

# Use of N-acetylcysteine in cannabis-dependent adolescents.

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**Clinical Question:** Can N-acetylcysteine use in conjunction with cessation therapy and contingency management improve successful cannabis cessation in cannabis-dependent adolescents?

## **Clinical Bottom Line**

1. In a double-blinded randomized controlled trial of cannabis dependent adolescents, findings support use of N-acetylcysteine (NAC) along with psychosocial treatment yield a positive primary cessation outcome.
2. NAC treatment group had greater than twice the odds compared with the placebo group of having negative urine cannabinoid tests while on treatment.
3. Secondary abstinence outcomes favored the NAC treatment group but were not statistically significant.
4. NAC was well tolerated with minimal adverse effects.

## **Evidence Summary**

1. 116 treatment-seeking cannabis dependent adolescents were enrolled in an 8-week double blind, randomized, placebo-controlled trial conducted between September 2009 and January 2011.
2. Exclusion criteria: Enrolled in substance use treatment, current co-morbid dependence aside from nicotine, acute unstable psychiatric or medical illness, history of adverse reaction to NAC, on carbamazepine or nitroglycerin, pregnant female participants.
3. Participants were randomly assigned to either N-acetylcysteine (1200 mg) or a placebo twice daily for 8 weeks along with weekly cessation counseling (<10mins) and a contingency management program. A follow up assessment was done 4 weeks post-treatment.
4. Efficacy was measured by urine cannabinoid testing (Twice weekly, one of which was random).
5. Intent-to-treat approach was used wherein those who were lost to follow-up or were absent from visits were coded as having a positive urine cannabinoid test at every missed visit.
6. Of 116 enrolled, 106 (92%) received at least 1 dose of study medication. 70 (60%) were retained through completion of treatment, and 54 (47%) were retained through post-treatment follow-up.
7. NAC treatment group had more than double the odds of negative urine cannabinoid tests during treatment compared with the placebo group. (Odds ratio = 2.4, 95% CI =1.1-5.2, p=0.029)
8. Negative urine cannabinoid testing at post follow up visit numerically favored the NAC treatment group but had no statistical significance. It was a similar case with the secondary efficacy measures such as time to first negative urine cannabinoid test and end of treatment abstinence.
9. The adjusted primary analysis model yielded the following results:
  - Participants with negative baseline urine cannabinoid tests had nearly 6 times the odds of negative tests during treatment. (OR = 5.9, 95% CI =2-17.7, p=0.020).
  - Participants with fewer baseline years of cannabis use had greater odds of negative urine tests during the study. (OR = 1.4, 95% CI=1.1-1.7, p=0.047).

- Participants with major depressive disorder had lower odds of negative urine test during the treatment, though this result had no statistical significance. (OR=0.3, 95% CI=0.1-1, p=0.062)
10. Intent to treat analysis yielded the Number Needed to Treat (NNT) to achieve negative cannabinoid testing was 7.3 for the treatment portion of the study and 11.6 for post-treatment follow-up visit.

## Comments

1. Reported to be the first double-blind randomized placebo controlled trial of pharmacotherapy for cannabis dependence in any age group yielding a positive primary cessation outcome via intent-to-treat analysis.
2. Limitations of the study include: single dosing regimen over a short treatment period studied, small sample size, narrow age range, and low rates of psychiatric comorbidities.
3. Other limitations are: a possible higher false positive rate due to coding positive urine cannabinoid test at every missed visit and those patients lost to follow-up or were absent from visits; a short (4 week) post treatment follow-up period versus a long-term 6-8 month follow-up to assess the true abstinence rate.
4. This study opens the possibility of using N-acetylcysteine as a possible adjunct to other psychosocial treatment offered for addictive behaviors .<sup>2,3,4</sup>

## References

1. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE: Monitoring the Future: National Results on Adolescent Drug Use: Overview of Key Findings, 2011. Ann Arbor, University of Michigan, Institute for Social Research, 2012
2. Moussawi K, Pacchioni A, Moran M, Olive MF, Gass JT, Lavin A, Kalivas PW: N-Acetylcysteine reverses cocaine-induced metaplasticity. *Nat Neurosci* 2009; 12:182–189
3. Zhou W, Kalivas PW: N-acetylcysteine reduces extinction responding and induces enduring reductions in cue- and heroin induced drug-seeking. *Biol Psychiatry* 2008; 63:338–340
4. Rodrigues-Barata AR, Tosti A, Rodríguez-Pichardo A, Camacho-Martínez F. *Int J Trichology*.2012 Jul;4(3):176-8. doi: 10.4103/0974-7753.100090. N-acetylcysteine in the Treatment of Trichotillomania. Department of Dermatology and Venereology, Hospital Universitario Virgen Macarena, Seville, Spain.