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N-Acetylcysteine Use in Treatment of Excoriation

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by

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Abstract

This paper examines the research for the use of *N*-acetylcysteine in patients diagnosed with excoriation disorder. Pubmed and CINAHL databases were searched finding articles for the last five years. Search terms included “excoriation,” “skin-picking disorder,” and/or “*N*-acetylcysteine” in varying contexts. Multiple articles were found with one specific randomized controlled trial identifying the use of NAC in excoriation disorder. Additional research was found on the use of NAC in other skin disorders and obsessive-compulsive related disorders. The research is generally positive but inconsistent due to the minimal studies conducted. Overall, the use of NAC for excoriation could provide positive benefit, but ultimately additional study is needed.

Background

Skin picking disorder is a common cause of physical and emotional distress dating back nearly 150 years (Jagger, Sterner, & William, 2016). Skin picking disorder, now known as excoriation disorder in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorder* (DSM-5), was originally thought to be a dermatological disorder rather than a psychiatric disorder (Jagger et al., 2016). Excoriation disorder includes repetitive behaviors of picking, scratching, squeezing, digging, rubbing, or biting at the skin resulting in tissue damage in which negative emotions both precede and follow the habit. Between 1.4% and 5.4% of the population suffer from this disorder, with it being more likely to occur in women. Due to the damage caused to the skin from the behavior, there is often negative outcomes such as infections, scarring, and ulcerations which cause increased distress in the patient (Selles et al., 2016).

Because of the emotional ties to the picking and the impaired functioning in multiple areas of the patient's life, this disorder is placed in the DSM-5 (5^{th} edition; American Psychiatric Association [APA], 2013) under obsessive compulsive and related disorders (Jagger et al., 2016). Additional criteria for excoriation disorder include multiple attempts to decrease or stop the behavior and the behavior must not be attributable to other medical or mental disorders or substance use (APA, 2013). Selles et al., (2016) reports there have also been some ties to body dysmorphic disorder, as the patient will frequently see flaws in the skin which leads to the picking behavior. Comorbidities of excoriation disorder include depressive disorders, anxiety disorders, obsessive-compulsive disorder (OCD), and trichotillomania (Jagger et al., 2016).

N-acetylcysteine (NAC) is an over the counter amino acid supplement which is generally easily accessible and affordable for use (Oliver et al., 2015). NAC increases the level of glutamate in the nucleus accumbens, thus may target the core symptoms of obsessive-

compulsive related disorders such as excoriation disorder (Amino acid reduces symptoms in persons with skin-picking disorder, 2016). NAC is generally safe for consumption with few common side-effects listed, including nausea, vomiting, foul taste, and constipation (Jones, Kuethen, & Greenberg, 2018). Most of these side-effects were mild and ceased after two weeks of use of NAC. Average dose range is 2400-3000 mg daily in divided doses, lower doses may be used if benefit is found or side effects are noted at higher doses (Oliver et al., 2015).

Case Report

C is a 26-year-old African American female who presents for ongoing depression and anxiety. She is seen for a medication evaluation after being referred from her therapist at the community health center. C recently moved back to the area to live with her mother after ending an abusive relationship in June of this year. She has a long history of anxiety and depression. She reports that she has always been a worrier since she was a child. She endorses symptoms of excessive anxiety and worry most days, difficulty controlling the worry, irritability, difficulty concentrating, and trouble falling asleep due to her thoughts racing. She calls herself moody and reports getting easily embarrassed which leads to her coming off as irritated to others. About one to two weeks out of the month, she reports periods of depressed mood, sadness, excessive crying, lack of interest and energy, hopelessness, worthlessness, guilt, and isolation. She reports these symptoms generally start the week prior to her menstrual cycle and are mostly improved by the time she has completed her cycle. From her report, it appears that this happens nearly every month and the symptoms never last more than two weeks.

C endorses sexual trauma as a child: she has ongoing intrusive thoughts, nightmares related to the events, flashbacks, and avoidance of situations that remind her of the events. She also reports picking at her legs and groin area, generally when there is an ingrown hair. She

endorses that this is nearly every day and can last up to a half-hour at a time. She reports significant distress related to this and reports that she feels ugly because of the sores that this has caused. In the past, she has developed sores so large that she had to seek medical care for treatment.

She denies any symptoms of psychosis, mania, or attention deficit hyperactivity disorder (ADHD). She reports being a binge-drinker in college but considers this age appropriate and consistent with her sorority activities. She reports she rarely drinks now and not to the point of intoxication. She reports using marijuana occasionally in college but did not like it. She denies any other drug use. She denies any suicidal thoughts; denies homicidal or violent ideation.

C endorses symptoms of anxiety and trauma since she was a child. She reports always being a worrier. She has a history of self-harm including cutting, hitting herself, scratching her face, and pulling her hair. She describes this as somewhat of a trauma response, as it is generally related to fighting with her mother or her ex-boyfriend. She reports one suicide attempt at the age of 20; stating she took 64 aspirin and a couple of her mother's sleeping pills to end her life after fighting with her mother. She did end up making herself vomit the pills and informed her mother who gave her activated charcoal pills for the next three days. She was not hospitalized and fully recovered. She reports no previous psychiatric hospitalizations.

C first saw a nurse practitioner (NP) two years ago who she reports diagnosed her with borderline personality disorder and post-traumatic stress disorder (PTSD). She reports taking bupropion SR and fluoxetine for the past two years, although she has not taken these consistently due to financial concern. She denies any history of psychosis, mania, or substance use disorders. In addition to the above medications, she reports taking another antidepressant in the past at a low dose but does not remember the name of it.

In regard to her family history, C indicates many of her family members likely have un-diagnosed psychiatric problems, as she grew up in a low socioeconomic area and most people she knows suffered from some type of abuse. She reports her mother is currently in outpatient treatment for trauma but is not sure she has been diagnosed with. She states that growing up, she frequently saw her mother struggling with her mental health and self-image. For example, C witnessed her mother punching herself in the stomach. There is no reported family history of psychosis, bipolar disorder, or suicide.

C's social history includes growing up with her mother in Iowa and living with her mother and grandmother for most of her younger years. She suffered from ongoing emotional, physical, and sexual abuse as a child. C does not have a relationship with her father and has no siblings from her mother but has some half-siblings from her biofather that she is not in contact with. She graduated from high school and completed her bachelor's degree in psychology. Since graduating from college, she has been working as a nail technician in between Florida, North Dakota, and Iowa, which she enjoys. She denies history of arrest. She has no children and has never been married.

Upon initial assessment, C is diagnosed with generalized anxiety disorder, post-traumatic stress disorder, excoriation disorder, and premenstrual dysphoric disorder. Recommendations for treatment at the initial visit include: Fluoxetine 20 mg every day, increased due to lack of benefit at a lower dose and ongoing depressive and anxiety symptoms. Discontinued bupropion due to the ongoing anxiety and lack of benefit for depressive symptoms. Continue with cognitive behavioral therapy (CBT) with her current therapist.

Literature Review

One randomized controlled trial has been completed on the use of *N*-acetylcysteine (NAC) for excoriation disorder. Grant et al. (2016) produced a randomized, double-blind trial including 66 adults that met criteria for excoriation disorder. Of those 66 adults, 31 were randomly assigned to the placebo and 35 assigned to NAC. The total population of the study consisted 59 women and seven men with a mean age of 34.8 years. The mean age for onset of the disorder was 12.2 years old and most (85%) had never sought mental health treatment for the disorder. None of the participants were receiving psychotherapy at the time of the study and 33% of the participants were taking a psychotropic medication for comorbid disorders. Each participant taking a medication prior to the onset of the study had to show stability on that medication for at least the past three months and changes could not be made during the time of the study without being dismissed. Thirteen participants withdrew throughout the course of the study, all giving the time needed to dedicate to the study as their reason for withdrawal.

The starting dose of NAC for the assigned group was 1200 mg per day and was increased to 2400 mg per day by week three; at week six the final dose of 3000 mg per day was reached. Researchers used the Yale-Brown Obsessive-Compulsive Scale modified for Neurotic Excoriation (NE-YBOCS) along with additional scales to measure severity of the illness, improvement in skin picking symptoms, anxiety, disability from illness, and quality of life. Using the Clinical Global Impression-Improvement scale, there was a significant improvement by the end of the study in those using NAC for treatment. Forty-seven percent (15 out of 32) of the participants assigned to the treatment group showed much or very-much improved compared with only 19% of the placebo group. The NE-YBOCS total score demonstrated a 38.3% decrease in skin-picking symptoms from the NAC group compared to 19.3% for the placebo group (Grant et al., 2016).

Grant et al. (2016) concludes NAC is safe and more effective for excoriation disorder. This study supports previous findings that manipulation of the glutamate system by pharmacotherapy may have effects on compulsive behavior. Because of the small number of participants in the study, the researchers encourage further study on this specific drug in larger placebo-controlled studies. Longer research times are also encouraged, as it is hypothesized that NAC would likely be needed long-term to control the symptoms of excoriation disorder.

A meta-analysis and systematic review of treatment for excoriation disorder completed in 2016 did not find much use of *N*-acetylcysteine (NAC), but rather pharmacologic treatments such as SSRIs and lamotrigine and the use of behavioral interventions (Selles et al., 2016). Behavioral treatments were shown to be the first line of treatment for excoriation disorder due to the effectiveness as well as the low risk for side effects. SSRIs, specifically fluoxetine, would also be recommended for use as they have been shown effective in randomized controlled trials, but the risks of side effects must be taken into consideration by both the clinician and patient prior to use. NAC did come up in the results for the treatment of excoriation disorders with recommendations for further study before recommendations could be drawn for use (Selles et al., 2016).

A case series for patients with Prader-Willi syndrome who suffer from excoriation disorder was completed and was mentioned in many of the systematic reviews but was unavailable to this author for review. According to Janeczek et al. (2019), a study was completed on 35 patients, all who improved or whose symptoms completely resolved with the use of NAC for excoriation disorder in patients also diagnosed with Prader-Willi syndrome. This review by Janeczek et al. (2019) was completed for the use of NAC in dermatology disorders and also found benefit for the use of NAC in disorders such as nail-biting behavior, trichotillomania,

bullous morphea, atopic dermatitis, and pseudoporphyria among others. This review concluded NAC could potentially serve as a safe and effective option for a variety of dermatologic disorders.

Recommendations for assessment and treatment of trichotillomania and excoriation were written by Jones, Keuthen, and Greenberg (2018). Their recommendations shared both therapy and pharmacotherapy treatment guidelines for patients suffering from these disorders. The first line of treatment for excoriation is habit reversal training and stimulus control followed by acceptance and commitment therapy (ACT) and dialectical behavior therapy (DBT). Pharmacologic interventions include the use of *N*-acetylcysteine (NAC), selective serotonin reuptake inhibitors (SSRIs), and antipsychotics. NAC has been shown more effective for use in treatment excoriation compared to placebo in one randomized controlled trial (RCT). Case study using therapeutic interventions along with fluoxetine and NAC showed a drastic reduction in the intensity and frequency of hair pulling and skin picking behaviors for an 18-year-old female patient. Although this patient was not completely in remission, she suffered less from the negative effects of the disorder.

It has been advised by Jones et al. (2018) to start NAC for any individual presenting with excoriation disorder as it has proven effective and has a favorable side-effect profile. Downsides to use of NAC include dislike of taste, adverse side effects, and expense due to lack of insurance coverage. Side effects may include nausea, vomiting, constipation, and diarrhea. Dose range of NAC is from 2400-2000 mg daily in divided doses. Because NAC is hypothesized to work on glutamate modulation, it may be more effective for patients performing skin picking behavior consciously versus those who perform these behaviors automatically while doing other things such as watching TV or driving (Jones et al., 2018).

A systematic review for the treatment of excoriation disorder was completed by Lochner, Roos, and Stein (2017) reviewing treatment suggestions from 1996 to 2017. Nonpharmacological treatment including cognitive-behavioral therapy, self-help treatments, habit-reversal therapy, and acceptance and commitment therapy have been found to have positive impact on excoriation disorder. SSRIs, lamotrigine, opioid antagonists, and inositol were found as possible treatments for excoriations disorder. Opioid antagonists and inositol have limited research available with case studies and uncontrolled trials. The randomized controlled trial completed by Grant et al. (2016) was referred to for the positive benefit found with the use of NAC for excoriation disorder as a glutamatergic agent. This systematic review does suggest that additional research and improvement of accessibility to efficacious treatments is needed for the treatment of excoriation disorder.

N-acetylcysteine in the treatment of obsessive compulsive and related disorders was reviewed by Oliver et al. (2015) and found promising results. NAC has demonstrated neurochemical, antioxidant, anti-inflammatory, mucolytic, and hepatoprotective activity with the additional benefit of ameliorating oxidative stress possibly providing benefits to brain health. NAC forms cysteine in the body which is used for glutathione (GSH) production. GSH is the most potent and abundant endogenous antioxidant in the body. Ultimately, NAC is responsible for restoring extracellular glutamate in the body.

Glutamate is hypothesized to play a role in obsessive compulsive disorder (OCD) and obsessive-compulsive related disorders (OCRD) (Oliver et al., 2015). Reduced levels of glutamate have been found in the anterior cingulate of women diagnosed with OCD. The neurotransmitter glutamate may also play a role in the poor cognitive processing in patients with OCD and evidence suggests glutamate metabolism abnormalities are evident in patients with

OCD. This systematic review found 11 studies, over half of which were case reports, and all results were promising but inconsistent. In the placebo-controlled studies reviewed, there were positive benefits for each NAC group, but there was not complete remission in either study. Differences in the lengths of studies, disease severity, co-morbidities, and neurobiological differences may account for the lack of consistent treatment responses in the cases identified.

Summary

Currently there is only one randomized controlled trial for the use of NAC in patients with excoriation disorder available. Further study must be completed on the use of NAC in this population to give definitive answers on the question of whether it is effective for treatment of excoriation disorder. Longer length of trials and larger cohorts with all ages and characteristics will provide more specific therapeutic indications of the use of NAC.

Implications

After the research was considered, NAC will be started on the above patient. Side effects, cost of treatment, and risks versus benefits were all weighed with the severity of the symptoms and psychosocial impact kept in mind. Initial dose to start will be 600 mg twice a day with an increase to 2400 mg per day in divided doses over the course of the next three weeks with a target dose of 3000 mg a day if tolerated. In addition to NAC, the patient should engage in cognitive behavioral therapy, as used in conjunction there will likely be a greater impact. With her therapist, the use of habit reversal training and stimulus control may also prove beneficial.

Conclusion

Grant et al. (2016) demonstrated a positive impact in the use of NAC for excoriation disorder and reminded researchers of the additional research that is necessary before this can

become a standard of care. The sample size was small, and the length of the trial could be extended for further benefits and risks to be identified. When utilizing NAC as a treatment option, there will be some unknowns due to limited research, but the risk is low considering the adverse effects that were found here and in previous uses of NAC.

Additional treatment methods were provided by other researchers with some benefit and possible risks noted. When treating a patient with excoriation disorder, it is imperative for the clinician to weigh the risks and benefits of treatment and use any possible treatment methods with caution, as there is not significant research in this area. Ultimately, patients should be given a full disclosure on the possible treatment options and risks and benefits of each, as they are the ultimate manager of their care.

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