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**Letter to the Editor**

# N-acetylcysteine in skin picking disorders

Sir,

We have come across a selection of case studies referencing the effective use of N-Acetylcysteine (NAC) in the treatment of skin picking disorder and other impulsive behaviours. NAC's pivotal roles in modulating oxidative stress, influencing inflammatory pathways and supporting skin barrier function are thought to be contributing factors in resolving skin picking disorders.[1] Skin picking disorder (SPD) is a "repetitive skin manipulation, resulting in visible tissue damage and the impairment of social functioning".[2] Despite the huge impact of this condition on quality of life, there have been inconsistent results in successfully treating this condition using current therapeutic modalities.[2]

NAC exerts its dermatologic effects through several fundamental mechanisms. Firstly, through its antioxidant activity, by its ability to donate cysteine. Cysteine is used in the production of glutathione, the body's most potent endogenous antioxidant, neutralising reactive oxygen species (ROS) and mitigating oxidative damage to skin cells. This likely works in SPD by reducing oxidative stress and subsequent damage to brain neurons, however more research is needed on the specifics of oxidative damage leading to impulse control disorders.[4]

Secondly, NAC acts as a neurotransmitter modulator, its hydrolysis yields cysteine which is then exchanged for glutamate in the brain. This has the cascading effect of inhibiting further glutamate release in the nucleus accumbens.[4]

Further, studies have shown excess of glutamate levels leads to neuronal damage, as evidenced by elevated levels of glutamate in the orbitofrontal cortex and caudate nucleus in people with obsessive-compulsive disorders (such as SPD).[1] Thirdly, through its anti-inflammatory action, NAC inhibits nuclear factor kappa B (NF-κB), reducing the expression of pro-inflammatory cytokines, such as TNF-α and IL-1β.[5] The decreased in the levels of TNF- α and IL-1β have been demonstrated in mice model studies treated with NAC.[6]

Moreover, by modulating oxidative stress and inflammatory mediators, NAC enhances keratinocyte proliferation and differentiation, aiding skin barrier repair and wound healing.[7]

It has been shown that NAC can be used via various delivery routes including oral, intravenous and topical. While topical NAC has a major limitation of its bioavailability being less than 3%, the main advantage is its safety and milder side effects (burning, erythema and pruritus).[1,3] The main disadvantages of oral NAC include that it is a white crystalline powder with a sour taste and the common side effect of gastrointestinal problems (occurring in 7.1% of patients in one study).[2] The sour taste can be countered by mixing with fruit juice or soft drinks.

The main advantages of the oral preparation are that it is cost effective, is generally well tolerated, with a bioavailability of around 5% and excretion through the renal (30%) and intestinal (70%) routes.[1] Intravenous NAC has the highest half-life and bioavailability, but the adverse effects are considered more severe which includes anaphylactoid reaction, urticarial rash, pruritus, angioedema, bronchospasm and hypotension. In addition, since NAC has not been studied sufficiently in pregnancy and breastfeeding, the current guidance suggests not use it unless necessary.[3]

There have been a multitude of studies performed and case reports outlining the effectiveness of N-Acetylcysteine in skin picking disorders. Miller and Angulo in 2014 found dosage of 450-1200 mg of NAC to be 71% effective at completely resolving skin picking (in a 12-week pilot study involving 25 paediatric and adult patients with skin picking and concurrent Prader-Willi syndrome).[8]

Silva-Netto et al, found that dosage of 1200-1800 mg of NAC for 10 months led to substantial to complete resolution of skin picking in the 3 adult patients involved in the case study.[9] The largest study we came across is a randomised double-blinded placebo-controlled trial in 66 adults with skin picking disorder using dosage of 1200-3000 mg/day of NAC orally for 12 weeks.

This study concluded there was statistically significant (using the modified yale-brown obsessive-compulsive scale and clinical global impression-severity scale) reduction in the urge or craving to pick the skin compared to placebo. Nonetheless, there was no significant improvement in quality of life or psychosocial functioning, which was attributed to a small sample size or short follow up length.[10]

In conclusion, N-acetylcysteine has shown to be a promising treatment option for skin picking disorder and we would recommend further research including randomised controlled trials in this subject. This should include a long follow up period (with regular interval follow-ups) and patients should be counselled of the importance of continuing to take the N-Acetylcysteine for the study duration.

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