Muscarinic blockade with oral hyoscine palliates angiotensin converting enzyme inhibitor induced cough

Sir, Angiotensisn converting enzyme inhibitors (ACEI) educe morbidity and mortality from cardiovascular and renal disease. Tolerability may, however, be limited by a persistent dry cough occurring in 27% of Nigerian patients and which may lead to discontinuation of these life-saving drugs in up to 4% of Nigerians [1]. The mechanism of ACEI-induced cough is still unclear although a role for badykinin accumulation and/or sensitization of vagal afferent nerves in the airwasy have been proposed [2,3]. Sodium cromoglycate has been reported to attenuate the cough [4], although the mechanism of this beneficial effect is unknown, an effect on vagal efferents has been speculated [4].

Since converting enzyme inhibitors may exert cardiac vagomimetic effect in healthy men [5] which is abolished by atropine [5], we examined the possibility that ACEI-induced cough may arise, also, from enhanced parasympathetic tone to sensory nerves in the respiratory tract.

We conducted a randomized, single blind, placebo controlled, cross-over study in six patients informed consent (5 stable heart failure patients and one hypertensive diabetic) aged 59(±10) years (4 females) who developed ACEI-induced cough, on enalapril treatment (4.4 ± 1.2 mg/day).

We compared the effects of placebo and an oral anticholinergic (m_1) blocker hyoscine-n-butyl bromide 10 mg administered orally twice dailyon cough severity as assessed both by a patient-rated ordinal scale of 0(absent), 1(mild) 2(moderate), 3(severe requiring stoppage) and a visual analogue scale of 0-10 cm, over a 2 week treatment period with a one-week washout interval. We excluded patients with COPD, pulmonary congestion and respiratory tract infection. Data are expressed as mean ± SD. Statistical analysis are by paired t tests and analysis of variance.

Hyoscine caused a reduction in cough severity with a fall in cough score from 2.2 ± 0.4 to 1.0 ± 0 ($P < 0.02$) and on the VAS score from 6.2 cm ± 0.9 to 1.8 ± 0.4 ($P < 0.01$).

There was no improvement on placebo by cough score (2.2 ± 0 to 2.2 ± 0) and slight deterioration by VAS score (5 ± 1.7 to 6 ± 1.1). Hyoscine caused a modest heart rate increase from 86 ± 4.2 to 96 ± 12.5 which was attributable in part to a large increase in one subject with atrial fibrillation. Two of the six patients on hyoscine complained of dry mouth One patient with a score of 3 (to be withdrawn from ACEI) showed a remarkable improvement to score of 1 allowing ACEI therapy continuation. Two patients have been on therapy hyoscine for 2 months with sustained benefit and tolerance.

Thus, muscanic receptor blockade with oral hyoscine palliates ACEI-induced cough and may become a practical therapy. It may, however, increase the ventricular rate in patients with atrial fibrillation. This finding is consistent with the priori hypothesis that increased central or peripheral parasympathetic activity in the respiratory tract contributes to the cough [2,3,4]. Enhanced tonic vagal discharged induced by ACEI may increase the sensitivity of vagal sensory unmyelinated C fibres which subserve the cough reflex to the stimulant action of accumulated bradykinin due to ACE inhibition [2].

Table

Cough Severity score	Baseline	5	10	15 (Days)
Hyoscine	2.2(0.4)	1.7(0.5)	1.0(0)	1.0(0)*
Placebo	2.2(0.4)	2.2(0.4)	2.2(0.4)	2.2(0.4)
Visual Analogue Score (cm)				
Hyoscine	6.2(0.9)	4.0(0.6)	3.0(0)	1.8(0.4)@
Placebo	5(1.7)	4.8(1.2)	5.0(0.9)	6.0(1.1)

n = 6 mean ± SD.
*$P < 0.02$ by ANOVA
@$P < 0.01$ by ANOVA
Oral hyoscine palliation of ACEI-induced cough.

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