

Hypoglycemic drugs and glycosylated hemoglobin into question: disappointing results and frequent serious adverse events

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Since the identification of the relationship between type 2-diabetes and a cardiovascular risk increase, several clinical trials have assessed the effect of treatments acting in reducing glycaemia, to lower cardiovascular risk in the same time. The resulting estimates of benefit to risk ratio were controversial, in particular on macro-vascular events, one of the most recent trials being prematurely stopped due to a significant increase in overall mortality.

Researchers from Claude Bernard Lyon 1 University, CNRS, Hospices Civils de Lyon and British Columbia University (Vancouver, Canada), among whom several from LBBE ([Theodora Bejan-Angoulvant-><http://lbbe.univ-lyon1.fr/-Bejan-Angoulvant-Theodora-.html>], Claire Bergeonneau, [Behrouz Kassai-><http://lbbe.univ-lyon1.fr/-Kassai-Koupai-Behrouz-.html>], [François Gueyffier-><http://lbbe.univ-lyon1.fr/-Gueyffier-Francois-.html>] et [Catherine Cornu-><http://lbbe.univ-lyon1.fr/-Cornu-Catherine-.html>]), conducted a systematic review of 13 trials on that topic.

Their results were published [in the issue of July 26th of the British Medical Journal-><http://www.bmj.com/content/343/bmj.d4169.full>] with [an editorial-><http://www.bmj.com/content/343/bmj.d4243.full>].

They showed that hypoglycemic agents do control glycaemia, but reduce myocardial infarction risk only by 15%, without clear benefit on stroke or cardiovascular mortality, and without total mortality reduction. This benefit was counterbalanced by severe hypoglycemic episodes or heart failure. Glycemic control, as assessed by glycosylated hemoglobin as a biomarker, is then rejected as an appropriate surrogate, and should not be considered as sufficient per se to deliver marketing authorization.

The important impact of this work is related to the rigorous approach, dealing appropriately with the difficult question of the level of evidence, thanks to the experience accumulated within the LBBE team in the meta-analysis techniques.

This work highlights the unmet need in terms of high level of evidence, to support the very large prescription of these drugs, with new well-conceived trials, so that to inform fully patients and physicians of the benefit risk ratio of treatments with type 2-diabetes.