Diabetologia (2015) 58:1374–1375
DOI 10.1007/s00125-015-3556-1

LETTER

Within-class differences of the sulfonylureas should be accounted for

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Received: 11 February 2015 / Accepted: 12 February 2015 / Published online: 24 March 2015

Keywords Cardiovascular events · Glibenclamide · Gliclazide · Hypoglycaemia · Sulfonylureas · Within-class differences

In a recent issue of *Diabetologia*, Riefflin et al published the results of their investigation into the effects of glibenclamide (known as glyburide in the USA and Canada) on insulin secretion in patients at different levels of glucose control [1]. We acknowledge that these results provide further evidence for the unique side-effect profile of glibenclamide. Unfortunately, in the discussion section, the results were repeatedly extrapolated to sulfonylureas as a class. For example, the final conclusion ends with 'This emphasises the need for cautious titration when using sulfonylureas as second-line agents after metformin when attempting to maintain tight glucose control.' The results of this study are largely confirmatory, given the overwhelming existing evidence that glibenclamide is associated with a higher risk of hypoglycaemia [2]. This extrapolation completely ignores important and clinically relevant within-class differences among sulfonylureas. It is well known that of all the sulfonylureas, glibenclamide in particular is associated with a high rate of side effects, for example, more severe hypoglycaemic events and an increased number of cardiovascular events [2].

There are many reports that patients using glibenclamide are at an increased risk of mortality, and in a recent large, observational cohort study monotherapy with glibenclamide was associated with a higher mortality and cardiovascular risks, while gliclazide was associated with a risk comparable to that of metformin [3]. In the Netherlands, these within-class differences are even incorporated in the guidelines [4]; here, gliclazide is the preferred second treatment option after metformin. One of the other main advantages of gliclazide is its safety in severe renal failure [5]. In addition, two meta-analyses have reported that of all the sulfonylureas, gliclazide is associated with the lowest risk of hypoglycaemia [6]. For example, the hypoglycaemic event rate for gliclazide is 50% lower than that for glimepiride [7] and is comparable to that for dipeptidyl peptidase-4 inhibitors [8, 9].

In summary, in our opinion, Riefflin et al [1] should not have discussed their findings as applying to the sulfonylureas as a class, and we urge investigators and editors to bear in mind within-class differences.

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Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

Contribution statement All authors were responsible for drafting the article and revising it critically for important intellectual content. All authors approved the version to be published.

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