OSA Associated with Diabetes Complications

Written by Lori Alexander

Obstructive sleep apnea (OSA), which is prevalent among patients with type 2 diabetes, has been found to be significantly associated with peripheral neuropathy and retinopathy—two diabetes-related complications that cause substantial morbidity. The findings are from two studies that were conducted in the diabetes clinic of a UK-based hospital, and Abd Tahrani, MD, MRCP, MMedSci, University of Birmingham, United Kingdom, reported the results.

OSA occurs in as many 86% of people with type 2 diabetes. Because OSA and diabetes complications share common inflammatory and molecular consequences, Dr. Tahrani and coinvestigators hypothesized that OSA may aggravate microvascular dysfunction and cellular damage in diabetes, resulting in peripheral neuropathy and retinopathy.

OSA in Patients with Type 2 Diabetes: A Novel Predictor of Peripheral Neuropathy

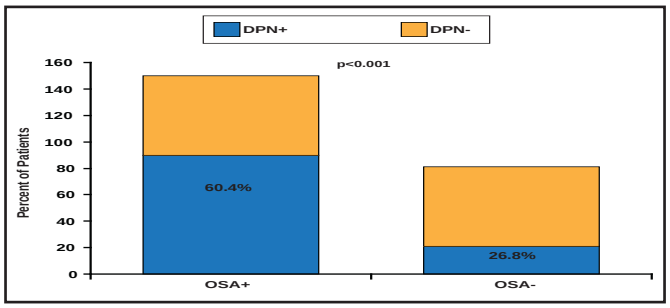
Data from 231 patients with diabetes were analyzed. Patients with known respiratory disorders (including OSA) were excluded, as were patients who were known to have neuropathy for reasons other than diabetes. Diabetic peripheral neuropathy (DPN) was diagnosed using the Michigan Neuropathy Screening Instrument, and OSA was assessed using home-based portable multichannel respiratory monitoring [ADA 2011. Poster 0388-PP].

The overall prevalence of OSA was 64.5%. Of the 149 patients with OSA, 59% had mild apnea, as measured by the apnea-hypopnea index (AHI 5 to <15 events); 23% had moderate apnea (AHI 15 to <30 events), and 18% had severe apnea (AHI ≥30 events).

The overall prevalence of DPN was 45%. The prevalence was significantly higher among patients with OSA than those without OSA (p<0.001; Figure 1). Patients with OSA reported more neuropathic symptoms, and all aspects of the foot exam and the prevalence of skin hypersensitivity were more common among patients with OSA. The severity of peripheral neuropathy was found to correlate with the severity of OSA.

The unadjusted odds ratio (OR) for peripheral neuropathy was 4.160 (95% CI, 2.309 to 7.494; p<0.001). After adjustment for possible confounders (including age, gender, waist circumference, smoking and alcohol, diabetes duration, medications, and other factors), OSA remained an independent predictor of peripheral neuropathy (OR=2.958; 95% CI, 1.416 to 6.178; p=0.004).

Figure 1. The Relationship Between OSA and DPN.



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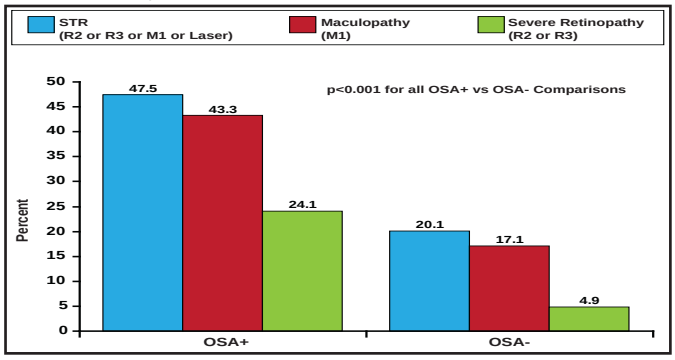
OSA in Patients with Type 2 Diabetes: A Novel Predictor of Sight Threatening Retinopathy

The results of a study on retinopathy were similar [ADA 2011. Poster 0391-PP]. Among 224 patients in the study, the overall prevalence of OSA was 63%. Of the 142 patients with OSA, 61.3% had mild apnea, 23.2% had moderate apnea, and 15.5% had severe apnea.

Rates of sight-threatening retinopathy, severe retinopathy, and maculopathy were determined on the basis of screening images or an ophthalmologist diagnosis. The overall prevalence of each oculopathy was 37.4%, 16.2%, and 33.7%, respectively. The prevalence of each oculopathy was significantly higher among patients with OSA than among those without OSA (Figure 2).

Figure 2. The Relationship Between OSA and Sight-Threatening Retinopathy, Diabetic Retinopathy, and Maculopathy.



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After adjustment for possible confounders, OSA was an independent predictor of each oculopathy:

- Sight-threatening retinopathy: OR=3.633 (95% CI, 1.642 to 8.037; p=0.001)

- Severe retinopathy: OR=5.057 (95% CI, 1.380 to 18.537; p=0.014)
- Maculopathy: OR=4.443 (95% CI, 1.925 to 10.253; p<0.001)

The data from the two studies suggest that OSA may play an important role in the development of both diabetic neuropathy and retinopathy. Prospective studies are needed to confirm this hypothesis. In addition, research is needed to determine the impact of treating OSA on both diabetic complications.

Insulin Delivery: Special Needs of Adolescents

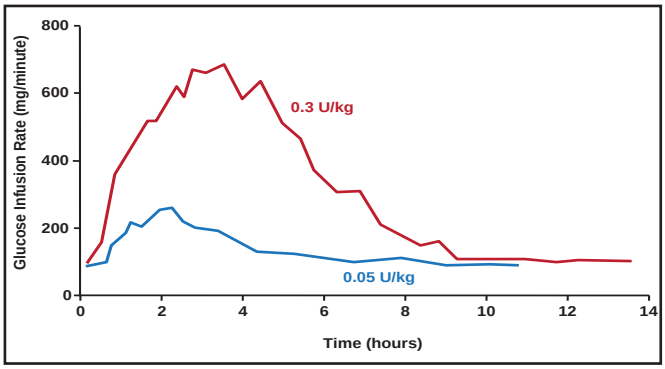
Written by Rita Buckley

In youth with type 1 diabetes (T1DM), increasing insulin resistance and decreased adherence to diabetes management tasks often occur during the adolescent years, leading to deterioration of glycemic control [Maffeis C et al. *Pediatr Diabetes* 2011]. William V. Tamborlane, MD, Yale School of Medicine, New Haven, Connecticut, USA, discussed the pharmacokinetic and pharmacodynamic properties of insulin, the need for fast-acting insulin in the pediatric T1DM population, and the latest approaches for accelerating the time-action profile of insulin.

Insulin sensitivity is reduced, even in healthy lean adolescents as they progress through puberty. This insulin resistance, which appears to be related to the puberty-associated rise in growth hormone levels, is exaggerated in teenagers with T1DM, especially adolescents who are overweight or obese [American Diabetes Association. *Diabetes Care* 2006]. There is a need for faster-acting insulins to address the challenges of insulin resistance in the pediatric population. Adolescents with T1DM require large (ie, 0.2–0.3 U/kg) premeal bolus doses of rapid-acting insulin to overcome peripheral resistance in puberty. But, there are negative clinical consequences that are associated with this strategy. They include delayed peak, with early postmeal hyperglycemia, and prolonged duration that suppresses hepatic glucose production, causing late postmeal hypoglycemia, especially after the last meal of the day (Figure 1).

The timely delivery of insulin in doses that match the increase in blood glucose after and between meals is a therapeutic challenge [Stote R et al. *J Diabetes Sci Technol* 2010]. Rapid-acting insulin analogs offer the possibility of immediate preprandial or even postprandial administration in children and adolescents, who often have unpredictable sleep patterns and eating behaviors [Danne T. *Diabetes Care* 2007].

Figure 1. Dose-Dependent Pharmacodynamics of Regular Insulin.



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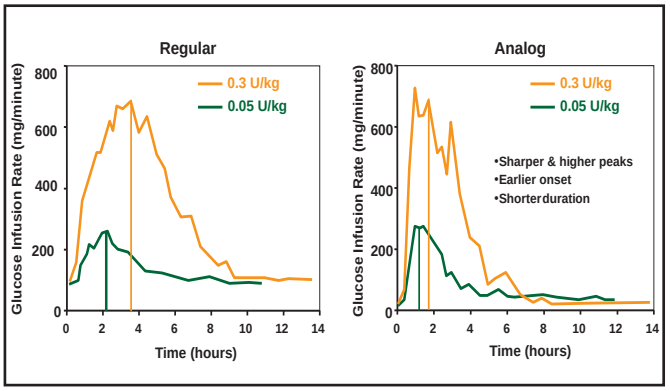
While rapid-acting insulin analogs have a more suitable pharmacokinetic and pharmacodynamic profile than soluble human regular insulin [Heller S et al. *Diabetes Metab Res Rev* 2011], even current insulins work too slowly and last too long for external closed-loop systems—once again resulting in exaggerated postmeal excursions, especially after breakfast, and vulnerability to late postmeal hypoglycemia, particularly after dinner.

More rapidly absorbed insulins can increase bioavailability and achieve greater within-subject consistency of bolus doses (Figure 2). Several approaches are being tested to accelerate the time-action profiles of fast-acting insulins. They include faster insulins; warming of the infusion site; coformulation with hyaluronidase; and alternate routes (microneedle infusion sets, inhaled insulin, and intraperitoneal insulin pumps).

Figure 2. Pharmacodynamics of Regular Versus Rapid-Acting Insulin Analogs.



Reproduced with permission from The American Diabetes Association, [Lys(B28), Pro(B29)]-human insulin. A rapidly absorbed analogue of human insulin. Howey DC et al; vol. 43, 396-402, March 1994.

The present status of these strategies varies. The first and only recombinant human hyaluronidase enzyme,