Reviewer's report

Title: Insulin Versus Oral Agents in the Management of Cystic Fibrosis Related Diabetes: A Case Based Study

Version: 1 Date: 8 March 2006

Reviewer: Emma Baker

Reviewer's report:

General

The authors performed a retrospective study comparing clinical outcomes in patients with cystic fibrosis related diabetes (CFRD) treated with insulin or oral hypoglycaemic agents.

The paper deals with an important and unanswered question in cystic fibrosis - what is the optimal treatment for diabetes in these patients? The rationale for the study is good - that oral agents may have insulin-sensitising and anti-inflammatory properties that may confer advantages over insulin. The approach - a retrospective review - is sensible as a preliminary investigation of the area.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Point 1. It was not at all clear how long patients in the study received treatment for. In table 1 there is a column called Rx course which is not explained. I interpreted this as duration of treatment on the blood glucose lowering agent stated – is that correct? If so patients received treatments for different lengths of time (e.g. I8 had insulin for 10 years and T2 had a glitazone for 1 year?)

This is particularly important when it comes to clinical variance over time (table 3). Were all patients followed up for 10 years or were they on treatment for different lengths of time? The clinical variance must be over a standard amount of time (e.g. over first year on treatment) for it to be meaningfully comparable between groups. This is also important for the figure where measurements are compared at the start and end of study – again this is meaningless if the study was of different durations for each patient.

Point 2. The methods are extremely brief and don’t explain how the study was done adequately – might help considerably with point 1 if these were clearer

Point 3. I am concerned as to the statistical methods used. The authors do not describe these adequately but appear to have used unpaired t tests which are not suitable for multiple comparisons. Additionally the numbers are so small in each group that non-parametric tests would be more appropriate. This is particularly important when looking at the baseline data. I think the groups are actually not matched for age, FEV1, weight or HBA1C which may be very important as it could influence the results. This is not statistically obvious due to small sample size and some statement about power may be useful.

With further regards to the baseline data, the patients on metformin had considerably less co-morbidity than the other groups – understandably as these may be contraindications to metformin therapy. However this further reduces the matching of the groups and would be worth commenting on in the discussion. Additionally weight is fairly meaningless as a baseline statistic (although
change is relevant on treatment). BMI would be helpful in assessing clinical state of patients at baseline.

Point 4. There is no mention of doses of the different agents that were used or protocols that were used to optimise therapy. This is important as again the groups are not comparable e.g. in terms of HBA1c reduction unless there is some information as to doses used/attempts to optimise glycaemic control. Additionally it would be worth discussing patient adherence/compliance with therapy. Did the metformin group have better HBA1c reduction than the insulin group because patients were happier taking tablets than injections.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Doesn't FEV1 stand for forced expiratory volume in 1 second, not forced expiratory vital capacity in 1 second (see background and legends for tables 2 and 3)?

2. I found the writing style a bit opaque in places and felt the grammar could be improved for the ease and pleasure of the reader.

For example in the background some sentences are long and difficult to follow. Some sentences such as those beginning "Investigators testing this therapeutic potential....." and "Dietary measures....runs..." and "Clinical outcome measures followed changes (doesn't make sense)" would benefit from careful proof reading and revision

The discussion is long and some of it is confusing. For example in paragraph 4 you seem to be saying that HBA1C is of no use for monitoring glycaemic control - then you say insulin is not a good treatment as it doesn't lower HBA1c.... (It may be helpful to note that we have recently shown that HBA1C <7.0 in CF predicts the same mean plasma glucose as HBA1C <7.0 in type I diabetes Brennan AL, Gyi KM, Wood DM, Hodson ME, Geddes DM, Baker EH. Relationship between glycosylated haemoglobin and mean plasma glucose concentration in cystic fibrosis. J Cyst Fibros. 2006;5:27-31).

In the figure the metformin graph should be labelled Therapy not Thearpy

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes

Declaration of competing interests:

I have published in the field as follows

Some of my opinions about HBA1c differ slightly from the authors