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Review

Hypoglycaemia: An overview

*Alex J. Graveling, Brian M. Frier**

Department of Diabetes, Royal Infirmary of Edinburgh, Edinburgh EH16 4SA, United Kingdom

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ABSTRACT

Hypoglycaemia is a frequent side-effect of treatment with insulin and sulfonylureas for people with diabetes, threatening potentially serious morbidity and preventing optimal glycaemic control. Fear of hypoglycaemia and development of syndromes such as impaired awareness and counterregulatory deficiency provide additional hazards for intensification of treatment. Rapid lowering of HbA1c may be potentially dangerous in type 2 diabetes because of the adverse cardiovascular effects induced by hypoglycaemia. Hypoglycaemia can disrupt many everyday activities such as driving, work performance and recreational pursuits. Measures to reduce the risk of hypoglycaemia are labour-intensive and require substantial resources.

Contents

* *Corresponding author*. Tel.: +44 131 242 1475; fax: +44 131 242 1485.
E-mail address: brian.frier@luht.scot.nhs.uk (B.M. Frier).

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1. Definition, quantification and identification

1.1. *Introduction*

The Diabetes Control and Complications Trial (DCCT) demonstrated the benefits of intensified insulin therapy in type 1 diabetes mellitus (T1DM) where strict glycaemic control was shown to limit the risk of vascular complications compared to conventional therapy and moderate glycaemic control [1,2]. However, these benefits came at a cost of a threefold higher rate of severe hypoglycaemia. The lasting value of strict glycaemic control on restricting the frequency and severity of vascular complications was also demonstrated in type 2 diabetes mellitus (T2DM) by the UK Prospective Diabetes Study [3,4]. Although hypoglycaemia did occur in the UKPDS in patients treated with insulin or sulfonylureas, the reported (and probably under-estimated) prevalences were much lower than in T1DM, reinforcing the misconception that hypoglycaemia is seldom a problem in T2DM.

Hypoglycaemia is the commonest side-effect of insulin and sulfonylureas in the treatment of diabetes, and is a major barrier to maintaining satisfactory long-term glycaemic control [5]. It remains the side-effect of insulin that is most feared by patients and their relatives [6], partly because of the debilitating loss of control that it causes the affected individual, but also because of its associated, and potentially serious, morbidity and risk of death.

1.2. *Definition*

Hypoglycaemia is defined by ability to self-treat when exposed to low blood glucose. If self-treatment is possible, the episode is termed "*mild*", irrespective of the nature or intensity of the symptoms experienced; "*severe*" hypoglycaemia is any episode that requires external assistance for recovery, and is not confined to the development of coma or a reduced conscious level [1]. This definition has international consensus and is both practical and clinically relevant. It does not depend on a definition using a pre-determined blood glucose level that has not been universally agreed [7,8].

1.3. *Frequency*

People with T1DM experience around two episodes of mild hypoglycaemia per week [6,9], a figure that has not changed over 20 years despite modern developments in insulin therapy. Differences in the reported frequencies of mild hypoglycaemia between clinical studies may be related to the heterogeneity of the populations studied and differing hypoglycaemia definitions [10]. The annual prevalence of severe hypoglycaemia in unselected populations (i.e. those including everyone irrespective of risk factors) has been reported consistently at 30–40% in several large studies [11], with an incidence varying from 1.0 to 1.7 episodes per patient per year. This rises to more than 3 episodes per patient per year in those with T1DM of >15 years duration (see Fig. 1) [12]. The distribution of severe hypoglycaemia is skewed in that most patients do not experience any episodes while a small number of individuals experience multiple events [13].

Many trials of insulin-treated T2DM have documented very low rates of severe hypoglycaemia, partly because of patient selection (excluding those at high risk) and short periods of study. Severe hypoglycaemia is less common in people with insulin-treated T2DM, but still represents a substantial clinical problem, with between 7% and 25% of patients experiencing at least one severe episode annually; the frequency increases with longer duration of insulin therapy [12,14,15]. Patients with insulin-treated T2DM are more likely to require emergency medical assistance for severe hypoglycaemia than those with T1DM (30% vs. 10% of episodes) [16]. Sulfonylureas cause much more hypoglycaemia than is generally recognised, with the annual prevalence of severe episodes in well-controlled patients being 7% (see Fig. 1) [12]. Long-acting agents such as glibenclamide are associated with a higher risk of hypoglycaemia and are particularly dangerous in the elderly [17]. A

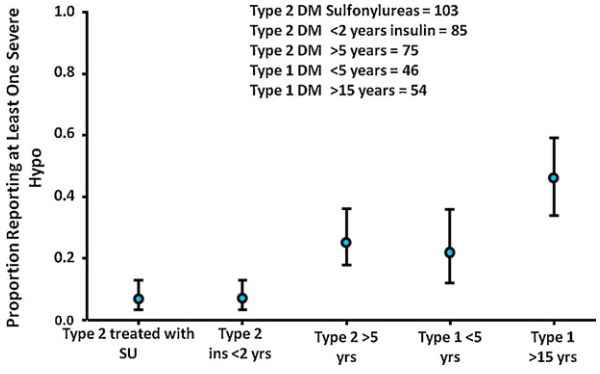

Fig. 1 – Prevalence of severe hypoglycaemia between differing treatment modalities (with kind permission from Springer Science+Business Media [12], Fig. 2).