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Commentary

Diabetes Management and Hyperglycemia in Safety Sensitive Jobs

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The chronic and acute effects of hyperglycemia affecting cognition and work are as important as those of hypoglycemia. Its impact, considering that majority of diabetic patients fail to reach therapeutic targets, would be potentially significant. Self monitoring of blood glucose, recognition of body cues and management interventions should be geared not only towards avoidance of disabling hypoglycemia, but also towards unwanted hyperglycemia. Over the long term, chronic hyperglycemia is a risk for cognitive decline. Acute episodes of hyperglycemia, above 15 mmol/L have also been shown to affect cognitive motor tasks. Maintaining blood sugar to avoid hyperglycemia in diabetic workers will help promote safety at work.

Introduction

The acute cognitive implications of hypoglycemia for safety sensitive work and activities in diabetic patients undergoing treatment are well recognized [1]. The converse of this - hyperglycemia and its workplace implications - probably does not receive as much attention as it deserves.

Physicians taking care of diabetic workers are rightly concerned about the acute disabling effects of hypoglycemia, which are often dramatic and self-evident. This could result in collusion with the diabetic worker to tolerate inappropriately high glycemic levels. The debilitating effects of hyperglycemia, which are subtle and insidious, perhaps experienced and expressed only as a vague sense of unease, should equally be a cause for concern especially because of its impact on cognition. When these effects coincide with times at work when cognitive demands are high, the consequences can be dire.

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The challenge becomes even greater if we consider the poorer glycemic status of younger patients of working age compared with that of older workers; in a study of 58,057 type 2 diabetes mellitus (T2DM) patients attending community care clinic, more than 70% of the diabetic patients below the age of 45 years were unable to achieve an A1C of 7.0% or below [2].

Long Term Effects of Hyperglycemia on Cognitive Domains

Various tests have been developed and validated for different domains of cognitive functioning, such as visuo-spatial performance, verbal and non-verbal memory, processing speed, executive function and mental state. In diabetes, scores in verbal memory, processing speed and brief cognitive screening (mini-mental state) are consistently more affected than in other domains.

Insulin resistance

Impaired glucoregulation, even before reaching the levels in diabetes, has been found to be associated with poorer performance on tests of executive function and working memory. This was demonstrated in a study of non-diabetic participants, aged between 55 years and 84 years, whose glucoregulatory status were ascertained by glucose tolerance tests and insulin levels. Those classified as poorer glucoregulators were found to have poorer performance scores [3].

T2DM patients at time of diagnosis, compared with non-diabetics, appear to be already worse off in terms of cognitive functioning, suggesting that etiological events may have been set in motion early [4,5]. This is not surprising, considering the long lead up of insulin resistance and compensatory hyperinsulinism. Insulin receptors are widely distributed in the brain, especially in the hypothalamus and hippocampal regions. Neural activity linked to learning and memory would be impacted by insulin resistance at the brain [6]. Furthermore, many of those with diabetes may have suffered from the disease for varying periods of time before diagnosis was confirmed and treatment initiated.

T2DM

Obese adolescents with T2DM (mean age 16.5 years, mean duration of diabetes mellitus [DM] 2.6 years) were found to perform consistently worse in all cognitive domains than obese controls without evidence of insulin resistance, matched for age, sex, school grade and other variables [7].

Reassuringly, once diagnosed and treated, the rate of cognitive decline among 68 T2DM patients compared with 38 non-diabetics in a four year follow-up did not reveal any difference after controlling for vascular factors and depression [4]. However, the diabetic participants (mean age 65 years) in this study had a baseline A1C of 6.9% and a four year follow-up A1C of 7.2%, generally indicating an optimal state of glycemic control. This should give cause for cautious optimism, but only for the diabetic worker, who has presumably been declared fit at pre-employment and whose diabetes is well controlled.

The Atherosclerosis Risk in Communities (ARIC) study compared differences in cognitive decline in the three domains of processing speed, verbal memory and executive functioning, between 516 diabetics and 8,442 non-diabetics at two time points over a six year period. Diabetics were noted to perform poorer than non-diabetic controls on tests of processing speed such by the digit symbol substitution test (DSST). This decline over the follow-up period was significantly faster in the diabetic participants, of whom 51% had an A1C between 8.9% and 10.9%. However, no trend of cognitive decline associated with A1C was noted within the diabetic group [8]. The participants in the ARIC study were middle aged with a mean age of 56 years and a mean duration of diabetes of 9.1 years.

An earlier study of community dwelling female participants aged 65 to 99 years found that cognitive decline among those with diabetes were significantly faster compared to those without the disease [9].

Every 1% increase in A1C was also associated with a 1.75 point lower DSST score in the Action to Control Cardiovascular Risk in Diabetes - Memory in Diabetes cross sectional study (population mean age 63 years, mean duration of DM 10.4 years). The DSST has been validated for testing in the cognitive domains of visual motor speed, capacity for learning, sustaining attention and working memory [10].

A relevant systematic review of 25 articles with follow-up periods between two to 18 years and involving 8,656 participants yielded pooled estimated cognitive decline rates, which were 1.2 to 1.5 times greater for diabetics than for non-diabetic controls [11]. Over the long term, it is conceivable that microangiopathy and oxidative stress may contribute by their effects on critical areas of the brain, as they do by affecting other target organs of diabetic disease [12].

Evidence would also suggest that optimization of blood glucose levels in the middle aged diabetic can attenuate or possibly reverse some of the cognitive deficits associated with hyperglycemia and insulin resistance [6]. To what extent this would apply to a young T2DM with an onset of impaired glucoregulation in the early teens and facing a longer duration of the disease will need to be further investigated.

With an ageing workforce, older diabetics may still be employed. The picture becomes considerably less optimistic for the elderly diabetic above 70 years, when cognitive ageing is accelerated by co-metabolic factors such as hypertension, dyslipidemia, cerebrovascular disease and depression [13].

Type 1 diabetes mellitus (T1DM)

Among T1DM patients with and without retinopathy (mean ages 44 and 39 years, respectively), hyperglycemia has been observed as a risk factor for cognitive impairment irrespective of microvascular complications [14].

The diabetes control and complications trial), conducted among 1,441 T1DM (entry age 13 to 39 years) over a mean follow-up period of 18 years, found that the recurrent hypoglycemia occurring under trial conditions of intensive treatment did not pose a risk of cognition impairment. Instead, it was those with an A1C above 8.8% who performed less well on tests of psychomotor efficiency, and motor speed [15].

Neuroimaging abnormalities

Moderate degrees of cerebral atrophy have been noted among middle-aged and elderly T2DM [16]. The finding of both reduced white matter volume and enlarged cerebrospinal fluid space among obese adolescent T2DM compared with obese controls [7] should be of concern, as would likewise the finding of different brain connectivity in imaging studies of T1DM. Functional connectivity, from magnetoencephalography studies, which provide an indication of the way different brain regions communicate, was also correlated with the cognitive functions of memory, executive functioning and processing speed [14].

Acute Short Term Effects

The issue of whether excursions above normoglycemia can immediately impact cognitive competence and disrupt work is still not definitely settled.

Experimental work has been performed, using insulin clamps to create varying bands of glycemia during which cognitive testing is carried out. Generally, none or minimal deleterious effects in complex cognitive processing were noted in earlier studies, even at glucose levels of 21.2 mmol/L (382 mg/dL) [17,18]. The participants in these studies, who had T1DM and were aged between 18 to 44 years, were notably chronically poor in their glucose regulation as evidenced by a high A1C (9.6-10.2%), prompting one to speculate that this may in part be due to cerebral adaptation.

Another study of both 196 T1DM participants (mean age 38 years) and 34 T2DM participants (mean age 50 years), which made use of self-administered cognitive testing done immediately before self-monitoring of blood glucose, reported cognitive effects of hyperglycemia affecting approximately 50% of the participants at levels exceeding 15 mmol/L (270 mg/dL) across all groups [19]. This study also noted a small positive correlation between greater cognitive impairments with more frequent exposures to hyperglycemic episodes, thus negating the adaptive theory.

Besides cognitive impairments, mood changes resulting in increased agitation and decreased alertness were also significantly associated with hyperglycemia clamped at 16.5 mmol/L (297 mg/dL) or more among type 2 diabetic participants [20].

Another exciting area of development is investigating the role of glycemic variation as a trigger factor for cognitive impairment [21]. Continuous glucose monitoring systems have now made possible the evaluation of the mean amplitude of glycemic excursions. Wide variations in glycemic excursions were found to be associated with cognitive impairment among a group T2DM patients (mean age 78 years). The findings were adjusted for markers of glycemic control (A1C, fasting and postprandial glucose) as well as other cognitive determinants (hypertension, dyslipidaemia, depression). Whether these findings can be replicated among a younger working age group remains to be seen. That reducing glycemic variability has some salubrious effect should come as no surprise, if we are to consider the evidence of its role in inducing oxidative stress and endothelial dysfunction. Perhaps this might also explain why we should encourage diabetic workers to avoid postprandial peaks.

What of the 'glucose memory facilitation effect'? An early report of this effect from a shot of glucose (usually 25 g) was in a 1981 study, which found that healthy adolescents with higher blood glucose levels following a carbohydrate-rich meal displayed enhanced recall of word pairs relative to a fasting control group [22,23]. Subsequently, several investigators have also found this improving effect to be operative in healthy elderly individuals tested for verbal episodic memory [23].

Glucose facilitation of memory by glucose rescue is part of the response of the diabetic patients to hypoglycemia, but would probably have no role under non-hypoglycemic conditions in the diabetic patient.

Summary of Risk Factors for Cognitive Impairment among Diabetic Patients

- Impaired glucose regulation
- Age
  Older patients are at increased risk, due to co-existing metabolic risk factors. The young T2DM with onset of impaired glucose regulation in his teens is also vulnerable.
- Glycemic control
  Chronic hyperglycemia
  Acute hyperglycemia
  Wide glycemic variation
  Treatment may reverse some of the adverse cognitive effects
- Co-morbidities
  Hypertension
  Dyslipidemia
  Depression
  Cerebrovascular disease

Occupational Health Implications for the Diabetic Worker and His Physician

Assessing the diabetic worker on fitness to work

The occupational physician has a role to assist diabetic workers in minimizing their risks of the medical consequences of their condition. Hyperglycemia is one of the many factors associated with cognitive decline. The magnitude of this impact in turn depends on many other factors such as age, state of diabetes control and the co-existence of vascular morbidity. This impact, seen against the wider holistic milieu of aptitude, attitude, skills and experience, may be small in the middle aged worker, but increases with age.

While the screening and selection based on skills and competence do not come within the purview of an occupational medical assessment, the medical aspects certainly do. Would there then be a case for suggesting a medical screening tool for cognitive competence, especially if the fitness in question is that involving a very senior or a safety sensitive position for the older diabetic worker?

In hyperglycemia, cognitive domains involving psychomotor skills and information processing appear to be most commonly impaired [20,24]. Perhaps the time has come for the wider adoption and adaptation of cognitive test batteries, currently commonly applied in research and very specialized settings (e.g., pilots), for the wider employment setting. The interpretation of the test results relevant to the requirements of the job will then have to be individualized.

Beyond that, decisions must also be made about the steps to be taken in the wake of unfavorable results. Repeating of the tests for trend or progression of a possible problem, optimizing diabetic management, proactive strategies and grounds for transfer to other duties are some of the issues to be considered.

Psychomotor and mental efficiency is a requirement in many jobs. Each cognitive domain is specific for the function being tested, and it is possible for a worker to score highly in memory but poorly in information processing and reasoning. On the other hand interrelationships between the various cognitive domains cannot be ignored; if people are to be able to reason and conceptualize information accurately (i.e., executive function performance), they must have a reasonable memory. Examples of such occupations include pilots, air traffic controllers, quality control technicians, refinery operators and intensive care unit staff, to name but a few. Many of these workers may also be required to operate independently. Their work can substantially be a process of receiving signals, retaining the information conveyed by these signals and subsequently processing the information in order for the correct response to be made in a timely manner.

Without doubt, the mitigating effects of experience in the job, having colleagues, supervision, shared decision making and other safeguards are not easily replicated in studies. In this respect, the hyperglycemic manager, even working under the most harried conditions of responding to a crisis, works in a team and in a sense is better protected against lapses than the hyperglycemic worker, who may be operating alone. Nevertheless, it is pertinent to note that, while hypoglycemia can be recognized by colleagues, the signs of hyperglycemia are comparatively more subtle and may be missed altogether, both by the diabetic worker and his colleagues.

However, that is not to say that the elder statesman in government or the captain in industry, who suffer from diabetes, are in any less vulnerable positions. They must use their judgment to make important decisions in a safe, responsible and rational manner. One could always speculate on how the course of history may have been influenced by the impact of a chronic disease like diabetes on the affected leadership.

Day to day glycemic management

Glucose homeostasis is a perpetual challenge for diabetic workers. A1C measurements, indicative of average glucose control over the preceding three months, must be complemented by timely blood glucose monitoring. Intensive glycemic control can reduce neurocognitive deficits, just as it can reduce micro and macrovascular risks and protect the eye, kidneys and the heart [25].

It would be ideal if all diabetic workers could keep their glucose levels within prescribed targets, pre-meal and post meal, but for the many who more often than not find maintaining these targets an onerous struggle, a good starting point may be to avoid all glucose levels of more than 15 mmol/L (270 mg/dL) [19], especially post meal or during compensation for hypoglycemia, when the tendency to hyperglycemia is greatest. For the time being, it would seem that this can protect psychomotor and mental efficiency in most people. Staying within a glucose variation of 2.2 mmol/L (40 mg/dL) is also a good practice [25]. To achieve this requires a multi-pronged approach requiring self recognition of cues, self monitoring of blood glucose and a management strategy combining physical activity, dietetics and medication.

Take Home Message for the Occupational Physician

- Occupational physicians and diabetic workers should be mindful of the implications of hyperglycemia for safety at work.
- The domains consistently affected in diabetes are processing speed and verbal memory. Working memory, attention span and learning can also be reduced as a result. The elderly diabetic is at increased risk.
- Optimizing glycemic control with treatment can attenuate some of these adverse impacts. Self-monitoring of blood glucose should be encouraged as part of the management strategy to avoid episodic hyperglycemia. A1C values indicate the average glycemic control over the preceding three months and do not capture these episodes.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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