

Abstract S29 Figure 1 Change in cough frequency over time (Full Analysis Set)

Introduction CS1002 contains diphenhydramine/ammonium-chloride/levomenthol in a demulcent preparation. We conducted a randomised controlled trial to compare the efficacy of CS1002 with Bell’s Simple Linctus (BSL).

Methods 163 subjects with acute cough associated with upper respiratory tract infection, URTI (onset ≤ 7 days and cough severity VAS ≥ 60 mm), presenting to pharmacists (64%) or general practitioners were randomised to CS1002 or BSL. The subjects (mean age 39 years, 57% female) were instructed to take their medication four times daily (5/5/10/10 ml) for 7 days or until resolution. Investigators were blinded to the treatment allocation. The primary analysis, cough severity VAS (0–100) was ANCOVA in an intention to treat population.

Results CS1002 (n = 82) compared to BSL (n = 75), after 3 days, was associated with a greater reduction in cough severity (adjusted mean(SE) difference 5.9 (4.3), p = 0.18), cough sleep disruption VAS (mean diff 11.6 (4.5), p = 0.01) and cough frequency VAS (mean diff 8.1 (4.1), p = 0.05, Figure 1). There was a greater improvement in QOL (LCQ-acute) with CS1002 compared to BSL after 5 days; mean diff 1.2 (0.6), p = 0.04. The reduction in cough severity with CS1002 was similar in dry/

chesty/tickly categories of cough. Cough resolved after 3 days in 24.4% of CS1002 subjects compared to 10.7% BSL, p = 0.02. CS1002 was well tolerated, similar to BSL.

In conclusion We have conducted the largest RCT in URTI with validated outcome measures. CS1002 reduced the impact of cough associated with URTI with a greater reduction in cough frequency and sleep disruption and improvement in QOL and cough resolution compared to BSL.

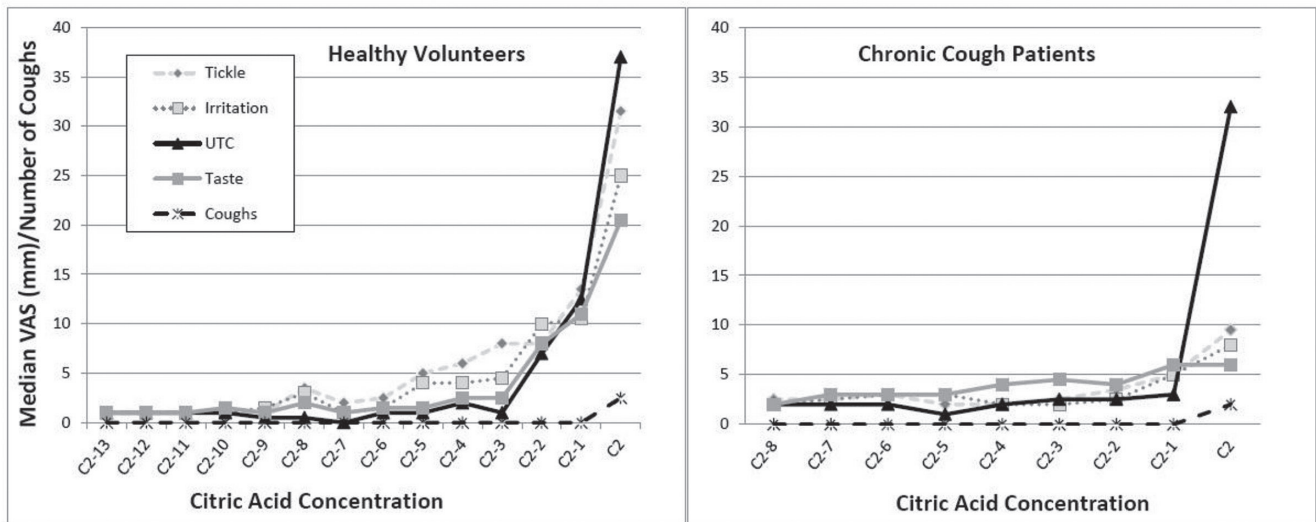
S30 SENSATIONS ASSOCIATED WITH EXPERIMENTALLY EVOKED COUGH: A COMPARISON OF CHRONIC COUGH PATIENTS WITH HEALTHY CONTROLS

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Introduction and objectives Cough is generally considered a protective airway reflex, however emerging evidence suggests chronic coughing is provoked by noxious sensations from the airway and serves to relieve these sensations. We have found patients with unexplained chronic coughing identify sensations of irritation, tickle (throat) and the urge to cough (UTC) as important sensations provoking coughing. We hypothesised that inhaling low dose tussive agents would evoke similar sensations and could provide a model for investigating chronic cough.

Methods Twelve chronic cough patients (mean age 61.4 yrs, 75% female, median cough duration 7 yrs) and 10 healthy volunteers (mean age 48.8 yrs, 40% female) inhaled increasing concentrations of citric acid from a dosimeter (0.01–4 M, 18 ascending concentrations). Following each inhalation subjects rated irritation, tickle, UTC and taste on 100 mm visual analogue scales (VAS; 0 mm = none and 100 mm = worst). The experiment continued until subjects coughed at least twice on any concentration of citric acid (C2). Somatosensory amplification score (SSAS) and State Trait Anxiety Index (STAI) were also collected. For the analysis, VAS data were aligned by the C2 concentration and sensation VAS scores compared using Mann-Whitney U tests. STAI scores were also compared with Mann-Whitney U tests and SSAS with an independent T test.



Abstract S30 Figure 1

Results The chronic cough patients had a much lower C2 than healthy controls (median 0.094 vs. 0.5M, $p = 0.009$). The UTC VAS and coughs evoked were similar at C2 and for the preceding concentrations in both groups, Figure 1. However, tickle, irritation and taste were rated more highly in healthy volunteers compared with chronic cough patients at C2 and for several preceding concentrations. For example, at C2, irritation VAS was significantly higher in healthy controls ($dp = 0.035$) and tickle VAS was borderline significant ($p = 0.052$) compared with chronic cough patients, however taste differences were not significant ($p = 0.29$). SSAS, STAI state and trait were not significantly different between the groups ($p = 0.23$, $p = 0.096$ and $p = 0.62$ respectively).

Conclusions These data suggest that as well as differences in cough threshold, chronic cough patients exhibit heightened urge-to-cough rather than other sensations in response to low level tussive agents.

S31 REPRODUCIBILITY OF FOUR CHALLENGE MODALITIES FOR CHRONIC COUGH

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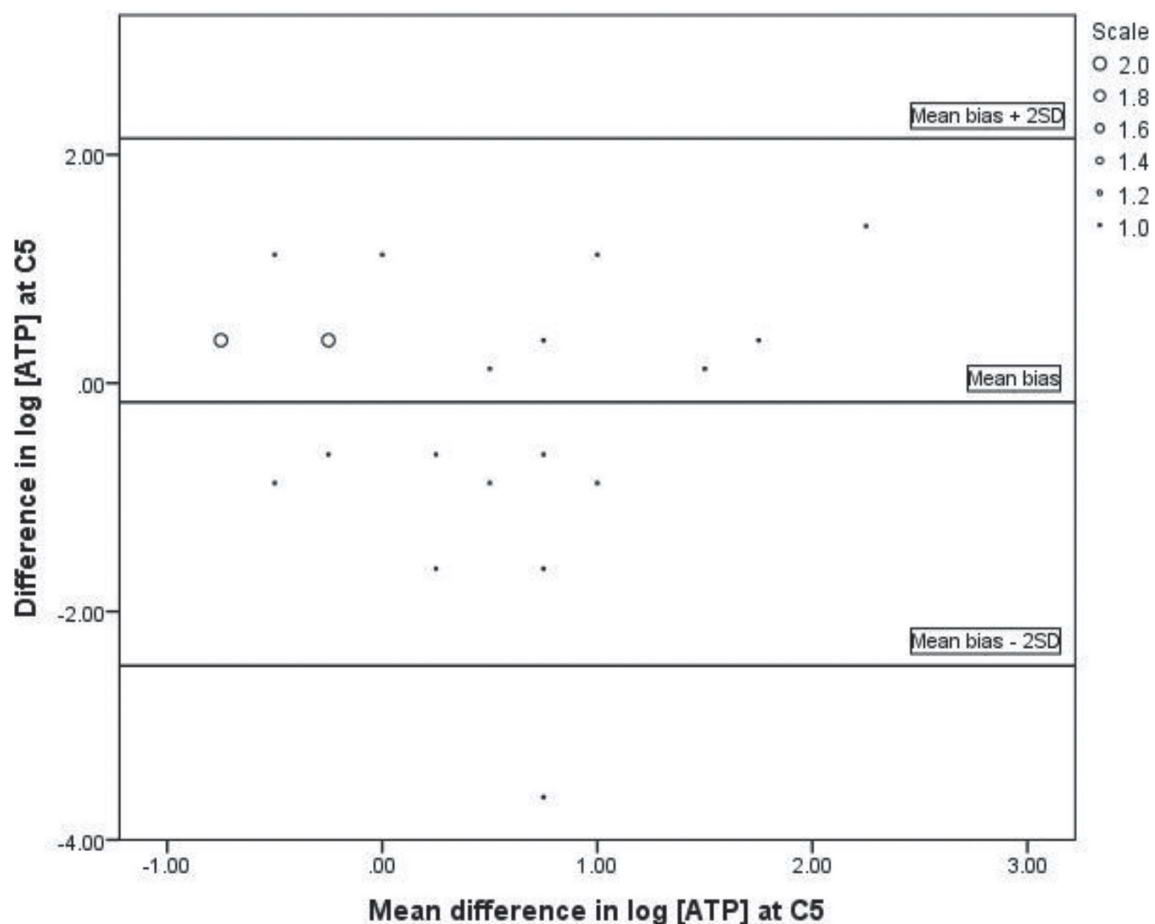
Background Cough challenges are utilised in clinical research to help determine efficacy of treatments for cough. Recently adenosine triphosphate (ATP) has gained interest as a potential tussive

agent. Previous research suggests such challenges are reproducible in healthy individuals, but little is known about their reproducibility in chronic cough patients, particularly the use of ATP as a tussive agent. This study aims to clarify if ATP is a reproducible tussive agent in chronic cough patients.

Method Data was collected on subjects undergoing cough challenges in the clinical trials unit. Subjects performed tussive challenges with four agents (capsaicin, ATP, citric acid and fog) in a randomly allocated order (visit 1); C2 and C5 were noted. This test was then repeated a week later (visit 2). Intra-patient variability was analysed using the Bland-Altman method for each tussive agent, presented as mean difference (95% limits of agreement). Inter-patient variability was analysed using paired t-tests. Pearson's correlation coefficient (r) between ATP and other agents was calculated.

Results 26 subjects were recruited; 21 with chronic cough. Average age of 57.4 ± 12.2 , mean BMI of 26.8 ± 5.7 , with an 85% female predominance. ATP showed a strong correlation with citric acid ($r = 0.76$, $p < 0.001$) and capsaicin ($r = 0.66$, $p < 0.001$). Bland-Altman analysis at C5 showed a 95% limit of agreement to be more than a two log dose difference except for fog: citric acid -0.07 (-1.7 to 1.5), capsaicin -0.1 (-1.5 to 1.2), ATP -0.2 (-2.5 to 2.1) (Figure 1), fog -0.01 (-0.3 to 0.3). Comparing visit 1 and visit 2 for each tussive agent showed no significant difference (p -value of 0.58, 0.80, 0.90, and 0.80 for ATP, fog, capsaicin and citric acid, respectively).

Conclusion ATP shows a strong correlation with other agents currently being utilised in cough challenges. This suggests direct



Abstract S31 Figure 1 Bland-Altman analysis of the 95% limit of agreement for ATP at C5