Aims: To investigate whether treatment of coexisting asthma has any effect on the incidence of hypoglycaemia and on glycaemic control in children with type 1 diabetes.

Methods: An observational study of children attending the paediatric diabetes clinics of five hospitals in the North Trent Region. Information on the frequency of hypoglycaemia in the preceding three months, treatment for asthma, and the individual’s latest HbA1c, was recorded when they attended for review.

Results: Data were collected on 226 children, of whom 27 (12%) had treated asthma. Only 11/27 children with asthma were taking their prescribed inhaled steroids. All used β agonists at least once a week. There was a reduction of 20% in the incidence of hypoglycaemia in the diabetic children with treated asthma. Of the children with diabetes and treated asthma, 52% reported an episode of hypoglycaemia in the previous three months compared to 72% of those with only diabetes. There was no difference in the proportion of children experiencing nocturnal or severe hypoglycaemia. Although not significant, those with asthma and diabetes also had better overall control (HbA1c 8.8%) compared to those with diabetes alone (HbA1c 9.3%).

Conclusions: Diabetic children with treated asthma have significantly fewer episodes of hypoglycaemia and better glycaemic control compared to children with diabetes alone. This observation needs further investigation but raises an interesting question. Do the drugs used to treat asthma, in particular β agonists, have the therapeutic potential to reduce hypoglycaemia and facilitate an improvement in glycaemic control?

Beta agonists, together with inhaled steroids, are widely used in the treatment of asthma in children. The effect of steroids on blood sugar is well documented. Beta agonists can also have a significant effect on blood sugar. They have a direct glycaemic effect and an indirect effect on blood glucose by enhancing sympathetically mediated counter regulatory responses to hypoglycaemia. Nebulised salbutamol can significantly increase blood glucose, and cases of ketoacidosis have been reported in diabetics. Terbutaline has been shown to be as effective as glucagon in reversing hypoglycaemia; in adults, under experimental conditions, it has proved effective in preventing nocturnal hypoglycaemia. The potential for asthma treatment to influence hypoglycaemia and diabetic control prompted us to study our paediatric diabetic population, to examine whether treatment of coexisting asthma had any effect on the incidence of hypoglycaemia and on glycaemic control.

Patients and Methods
All children had type 1 diabetes and were attending the paediatric diabetes clinics of five hospitals in the North Trent Health Region of the UK. Information on the incidence of hypoglycaemia within the past three months, asthma treatment if any, and the individual’s latest HbA1c, were recorded for all children with diabetes when they attended for review. The results for those children on treatment for asthma were compared to those of the clinic population as a whole using χ² tests and unpaired t-tests. Treated asthma was defined as being prescribed inhaled steroids or using β agonists at least once a week. Individuals who used treatment only during viral exacerbations or who had been treated for asthma in the past were not considered to be currently on treatment. Few children check their blood glucose during episodes of hypoglycaemia, so a pragmatic approach to the definition of hypoglycaemia was adopted. Episodes reported by the child and their family as “hypos” were accepted as such. Only for severe hypoglycaemia was a definition stipulated, which was an episode requiring glucagon or dextrose gel.

Results
Data were collected on 226 children with diabetes. Twenty-seven children were on treatment for asthma and the prevalence of asthma reflects that of the general population at 12%. Interestingly only 11/27 children prescribed inhaled steroids were using them regularly, although they used β agonists at least once a week. The mean age for those with both asthma and diabetes was 11.3 years (SD 3.3) compared to 11.5 years (SD 3.6) for those with diabetes alone. Table 1 presents details of the impact of treated asthma on hypoglycaemia and glycaemic control. There was a statistically significant reduction of 20% in the incidence of hypoglycaemia in those diabetic children with treated asthma. Of those children with both diabetes and treated asthma, 52% reported an episode of hypoglycaemia in the previous three months compared to 72% of those with diabetes alone (p < 0.05). There was no difference between the groups in the proportion of children experiencing nocturnal hypoglycaemia or severe hypoglycaemia. Although not statistically significant, those with asthma and diabetes also tended to have better overall control (HbA1c 8.8%, 95% CI 8.4 to 9.3) compared to those with diabetes alone (HbA1c 9.3%, 95% CI 9.0 to 9.5).

Analysis of the influence of age, frequency of β agonist use, and of inhaled steroids on hypoglycaemia in asthmatics was limited by the small sample size. There were no statistically significant differences, but this may be a consequence of the small numbers. Hypoglycaemia was reported by only 30% (3/10) of frequent users of β agonists compared to 58% (7/12) of less frequent users (p = 0.18). Of those using inhaled steroids, 63% (7/11) reported hypoglycaemia compared to 38% (5/13) of those not taking inhaled steroids (p = 0.29). Mean HbA1c was 9.0% (0.6%) and 8.6% (0.7%) respectively.

Discussion
Given the tendency of both steroids and β agonists to elevate blood glucose, we had anticipated that if coexistent treatment for asthma were to influence diabetic control, we would
perhaps see a reduction in the incidence of hypoglycaemia but
at the expense of an elevation in HbA1c. We observed a
significant reduction in hypoglycaemic episodes associated
with a tendency to improvement in HbA1c. It may be that it is
the pathological process associated with asthma that facili-
tates a reduction in hypoglycaemia, but we are not aware of a
mechanism to explain this phenomenon. It is more likely that
there is a beneficial effect of the treatment associated with
asthma. This finding, if confirmed, has potential for the man-
gement of type 1 diabetes.

The study does have methodological weaknesses, which
need to be acknowledged, but which should not adversely
affect the results. This was an observational study of our local
paediatric population and different laboratories were used for
HbA1c measurements. As the proportion of children with
treated asthma was similar between the centres, any discrep-
ancy in HbA1c assays should be equally represented in both
groups and should not influence the study’s findings.
Similarly we adopted a pragmatic definition of hypoglycae-
ia, relying on children and their families to define an
episode. Any variation in definition of hypoglycaemia should
again be consistent across the patient population and should
not bias the results.

An alternative explanation is that the relation between
asthma and diabetes may in some way modify compliance
with insulin therapy, alter patterns of exercise, and influence
parental involvement. Children with symptomatic asthma
may exercise less and as a consequence experience less
exercise related hypoglycaemia. Having two chronic condi-
tions may increase parental imput and hence improve diabetic
control. It is possible that these factors rather than treatment
for asthma may be influencing hypoglycaemia, but we did not
attempt to address them in this study.

Considering the potent direct and indirect glycaemic effects
of β agonists, we would suggest that they are the most prob-
able candidate as mediator of the reduction in hypoglycaemia
we observed. Fewer than half the children in the study with
asthma were using inhaled steroids, and although not statisti-
cally significant, there was an increased incidence of hypogly-
caemia in those asthmatics using inhaled steroids compared
to those who did not. Frequent users of β agonists had fewer
episodes of hypoglycaemia than less frequent users. Reducing
hypoglycaemia may facilitate an improvement in overall
glycaemic control, perhaps by reducing hypoglycaemia
unawareness.7 Such a mechanism would explain the small
improvement in HbA1c we observed.

Hypoglycaemia remains one of the principle obstacles to
tight glycaemic control. The evidence is by no means
conceivable and these observations need further investigation,
but they raise an interesting question. Do the drugs used to
treat asthma, in particular β agonists, have the therapeutic
potential to reduce hypoglycaemia and facilitate an improve-
ment in glycaemic control?

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