Brief Literature Review: The Potential of Diabetes Technology to Improve Sleep in Youth With Type 1 Diabetes and Their Parents: An Unanticipated Benefit of Hybrid Closed-Loop Insulin Delivery Systems

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Sleep has recently gained attention as a risk factor for higher A1C levels and problems with the management of type 1 diabetes, especially in the adolescent population (1). Sleep has also become a prime target for interventions because it has been established as a risk factor for obesity, insulin resistance, and type 2 diabetes (2), and the most recent American Diabetes Association *Standards of Medical Care in Diabetes* recommends that providers assess sleep quality as part of routine diabetes management (3). It is important to develop behavioral sleep-promoting interventions specific to type 1 diabetes because of the management and nocturnal issues that are unique to this disease. However, although behavioral modifications may improve sleep habits and increase sleep duration, these changes do not address the underlying physiology, including constantly fluctuating blood glucose levels and the need to make frequent treatment decisions overnight. Thus, we believe that one of the potential benefits of new hybrid closed-loop insulin delivery systems, which reduce glycemic variability by automatically adjusting basal insulin doses based on continuous glucose monitoring (CGM) readings, is a positive impact on the sleep of patients with type 1 diabetes, as well as their caregivers.

Effects of Poor Sleep on Type 1 Diabetes

It is well known that sufficient and good-quality sleep is essential for maintaining optimal physical and mental health (4). In adults, poor sleep has been identified as a risk factor for diseases such as hypertension, insulin resistance, type 2 diabetes, and coronary artery disease (5,6). Furthermore, a meta-analysis of data from international studies indicates that short sleep duration is linked to obesity in both children and adults (7). Sleep restriction and sleep disturbances increase insulin counter-regulatory hormones such as cortisol and growth hormone and therefore increase insulin resistance (8,9). In addition, experimental studies of sleep restriction demonstrate links between poor sleep and problems with memory, cognition, and mood disorders (10,11).

Because type 1 diabetes is a complex disease that requires constant evaluation, the effects of poor sleep on cognition and mood likely have a significant negative impact on diabetes management. For example, Jaser and Ellis (12) showed that increases in sleep duration correlated with improvement in self-management of type 1 diabetes, suggesting that sleep has an effect on the behavioral aspects of diabetes management. The relationship between sleep and A1C appears to be a bi-directional one, in which sleep disturbances may contribute to higher A1C and blood glucose variability may disturb sleep. Thus, the use of a hybrid closed-loop system may be one approach to decreasing blood glucose variability to improve sleep quality.

Effects of Insufficient Sleep in Adolescents With Type 1 Diabetes

Insufficient sleep has been identified as a public health problem for children and adolescents in the general population (13), and it is especially prevalent in those with chronic diseases, including type 1 diabetes (14,15). A meta-analysis of sleep patterns found that children and adolescents with type 1 diabetes sleep significantly less than those without diabetes (by ~26 minutes per night) (16). Furthermore, Perfect et al. (17) conducted a study using polysomnography and found that adolescents with type 1 diabetes spend more time in stage N2 sleep (the middle stage of three progressively deeper stages of non-REM sleep) and less time in stage N3 sleep (the deepest stage of non-REM sleep, also known as slow wave or "deep sleep") than healthy peers. This is important because stage N3 sleep is generally thought of as the most restorative of the sleep stages, when the body can regenerate. In adolescents with type 1 diabetes, this difference in sleep architecture was associated with higher A1C levels and worse quality of life.

Diabetes-related sleep disturbances, including nocturnal caregiving behaviors frequently related to hypoglycemia, are common in youth with type 1 diabetes and can greatly affect sleep quality (18). However, it is not only hypoglycemia that causes nighttime awakenings, but also rapid glucose changes that are associated with a sensation of hypoglycemia even when glucose levels are within the normal range (19). Sleep disturbances are related to both physiological changes in glucose levels and the psychological impact of managing diabetes (i.e., frequent nighttime blood glucose checks related to fear of hypoglycemia). Therefore, advances in technology that increase time spent in the target blood glucose range could reduce these disturbances.

Importance of Sleep for Parents of Adolescents With Type 1 Diabetes

Caregivers who are responsible for the diabetes management of their children are also not meeting recommendations for sleep duration (15) and are therefore an important population to consider. When parents do not get sufficient sleep and parental stress is increased, the diabetes management of the child is negatively affected (18).

Nighttime has been identified as a particularly stressful time for parents (20) because one of the most concerning aspects in caring for a child with diabetes is the fear of nocturnal hypoglycemia (18). This fear is not entirely unfounded given that the risk for hypoglycemia in children with diabetes is increased during sleep (19). Pillar et al. (19) found that hypoglycemia during sleep, especially recurrent hypoglycemia, results in decreased awakenings, suggesting that sleep itself inhibits counterregulatory responses to hypoglycemia. Parental fear of hypoglycemia may lead to frequent and often unnecessary nighttime checks. Even in families using CGM systems, parents still frequently wake to check glucose data. Hybrid closed-loop systems have the potential to improve parental sleep by allowing for basal insulin delivery to be modulated based on glucose levels, reducing the occurrence of nighttime low glucose levels and possibly reducing fear of nocturnal hypoglycemic episodes.

Technology in Diabetes Management

Although the use of technology has led to decreases in blood glucose variability and reductions in A1C (21), patients and their families must develop enough trust in diabetes devices to allow them to function as they were intended. In addition, these devices come with the potential for additional disturbances, including frequent alarms (22). In fact, results from a recent study (23) indicated that children using insulin pumps and CGM systems reported greater sleep disturbances. Difficulty initiating and maintaining sleep was also significantly higher in children using insulin pumps compared to those using injections, children using CGM devices compared to those using glucose meters, and those who experienced nocturnal hypoglycemia compared to those who had not (23).

Although the use of insulin pumps and CGM systems has been associated with greater sleep disturbances in children and parents, there may be a beneficial effect on sleep with the use of hybrid closed-loop technology. For example, in one recent study (24), parents of children using a hybrid closed-loop system reported decreased fear of hypoglycemia as the families developed trust in the device. This indicates the potential for technology to play a role in improving sleep, because of both the physiological effect on glucose levels and the psychological effect on fear of hypoglycemia and diabetes distress for patients with type 1 diabetes and their caregivers.

The Newest Diabetes Technology: Hybrid Closed-Loop Insulin Delivery Systems

In the United States, there is currently only one "artificial pancreas" device that is approved by the U.S. Food and Drug Administration and available outside of research settings. This device is considered a "hybrid" closed-loop system because it still requires the wearer or caregiver to be involved with glucose monitoring for calibrations and input of carbohydrates for meals rather than fully automating insulin delivery. In a review from 2015 (25), there were 18 devices in development with wide variability in functionality, so more options are likely to become available.

Hybrid closed-loop systems have been extensively studied for safety and efficacy under various conditions (24,26,27). These studies demonstrated that the devices are safe without causing excess ketone production during times of insulin suspension and without leading to excess insulin administration and subsequent hypoglycemia. They are also effective in decreasing blood glucose variability and A1C levels and reducing hypoglycemic events. The effects have been particularly significant during the nighttime hours (27), and results have been consistent across hospital settings, home settings, and camps (26).

The Future of the Artificial Pancreas and the Potential Role in Improving Sleep

The ongoing development of an artificial pancreas is an exciting prospect, not only for its potential to decrease glucose variability, but also for the potential positive impact it could have on the psychosocial aspect of managing diabetes, and specifically for improving sleep. As previously demonstrated, however, technology itself has the potential to cause sleep disruptions due to frequent alarms during the night. Therefore, mechanisms to reduce nocturnal alarms, such as alternate hyper- and hypoglycemia settings for nighttime or reminding patients before bedtime about a pending overnight calibration, would be beneficial. For safety purposes, glucose confirmation may be necessary overnight; however, routine calibrations should be programmed to occur only during daytime hours. Alternatively, sensors that do not require calibration would reduce alarm fatigue by limiting alarms solely to glucose level alerts. Sensor accuracy is an ongoing area of improvement, and better glucose sensor accuracy would reduce excess alarms and increase the ability of the system to function as intended to reduce blood glucose variability. In addition, better sensor accuracy may increase trust in the system and further reduce the fear of nocturnal hypoglycemia.

Continued development toward a fully automated closed-loop system is still needed because there is frequent human error involved in the current systems that can result in a user being "kicked out" of the automatic mode and no longer being able to benefit from the system's ability to regulate glucose levels automatically. Reducing the need for users' active involvement will increase the devices' ability to function properly and will likely increase uptake of device use. In addition, multiple hormone systems (i.e., those that also deliver glucagon), can further reduce the occurrence of hypoglycemia and decrease overall blood glucose variability.

Conclusion

Sleep is becoming recognized as an important component of type 1 diabetes care and deserves increased attention as the target of interventions aimed at decreasing long-term complications. Given that blood glucose variability, especially hypoglycemia, and the fear of hypoglycemia often result in nighttime glucose monitoring, this is an area of particular interest. Hybrid closed-loop systems have demonstrated a significant ability to reduce blood glucose variability during the nighttime, and therefore, in addition to reducing A1C levels and the risk for diabetes complications, these systems may also have a significant impact on sleep in adolescents with type 1 diabetes and their caregivers. However, further research is needed to evaluate this potential. In addition, the use of hybrid closed-loop systems may have a positive impact on health care providers' sleep by improving patients' medical care and reducing the need for nocturnal emergency calls. Currently, inherent device issues such as sensor inaccuracy, nocturnal alarms, human error, and difficulty keeping the systems in automatic mode limit the potential effect the devices can have on sleep. Over time, however, with improvement in the devices, we may see that one of the unanticipated but welcome benefits of closed-loop systems will be improvements in sleep.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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Author Contributions

E.C.C. wrote the manuscript and approved the final version. S.S.J. wrote and revised the manuscript and approved the final version. E.C.C. is the guarantor of this work. No data were included in this manuscript.

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