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Preliminary asthma-related outcomes following glucagon-like peptide 1 agonist therapy

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Dr M.W.B. had full access to all the data and takes responsibility for the integrity and accuracy of the data analysis, including and especially any adverse effects.

The QJM has recently published reviews of novel therapies in chronic airways disease.[1] There is a potentially novel role for glucagon-like peptide 1 (GLP-1) agonists in obesity-related, metabolic asthma, though clinical trial data are lacking.[2] On the basis of work with other inflammatory states, we hypothesised that clinically-indicated use of GLP-1 agonists for glycaemic control in type 2 diabetes mellitus (T2DM) would be safe in those with concomitant asthma, potentially leading to improved asthma control and fewer asthma exacerbations.[3] In a pilot observational cohort study, we prospectively identified nine patients with pulmonologist-diagnosed asthma (never-smokers) and concomitant T2DM who were about to be initiated on clinically-indicated liraglutide for T2DM in the course of routine clinical care, and assessed them for asthma-related indices at baseline and 52 weeks after initiating liraglutide. All received routine asthma care. Baseline characteristics of the study cohort are as shown (Table 1). Seven of the nine subjects who commenced therapy with liraglutide remained on therapy for the 52 week duration of the study (i.e. 'adherent'), while two subjects ('non-adherent') came off liraglutide before 8 weeks due to non-asthma-related side effects (diarrhoea, epigastric discomfort, night sweats, hypoglycaemia and headaches) but were included in the analysis. At week 52 of liraglutide therapy, the mean weight loss was 4.9 kg (5.6% of baseline mean weight) with median weight loss value of 2.9 kg. HbA1c at week 52 fell to 51.9 mmol/mol (mean). Over the 52 weeks of therapy, the greatest falls in weight and HbA1c were in those who remained adherent to liraglutide, accompanied by clinically significant improvements in asthma control including asthma symptoms and exacerbations (Figure 1). No subject adherent to liraglutide had a clinically significant deterioration of asthma. One non-fatal severe exacerbation occurred, which happened several weeks subsequent to early discontinuation of liraglutide in the (non-adherent) subject, who had 2.9 kg of weight loss in the study. This could reflect withdrawal of liraglutide or poor-adherence to other asthma controller medicines. The changes in asthma-related outcomes could not be linked to changes in dosage of other asthma controller medicines. We conclude that use of liraglutide to treat concomitant T2DM was safe and potentially helpful for co-morbid overweight/obese asthma. This is consistent with animal/*in vitro*/*ex vivo* studies that have assessed the effects of GLP-1 analogues in asthma, but could also be coincidental or represent an observer effect in a small uncontrolled cohort study.[4,5] Given the growing clinical exposure of patients to GLP-1 agonists, the proof of concept data herein provides a further imperative for large randomised controlled studies assessing the role of GLP-1 analogues in overweight/obese asthma patients with and without T2DM.

Authors' contributions

M.W.B. and D.O.S. conceived the study design, interpreted data and assisted in manuscript preparation. F.K., A.M. and B.K.

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Table 1. Baseline demographic and other clinical variables among T2DM participants with concomitant asthma completing 52 weeks of follow up

Parameter	Value
N	9
Gender (male/female)	4/5
Age (yr)	61.9 ± 2.3
Smoking status (never/former/current)	9/0/0
Family history of asthma (yes/no)	3/6
Asthma onset (youth onset/late onset	5/4
Weight (kg)	88 ± 5
BMI[a] (kg/m^2)	32.3 ± 2.5
Asthma acute exacerbation rate (annual)	2.6 ± 0.62
Asthma controllers, *n* on any ICS[b]	8
GINA[c] treatment step (step 1/2/3/4/5)	1/1/3/4/0
ACQ[d] score	1.03 ± 0.1
AQLQ[e] overall score	5.59 ± 0.2
AQLQ symptom score	5.80 ± 0.2
AQLQ activity score	5.57 ± 0.3
AQLQ emotional score	5.56 ± 0.4
AQLQ environmental stimuli score	5.06 ± 0.3
Severe asthma (*n*)[f]	4
FVC[g] (post-bronchodilator) L	3.5 ± 0.3
FEV1[h] (post-bronchodilator)L	2.34 ± 0.2
% FEV1/FVC (post-bronchodilator)	67.8 ± 3
HbA1c[i] (<48 mmol/mol)	57.0 ± 1.7

[a]BMI, body mass index.
[b]ICS, inhaled corticosteroids.
[c]GINA, Global Initiative for Asthma.
[d]ACQ, Asthma Control Questionnaire.
[e]AQLQ, Asthma Quality of Life Questionnaire.
[f]Severe asthma defined as per International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma.
[g]FVC, forced vital capacity.
[h]FEV1, forced expiratory volume of air in 1 s.
[i]HbA1c, glycated haemoglobin (A1c).

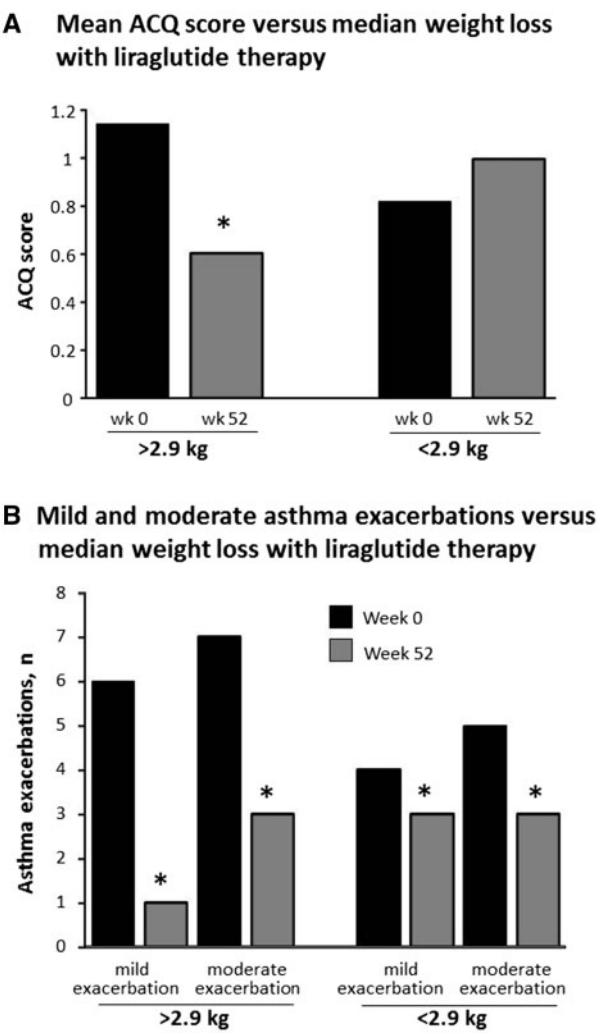

Figure 1. Asthma-related outcomes in subjects whose weight loss was greater or less than the median weight loss of 2.9 kg. **A.** Mean ACQ score pre- and post-52 weeks of liraglutide therapy, parsed on the ordinate by those with greater-than-median weight loss of 2.9 kg and those with less-than-median weight loss. **B.** Similar to A, but showing the number of asthma exacerbations in the year prior to (week 0, black bars) and the year following initiation of liraglutide (week 52, grey bars), and parsed into mild and moderate exacerbations for each weight grouping (the only severe exacerbation observed in the study occurred in a non-adherent subject post-discontinuation of liraglutide). In panels A and B, an asterisk (*) denotes a clinically significant change, reflecting minimal clinically important difference (MCID) where known. ACQ, Juniper Asthma Control Questionnaire.

collected the data, interpreted data and assisted in manuscript preparation.

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Ethics committee approval

The study attained prior ethics approval from the St. Vincent's University Hospital Research Ethics Committee. The Committee does not utilise approval numbers.

Conflict of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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