P237 COUGH FREQUENCY IN ACUTE STROKE

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10.1136/thoraxjnl-2015-207770.373

Introduction and objectives Few studies have investigated cough frequency in neurological patient groups, in which cough may be impaired or increased in the presence of aspiration. This study aimed to (1) validate the Leicester Cough Monitor (LCM) on a stroke unit, where background coughs might contaminate one patient's cough recordings; and (2) observe cough frequency longitudinally in a convenience sample of acute stroke survivors.
Methods To validate the LCM, 15-minute recordings were made from 5 patients on a stroke unit. LCM results were compared with real-time cough counts by a researcher present in the room (visual and auditory). To observe cough frequency longitudinally, 21 stroke survivors underwent 24-hour LCM recordings at baseline (<2 weeks post stroke), week 1 and 4. Participants (14 men, mean (SD) age 60 (15) years) had moderate stroke impairment (median (IQR) NIHSS score 8 (5, 11)) with cortical (n = 9), subcortical (n = 9), brainstem (n = 2) and cerebellar (n = 1) strokes. Five randomly selected recordings were analysed by a second researcher, blinded to subject characteristics and not present during the recordings.
Results In the validation study, the real-time observer counted 67 subject coughs plus 81 background coughs in total. The LCM returned a subject cough count of 68, not significantly different to the observer's count (p = 0.99) with excellent agreement (ICC 0.996, 95% CI: 0.967, >0.999). Inter-rater reliability for LCM hourly cough counts was good (ICC 0.973, 95% CI: 0.789, 0.997). In the longitudinal cohort, average cough frequency was higher at baseline and reduced over time, with wide individual variability (Table 1) and higher cough frequency during day-time. There were no significant associations between cough frequency and sex, age, stroke site, stroke severity, swallowing safety, smoking status or ACE-inhibitor use.

Abstract P237 Table 1 24-hour cough frequency (median, range) following acute stroke. Baseline assessments were conducted within 2 weeks of stroke

24-hour cough frequency	Baseline (n = 21)	Week 1 (n = 20)	Week 4 (n = 17)
Total number of coughs	118 (4, 375)	60 (6, 217)	56 (1, 186)
Hourly coughs	5 (0, 16)	2 (0, 9)	2 (0, 8)
Day time coughs[a]	86 (4, 282)	30 (6, 159)	41 (1, 108)
Hourly day time coughs	6 (0, 20)	2 (0, 11)	3 (0, 8)
Night time coughs[a]	21 (0, 112)	18 (0, 58)	9 (0, 90)
Hourly night time coughs	2 (0,11)	2 (0, 6)	1 (0, 9)

[a]day time: 08:00–22:00, night time: 22:00–08:00.

Conclusions This study is limited due to the small sample size and should be regarded as exploratory. It was possible to validate the LCM for application on an acute stroke unit. The findings might serve hypothesis-generation: For example, is cough frequency after stroke increased, indicating sub-clinical levels of swallowing impairment and aspiration threat, which trigger frequent protective coughs?

P238 A RANDOMISED, DOUBLE-BLIND (SPONSOR-UNBLIND), PLACEBO CONTROLLED, CROSS-OVER STUDY TO INVESTIGATE THE EFFICACY, EFFECT ON COUGH REFLEX SENSITIVITY, SAFETY, TOLERABILITY AND PHARMACOKINETICS OF INHALED GSK2339345 IN PATIENTS WITH CHRONIC IDIOPATHIC COUGH USING AN AQUEOUS DROPLET INHALER

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10.1136/thoraxjnl-2015-207770.374

Introduction and objectives Voltage gated sodium channels (VGSC) are important in the initiation and propagation of action potentials in the afferent sensory nerve fibres innervating the airways responsible for evoking cough. Therefore a VGSC inhibitor may be an effective anti-tussive agent, inhibiting cough irrespective of the type of stimuli. We aimed to investigate the efficacy of a novel use-and frequency-dependent VGSC inhibitor (GSK2339345) in patients with chronic idiopathic cough.
Methods We performed a two-part randomised, double-blind, placebo-controlled, cross-over study recruiting patients with chronic idiopathic cough from two specialist clinics. In the first part of the study, patients were randomly assigned to receive two inhaled doses of either GSK2339345 or placebo, 4 h apart during three study periods. The primary endpoint was the objective cough frequency (VitaloJAK, Vitalograph Ltd) during the 8 h post-treatment (4 hrs following each dose). The difference between GSK2339345 and placebo in log-transformed cough counts was investigated using a mixed effects model with fixed effects terms for treatment and period, and subject fitted as a random effect. In the second part, subjects attended on four study days, and underwent full dose-response cough challenges with capsaicin and citric acid following single doses of GSK2339345 or placebo. This was analysed using dose response modelling.
Results Of 16 patients enrolled (56.7 ± 9.6 yrs; 13 female), 11 completed the study. Eight hour cough counts showed a 26% increase in cough counts with GSK2339345 vs placebo. However, on exclusion of the coughs occurring within 2 min of inhalation of the study drug, there was only a 1.6% increase in coughs; see Table 1 for ratio of adjusted geometric means. There appeared to be no impact of GSK2339345 on either of the cough challenges however, the dataset was too small to draw definitive conclusions.

Abstract P238 Table 1

Endpoint	Treatment	Adjusted geometric mean	Ratio of adjusted geometric means (90% credible intervals)	% Increase from placebo
8 h cough count	GSK2339345	192.5	1.26 (1.10, 1.44)	26%
	Placebo	152.7		
8 h cough count excluding transient coughs	GSK2339345	153.9	1.02 (0.87, 1.19)	1.6%
	Placebo	151.5		

Based on data from 14 subjects – 21 8h counts per treatment due to replicate period. Transient coughs are the number of coughs occurring in the first 2 min following each dose.

Conclusion There was no evidence of an anti-tussive effect of GSK2339345 over the 8 h analysis for any subject, despite cough frequency being highly reproducible within patients. Inhalation of GSK2339345 had a pro-tussive effect in all subjects following actuation of the device, not seen with placebo. The novel cough challenge methodology warrants further investigation as a development tool.

P239 LOW PREVALENCE OF EXTRA-THORACIC AIRWAY HYPER-RESPONSIVENESS IN UK PATIENTS WITH CHRONIC REFRACTORY COUGH

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10.1136/thoraxjnl-2015-207770.375

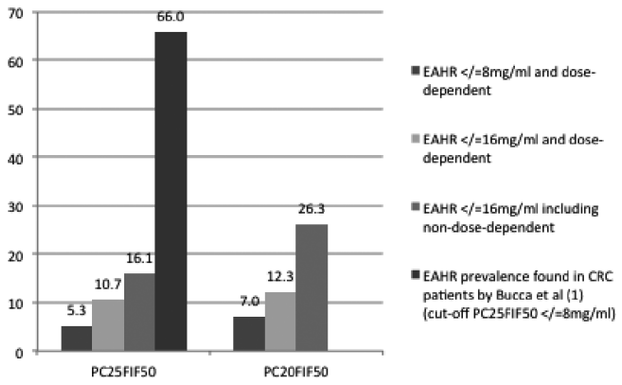
Introduction Prior research indicates that chronic refractory cough (CRC) is associated with a high prevalence of extra-thoracic airway hyper-responsiveness (EAHR).[1] This heightened laryngoconstrictor reflex can be characterised using standard bronchoprovocation tests (e.g. histamine or hypertonic saline); whereby attenuation in the inspiratory component of the flow-volume curve is evaluated in response to escalating doses of the stimulus.

Aims and objectives To determine the prevalence of EAHR in a cohort of CRC patients in the UK undergoing cough assessment, and to relate EAHR to other disease characteristics.

Methods Data was retrospectively evaluated for all CRC patients completing cough assessment with histamine bronchoprovocation challenge, between 2013 and 2015. EAHR was defined by a 25% dose-responsive fall in the mid-inspiratory flow (PC25FIF50) in response to ≤ 8 mg/ml histamine.[2] EAHR data was compared with other simultaneous investigation results, including overnight pH/impedance results and co-existing nasal disease.

Results We studied 57 adult CRC patients (n = 42, female; 74%), mean ±SD age 54.6 ± 12.4 years, BMI 28.2 ± 5.9 kg/m^2, reporting a duration of cough 5.5 years (0.8–50) with a median cough VAS score of 57 (16–90). The majority of patients (56%) reported cough without other respiratory symptoms, whereas 12 (21%) reported cough with dyspnoea and wheeze. Evidence of EAHR was found in three patients (5.3%). At a reduced cut-off (PC20FIF50 ≤ 16 mg/ml) the prevalence of EAHR was greater (12%) (Figure 1). Patients with a positive EAHR test at this cut-off were younger ($p < 0.01$, mean age 44 yrs versus 56 yrs) and more likely to report respiratory dyspnoea and wheeze ($p < 0.05$). In patients completing an overnight reflux study (n = 52), 32 (62%) had evidence of reflux. 21 (37%) patients had co-existing nasal disease. However, presence of reflux or nasal disease was not predictive of EAHR (both $p > 0.05$).

Conclusion EAHR was not prevalent in CRC patients, completing assessment at a specialist cough service, when using a standard histamine bronchoprovocation test. Differences from prior published data may be explained by methodological differences, specifically the application of stringent control of the measures of reproducibility of inspiratory flow parameters and dose response criteria.



Abstract P239 Figure 1

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P240 VALIDATION OF THE LEICESTER COUGH QUESTIONNAIRE IN PULMONARY TUBERCULOSIS

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10.1136/thoraxjnl-2015-207770.376

Introduction and objective Cough is prominent in pulmonary tuberculosis (TB) and transmits infection, yet no tool has been validated for assessing cough symptoms. We evaluated the Leicester Cough Questionnaire (LCQ) for measuring cough-related quality of life (QOL) in TB.

Method The face validity of the LCQ was evaluated by structured interviews with patients and a multi-disciplinary team (MDT) discussion (respiratory physicians and nurses). Consecutive patients with TB completed the LCQ just before or within 7 days of starting therapy; a subgroup completed a repeat questionnaire approximately two weeks after the first. Internal reliability (inter-relatedness between items), concurrent validity (association with cough severity visual analogue scale [VAS] score and 24-hour cough frequency measured with the Leicester Cough Monitor), and responsiveness were evaluated.

Results The MDT and patients thought the LCQ to be relevant, comprehensive and useful in TB and no modifications were suggested. Forty patients completed the questionnaire before (n = 29) or just after (n = 11) the start of treatment. Internal reliability of responses was high (Cronbach's $\alpha = 0.93$). LCQ scores were correlated with both the VAS (Spearman's $\rho = -0.69$ [95% confidence intervaI -0.83 to -0.46], $p < 0.0001$) and 24-hour cough frequency ($\rho = -0.36$ [-0.62 to -0.04], $p = 0.023$), and were worse pre-treatment in culture-positive compared to culture-negative disease (median 12.4 [IQR 8.5–17.4] *vs* 18.7 [17.8–19.6] respectively, $p = 0.052$). There was no evidence of association with other markers of disease severity (sputum smear positivity, lung cavities and radiographic extent of disease), but a trend towards worse LCQ scores amongst current smokers than non-smokers (12.6 [8.3–14.4] *vs* 17.1 [11.1–21.0] respectively, $p = 0.075$).