nausea. However, taking the medication with food can relieve discomfort.

Doxepin*:* An alternative to SSRIs as first line therapy is doxepin (Sinequan ®). It has both antidepressant and strong antipruritic effects because it is a tricyclic antidepressant (TCA) as well as an H1 antihistamine. Therefore, doxepin is a preferable medication for depressed patients with neurotic excoriations. A common side effect for doxepin is sedation, which may be therapeutic for patients with agitated depression. The starting dose is 10 to 25 mg each day at bedtime for depression. It may be titrated up by 10-25 mg increments every two weeks to an antidepressant therapeutic range between 75 to 300 mg per day. It typically takes 2 weeks or more after the therapeutic dose is reached for its antidepressant properties to go into effect. If patients do not show a therapeutic response despite a large dose of doxepin for many weeks, a serum doxepin level should be tested to ensure that it is within the therapeutic range for depression; there is a wide interindividual variation [3]. In addition to sedation as a side effect, doxepin has other side effects similar to other TCAs, such as cardiac conduction disturbances (prolonged QT interval, atrioventricular block, intraventricular conduction delay), orthostatic hypotension, weight gain, and anticholinergic adverse effects (dry mouth, constipation, urinary retention, blurry vision).

Venlafaxine*:* Another medication to consider for depression is venlafaxine (Effexor ®). It is used for depression and anxiety [4-7]. Venlafaxine selectively inhibits serotonin and norepinephrine reuptake as a serotonin-norepinephrine

reuptake inhibitor (SNRI) [8]. It is produced in two formulations: an immediate release form and extended release (XR) form. For the immediate release formulation, the initial dosage is 75 mg/day in two separate doses with food. Then, the dose can be increased by 75 mg/day for partial responders. The therapeutic dose for the immediate release formulation is 75-225 mg/day twice daily. For the XR formulation, the initial dosage is 37.5 to 75 mg/day with food, with a maximum dose of 225 mg/day. In general, venlafaxine has benign side effects. Its most common side effects are nervousness and insomnia. Other common side effects include fatigue, nausea, sweating, dizziness, headaches, constipation, dry mouth, loss of appetite, and sexual dysfunction.

Buproprion*:* Buproprion (Wellbutrin ®) is a weak inhibitor of dopamine reuptake with some effects on norepinephrine uptake [9]. It is administered for depression. Notably, it has few sexual side effects as compared to SSRIs, and can promote normal sleep patterns for those with sleep difficulties [10-13]. Bupropion is administered in two formulations: immediate and sustained release. For immediate release, the initial dosage is 200 mg /day and may be taken as 100 mg twice daily. After four to seven days, the dosage can be increased to a total of 300 mg/day, divided into three times per day. The typical therapeutic dose is 200 to 300 mg/day, divided into two or three daily doses. For sustained release, the initial dosage is 150 mg/day in the morning. The therapeutic dose is 300 mg/day, given as 150 mg twice daily. Buproprion is well tolerated, but common side effects include headache, insomnia, agitation, dry mouth, nausea, tremor, and constipation. Seizure induction is a rare but serious side effect at doses of usually over 300 mg/day [14]. Therefore, it should be avoided in alcohol or drug abusers, or in bulimic patients because this condition can lower the seizure threshold.

Treatment of Anxiety

Dermatologists often have patients with anxiety disorder, excessive anxiety and stress that may be secondary to the negative social impact of a skin condition. They may also have agitation, difficulty concentrating, restlessness, and irritability. Somatic symptoms of anxiety include palpitations, dizziness, sweaty palms, lightheadedness, muscle aches, soreness, sleep disturbance, trembling, and difficulty breathing. These symptoms may cause impairment in functioning and subjective distress. The correct reatment of anxiety may depend on whether it is acute (short-term), often due to a specific situational stressor, or chronic. Anxiolytics, such as benzodiazepines and buspirone, and antidepressants may be prescribed.

Benzodiazepines*:* Benzodiazepines are typically used to treat acute situational anxiety, in which patients have adequate coping skills and typically recover after a few weeks. However, anxiety may exacerbate a skin disorder. Therefore, for patients with acute anxiety who have not used benzodiazepines before, the initial dosage with alprazolam (Xanax ®) of half a 0.25 mg tablet up to four times daily as needed is recommended. Although well tolerated, a common side effect for short-term benzodiazepine use is sedation, which resolves after several days of treatment. Initial administration of the medication, therefore, may be at night. Benzodiazepines may be addictive if used long-term, and thus, treatment should be limited to less than three to four weeks.

Buspirone*:* For chronic anxiety, the preferred medication is buspirone (Buspar ®) because it does not cause dependency or sedation. However, it has a delayed onset of action, and therefore, it cannot be administered on an as needed basis. It also cannot be used for acute situational stress because of its slow onset of action. It should be prescribed for at least two weeks before significant therapeutic effect is reached. Initial dosage is 15 mg/day divided into two doses. It can be increased to 15 mg twice daily after one week. The maximum therapeutic dosage is 60 mg/day. Buspirone has no serious adverse side effects. However, common adverse effects include fatigue, headache, dizziness, and nausea.

Antidepressants*:* For chronic anxiety, paroxetine at 20 to 50 mg/day, venlafaxine XR at 75 or 150 mg/day, and low-dose doxepin at less than 50 mg/day can be prescribed [15,16].

Treatment of Delusional Disorder

The most common delusional disorders encountered by dermatologists are the monosympotmatic hypochondriacal psychoses (MHP). Patients with MHP have “encapsulated” delusions, in which they have one specific hypochondriacal concern. The most common type of MHP is delusions of parasitosis (DOP), in which patients often have cutaneous sensations of crawling, biting, and stinging in addition to their delusion. Antipsychotics are recommended to treat delusional disorder.

Pimozide*:* Pimozide (Orap ®) is the most frequently used psychotropic treatment for DOP. It can be prescribed with a

starting dose of as low as half a tablet, 0.5 mg, daily. Extrapyramidal side effects such as restlessness and stiffness may occur, and therefore, the initial dose of pimozide should be low. Extrapyramidal side effects can typically be controlled with diphenhydramine (Benadryl ®) 25 to 50 mg every four to six hours as needed or benztropine (Cogentin ®) 1-2 mg four times daily as needed. The risk of tardive dyskinesia also exists, but the rate of occurrence is very rare owing to low dosage and short-term use.

Pimozide dosage can be increased by as little as half a tablet, 0.5 mg, increments; this is done slowly on a biweekly basis. Clinical improvement is usually observed when the patient reaches 3 to 5 mg of pimozide daily. The provider should consider checking an EKG at baseline to ensure the patient does not have an arrhythmia or prolonged QT interval. Even for patients without cardiac conduction abnormalities, it may still be worthwhile to obtain a pre-treatment EKG.

When the therapeutic dose of pimozide is reached, it should be maintained for one to three months. If the patient continues to show improvement whereby formication becomes minimal, the dosage can then be gradually decreased by 1 mg every two to four weeks. Often, the patient remains convinced that he or she did have an infestation. Even though these patients usually never change their mind, successful treatment with pimozide typically produces a situation in which the patient continues to believe that he or she did have an infestation but that it no longer matters because the patient now is convinced that the organism has been destroyed.

***Atypical antipsychotics**:* Atypical antipsychotics that are most commonly administered for delusional disorder include risperidone (Risperdal ®), olanzapine (Zyprexa ®), and quetiapine (Seroquel ®). They are effective as dopamine and serotonin receptor antagonists. Collectively, these medications are less likely to cause extrapyramidal side effects and tardive dyskinesia because they are more selective in binding to receptors related to the antipsychotic effects but not to receptors related to extrapyramidal effects or tardive dyskinesia as compared to other psychotropic medications [17-20]. However, these medications should be cautiously used in those with a history of seizures or other conditions that may lower the seizure threshold such as Alzheimer's disease.

Risperidone is started at 1 mg daily, and may be gradually increased every two weeks to 3 to 5 mg/day in divided doses. The most common side effects of risperidone are dizziness, anxiety, and rhinitis. Risperidone may also induce QT interval prolongation. However, risperidone may be recommended for the elderly because it is the only atypical antipsychotic with limited anticholinergic side effects [21].

Olanzapine is started at 5 to 10 mg/day. The therapeutic dosage is typically 10 to 15 mg/day. The most frequent adverse effects are sedation, weight gain, and anticholinergic effects.

Quetiapine is initiated at 25 mg twice daily. Therapeutic dosage is usually 150 to 750 mg/day. The most common side effects are anticholinergic effects and somnolence. Quetiapine has also been known to cause orthostatic hypotension [22].

Treatment of OCD

Patients with OCD have an obsession, or an intrusive thought, and a compulsion, which is a stereotyped, repeated behavior that is difficult to control. Some examples of OCD in dermatology include hair loss caused by trichotillomania or compulsive hair pulling, excoriations associated with compulsive skin picking or neurodermatitis, and eczema related to excessive washing. SSRIs are considered a first-line treatment for OCD. However, patients with OCD may need higher doses of SSRIs than are required for depression; they may also take longer to respond. Therapy may be continued for at least six months to one year after therapeutic response is reached [23].

Psychotropic Agents to Treat "Traditional" Dermatological Conditions

The most well documented psychotropic medications that are useful in treating actual dermatologic conditions are TCAs, doxepin, and amitriptyline [24-29]. Doxepin is used for pruritus and urticaria. Doxepin may be prescribed in a dose as small as 10 mg daily at bedtime and titrated to an optimal dose with a maximum dosage of 300 mg at bedtime if tolerated. Amitriptyline is preferred for cutaneous manifestations of pain, including burning, biting, stinging, and chafing. Amitriptyline can be initiated at a dose of 25 mg at bedtime and titrated up. As an analgesic, the usual dose is 50 mg per day or less. Side effects are similar to doxepin and include anticholinergic, cardiac, sedative, and alpha-adrenergic side effects.

Discussion and Conclusion

There is a high prevalence of dermatology patients with psychiatric disorders or psychosocial issues. Commonly, SSRIs are the first-line pharmacological therapies for depression and OCD symptoms. Anxiolytics are preferred for anxiety and pimozide and atypical antipsychotics are preferred for delusional disorders in dermatology.

Although psychiatric referral is generally preferable for patients with psychodermatological conditions, these patients often refuse the referral. Therefore, it is important for dermatologists to be familiar with and possibly prescribe psychotropic medications, which may be the only source of help for many of these patients who will not go to a mental health professional. Although we provide a comprehensive and up-to-date guide for using psychotropic medications here, we recommend that the reader consult the *Physician's Desk Reference* for a more detailed description of administration of these therapies for further enrichment.

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