Side- effects of nasal steroids use to treat pediatric obstructive sleep apnea syndrome

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns. Adenotonsillectomy is the primary treatment for childhood OSAS which is expensive and invasive. So, alternative treatments like intranasal corticosteroids are desired. However, the side effects of this treatment need to be studied given that exposure to systemic corticosteroids is directly related to the development of side effects including suppressing the hypothalamic–pituitary–adrenal-axis leading to adrenal crisis and growth suppression. This project aimed to study the side effects of intranasal corticosteroids (NCS) by evaluating growth and adrenal suppression. We hypothesized that NCS in the dosage used will result in a significant number of serious adverse events in the NCS group compared to the placebo group.

Methods

- Secondary analysis of a randomized double-blind, placebo-controlled trial designed to analyze the efficacy of NCS to treat OSAS in children
- Participants: Children aged 5-12 years (n=134)
- Children were first randomly assigned in 2:1 fashion to a 3-month course of NCS or placebo, at which time PSG and baseline tests were repeated
- Children in the NCS group were further randomized in 1:1 fashion to ongoing NCS vs placebo for an additional 9 months (a total of 12 months in the trial). See Figure 1.
- Blood was drawn at patient visits to be tested (cortisol and adrenocorticotropic hormone (ACTH)) at the lab and its results were stored in Redcap database.
- Collected data was analyzed using **Stata 16.0** with t-tests and a p-value < 0.05 as the criterion for statistical significance.

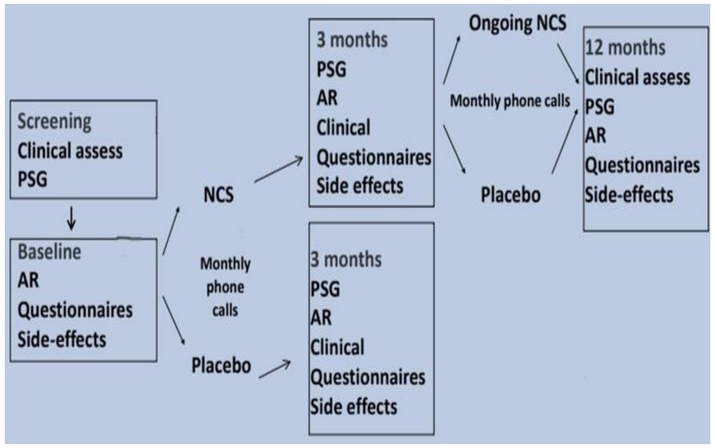


Figure 1: Randomization process of this study at 3 months, 9 months and 12 months

Results

Characteristic	INCS Arm	Placebo Arm
N	91	43
Age (yrs.)	8.2 ± 2.2	8.1 ± 2.0
Gender		
Females	47 (52%)	20 (47%)
Race		
African American	74 (81%)	35 (81%)
Caucasian	11 (12%)	5 (12%)
Other	6 (7%)	3 (7%)
Hispanic Ethnicity	7 (8%)	5 (12%)
Anthropometric Measures		
Weight (kg)	37.5 ± 18.2	36.3 ± 15.8
Height (cm)	131.9 ± 15.5	131.5 ± 13.5

Table 1: Baseline characteristics of the study group

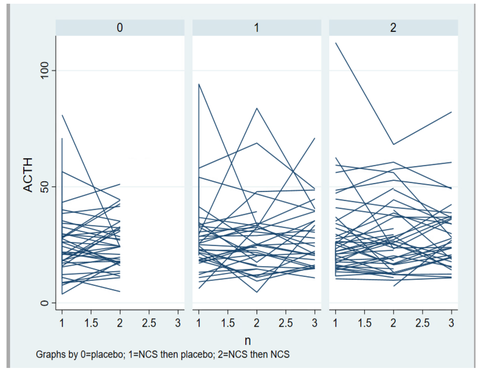


Figure 2: Comparison model that shows change in ACTH levels over time by treatment group adjusted for age and sex. Note: X-axis is labeled as visit, so 1= base line visit, 2= 3-month visit…

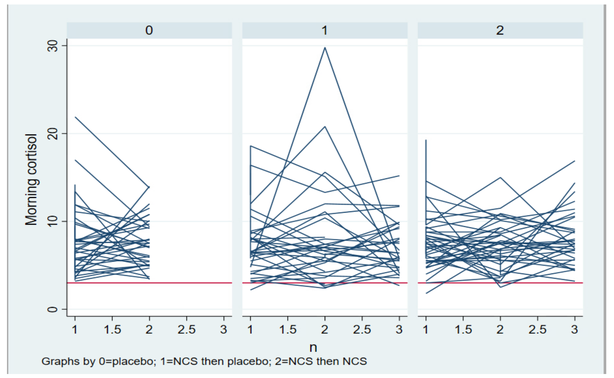
	Morning Cortisol	ACTH	Spine BMD
Baseline	7.93 (7.41, 8.46)	27.73 (26.00, 29.45)	0.087 (-0.089, 0.26)
3 months	8.18 (7.87, 8.48)	27.57 (26.69, 28.44)	0.16 (-0.018, 0.34)
P value	0.47	0.87	0.55

Table 2: Comparison of baseline and three-month adrenal and growth parameters after the administering of NCS

Analysis done using Stata after collecting and verifying data through Redcap

- No real association between the adrenal suppression and NCS use
- No significant difference (P > 0.05) in the cortisol and ACTH levels between placebo and NCS groups
- No significant correlation (P = 0.55) was found between the spine BMD measurements before and after the NCS treatment of the participants.

Figure 3 : Comparison model that shows change in cortisol levels over time by treatment group adjusted for age and sex. Note few values dropped below the threshold for adrenal suppression for any treatment group. X-axis is labeled as visit, so 1= baseline visit, 2=three-month visit…



Conclusions

- No association between ACTH, cortisol, or DXA measurements and NCS use suggests that there is not a relationship between NCS and adrenal or growth suppression; therefore, clinicians may consider risk-benefit ratio before recommending NCS treatment for OSAS.
- There is no statistically significant change from baseline to 3-month values for morning cortisol or ACTH which signifies that NCS usage does not cause adrenal suppression.
- There is no statistically significant change from baseline to 3-month values for spine bone mass density, suggesting that NCS usage does not induce growth suppression.
- In summary, although the overarching, primary trial does not support NCS usage to treat OSAS, usage does not seem to negatively impact the child.

Next Steps

- Finalize and further current data analysis of adrenal suppression and growth measurements using STATA
- Future prospective studies could evaluate long term side effects of NCS as a treatment of childhood OSAS by following subjects for years and investigate NCS in infants and toddlers
- Pursue paper publication in a peer-reviewed journal

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References

Bensch, Greg W. "Safety of intranasal corticosteroids." *Annals of Allergy, Asthma & Immunology* 117.6 (2016): 601-605.

Dahl, Ronald. "Systemic side effects of inhaled corticosteroids in patients with asthma." *Respiratory medicine* 100.8 (2006): 1307-1317.

Kuhle, Stefan, et al. "Anti-inflammatory medications for obstructive sleep apnoea in children." *Cochrane Database of Systematic Reviews* 1 (2020).