



Non-Insulin Dependent Diabetics for Longer than Twenty Years without Diabetic Retinopathy have Decreased Rates of Peripheral Neuropathy

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Abstract

Purpose: The purpose of this article is to determine if individuals with NIDDM for greater than twenty years without diabetic retinopathy (DR) had a lower prevalence of symptomatic diabetic peripheral neuropathy (DPN) than the NIDDM population. We hypothesized the prevalence of DPN would be lower in patients with NIDDM for greater than 20 years without DR possibly due to similar protection against complications of NIDDM.

Methods: NIDDM patients without DR were identified by Medicare ICD code 11.9. The lack of DR was determined by dilated fundoscopic exam. The duration of diabetes and symptoms of DPN were determined by survey. Results were compared to a prevalence of DPN of 50% that was determined from extensive literature review.

Results: Patients with NIDDM for greater than 20 years duration had a statistically lower prevalence of DPN 24% (5/21) than in the control group (50%). A one-tailed binomial test was utilized ($p=0.013$).

Conclusion: Our results are suggestive of some intrinsic protective effects of diabetic complications due to a decreased prevalence of DPN in patients with NIDDM for greater than 20 years without DR apparently independent of effective glycemic control.

Keywords: Diabetic retinopathy; Diabetic peripheral neuropathy; Non-insulin dependent diabetes mellitus

Introduction

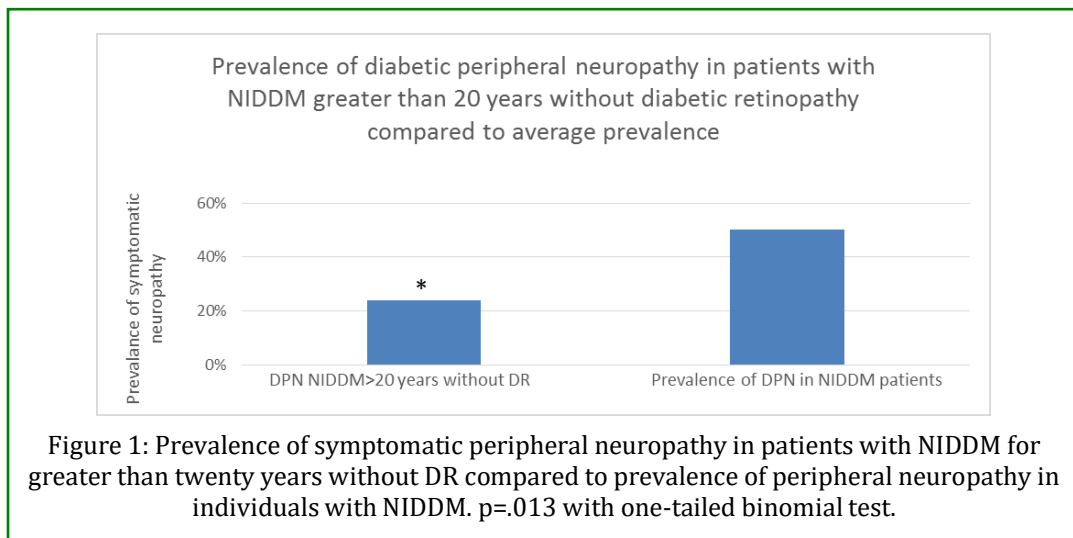
Diabetic retinopathy (DR) is a chronic condition and can cause gradual and progressive damage to the microvasculature of the retina leading to retinal ischemia and permanent vision loss. It has been reported that nearly all patients with insulin dependent diabetes (IDDM) for more than 20 years and 60% of patients with

non-insulin dependent diabetes mellitus (NIDDM) for longer than 20 years develop some degree of diabetic retinopathy [1]. However, there is great variability in the reported prevalence of diabetic complications. One study documented clinical signs of DR in 72% of their patient population after 15 years. The 50 year Medalist study, revealed 46.8% of individuals with IDDM for duration of greater than 50 years reported no significant

microvascular complications of diabetes. Additionally, individuals with 50-60 year durations of IDDM had a 50% prevalence of diabetic retinopathy (DR) while the rate of DR decreased to 44% in individuals with IDDM for 60-70 years and to 27% in individuals with IDDM for greater than 70 years [2]. After 17 years of follow-up, those without advanced retinopathy had a low likelihood of having worsening retinopathy [2]. DR in this patient population was independent of glycemic control [2].

Therefore, this landmark study suggested the Medalist population has intrinsic protective factors against the vascular complications of IDDM. Although the Medalist study identified a patient population that escaped many complications of IDDM, our study identified a correlation between the lack of DR and a lack of symptomatic diabetic

peripheral neuropathy (DPN) in individuals with NIDDM for greater than 20 years. A study by Mohan et. al specifically determined the prevalence of diabetic complications in individuals with NIDDM for longer than forty years. The prevalence of retinopathy and peripheral neuropathy was 76% and 87% respectively [3]. However, this study did not further study patients who had not developed either of these microvascular complications. It remains to be answered why some individuals do not develop systemic complications of diabetes. We hypothesize that individuals without diabetic retinopathy for 20 or more years will have a decreased prevalence of symptomatic peripheral neuropathy due to similar protection against microvascular complications associated with diabetes.



Methods

Our study is a cross-sectional study utilizing the patient population at Eye Specialists of Illinois, a multispecialty ophthalmology practice located in Park Ridge, IL. Patients without DR were identified based upon the Medicare ICD code 11.9 (diabetes without retinopathy). This diagnosis is determined by a dilated fundoscopic examination to ensure no signs of DR were present. The search criteria then returned a list of patients who met these criteria and had been seen within the last 12 months at the ophthalmology office. Patients that could not be reached were not included. The consent was verbally received by patients prior to answering questions. The study is in accordance with HIPPA regulations and adherent to the tenets of the Declaration of Helsinki. The data was obtained via telephone survey. All calls were completed by a single individual asking pre-determined questions to ensure consistency. The questions asked were in regards

to the type of diabetes, duration of diabetes, last A1C received within the last three months prior to the exam, and whether they had symptoms of peripheral neuropathy. Therefore, all information was obtained directly from patients. To test our hypothesis, the percentage of patients who have DPN after twenty years of being diagnosed with NIDDM and lack of DR was compared to multiple studies that have demonstrated rates of diabetic peripheral neuropathy (DPN) of 50% [4-7].

This was done with a one-tailed binomial test. Individuals with NIDDM for greater than 20 years without DR who responded "yes" to symptoms of peripheral neuropathy were compared to the pre-determined frequency of "yes" to symptoms of peripheral neuropathy. Unfortunately, few studies have solely looked at prevalence of developing DPN after having NIDDM for greater than 20 years or having DPN and DR after having NIDDM for

greater than 20 years. Statistical analysis was conducted using SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

Results

The prevalence of DPN in our patient population was 24% (5/21) which was statistically significant (p -value= 0.013) to the prevalence of DPN of 50% determined by literature review. This was determined by a one-tailed binomial test as previously noted. The average A1C was 7.2% with a standard deviation of 1.4% and the range of our A1C was 5.5 to 13%. All of these A1Cs were measured within a year of speaking to each patient. The average age our patient was 74 years old with a standard deviation of 10.5 years. The average duration of diabetes was 23.5 years with a standard deviation of 5.2 years (Table 1).

Statistics of our patient population		Std. Deviation
Sample Size (n)	21	
Prevalence of Peripheral Neuropathy	(5/21) 24%	
Average Duration of NIDDM (years)	23.5	5.2
Average A1C (%)	7.2%	1.47%
Average Age (years)	73.95	10.52
A1C range (%)	5.5-13%	
Age Range (Years)	59.5-93	

Table 1: Statistics of our patient population.

Discussion

The purpose of our study was to determine if individuals with NIDDM for greater than 20 years without evidence of DR had a lower prevalence of DPN than in the average NIDDM population with NIDDM for twenty or more years. It was challenging to determine a number to compare our results to because we were unable to find a study determining the prevalence of DPN in NIDDM for over twenty years with DR. However, multiple clinical trials demonstrated a prevalence of peripheral neuropathy of 50% [4-7]. One of these studies reported prevalence greater than 50% in NIDDM patients over the age of sixty [7].

The average age of patients in our study population was nearly 74. Thus, utilizing a prevalence of DPN of 50% is supported by multiple independent sources and is most likely higher than 50% in all patients with NIIDM for greater than 20 years. Our data indicates individuals without diabetic retinopathy for twenty or more years are less likely to develop DPN. Although previous studies have

indicated the importance of glycemic control in the prevention of microvascular complications of NIDDM, our patient population has a decreased prevalence of DPN apparently independent of effective glycemic control. As previously noted, The A1C in our population ranged from 5.5-13% with an average of A1C of 7.2%. Therefore, patients may contain intrinsic protective factors helping limit microvascular complications from NIDDM. Multiple studies have looked at a variety of genetic factors either promoting or protective against microvascular complications of NIDDM. Therefore, protection against complications of NIDDM appears to be multifactorial in nature [8]. Since our patient population lacks complications of NIDDM independent of glycemic control, we hypothesize our identified patient population may contain a variety of protective genetic factors against microvascular complications of NIDDM.

There were several limitations to our study. Despite our results, our sample size of 21 individuals was small. It was challenging to identify many patients who have been diagnosed with NIDDM for greater than twenty years and lack clinical findings of DR. Additionally, surveying patients to determine whether they have symptoms of DPN could have led to a falsely low prevalence of peripheral neuropathy. It is possible patients who did not report symptoms of peripheral neuropathy would test positive for peripheral neuropathy if monofilament testing was used or a more rigorous peripheral neuropathy survey was employed. Due to years of asymptomatic hyperinsulinemia, average duration of our population's diabetes may be falsely decreased as well. Finally, few studies have investigated patients with NIDDM diabetes for greater than twenty years. Therefore, it was challenging to obtain valid data we could compare our results to.

We are interested in continuing to follow our patient population to monitor whether they do indeed develop clinical signs of DR or DPN. Previous literature has demonstrated that diabetic complications are directly proportional to duration of the disease. Additionally, we will continue to identify new patients who meet our criteria's study as they are evaluated in our clinic. Our goal for this project is to bring attention to the patient population that has eluded the systemic complications of diabetes. We hope this helps the medical community continue to develop therapies to improve the quality of life for the hundreds of millions of patients who are debilitated by diabetes and leads to the discovery of protective genetic markers in systemically asymptomatic patients which can be used to help diabetics and protect them from the systemic manifestations of this disease.

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