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LETTER

Within-class differences of the sulfonylureas should be accounted for. Reply to Schrijnders D, Kleefstra N and Landman GWD [letter]

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To the Editor: Schrijnders et al [1] express concern that the findings of our paper [2], highlighting the continued enhancement of insulin secretion by glibenclamide at near-normal glucose levels, may have been unduly extrapolated to other drugs in the sulfonylurea class. Whilst we emphasised (correctly in our view) in the discussion 'the need for cautious titration when using sulfonylureas as second-line agents after metformin when attempting to maintain tight glucose control', our abstract conclusion was specific to glibenclamide stating: 'This study highlights the risks of hypoglycaemia when aiming for tight glucose control on this agent.'

We chose to study glibenclamide as it was the most commonly used sulfonylurea agent at the time, and because its principal mechanism of action on the pancreatic beta cell, namely to inhibit the sulfonylurea receptor (SUR)/inward rectifying potassium (KiR6.2) channel to depolarise the cell, is shared by the sulfonylurea class as a whole [3]. Similar results have been shown with other members of the class, such as gliclazide, in hyperglycaemic conditions [4]. In clinical practice, glibenclamide is well known to be particularly prone to cause hypoglycaemia and has pharmacokinetic and pharmacodynamic properties that are likely to underlie this. However, while the degree to which glibenclamide and other sulfonylureas are related to mortality rates and cardiovascular risk may differ, they are all associated with an increased risk of hypoglycaemia [5]. It is also known that glibenclamide has effects on cardiac potassium channels not shared by some of the other sulfonylureas, but the association between severe hypoglycaemia and increased mortality in large scale trials [6] cannot be attributable wholly to this property of this particular drug.

We acknowledge that there are intraclass differences in the degree to which sulfonylureas promote hypoglycaemia, but we do not believe that the enhancement of insulin secretion we have demonstrated at near-normal glucose levels is unique to glibenclamide, and we consider that our advice concerning cautious titration of these agents remains entirely appropriate.

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