Turk J Med Sci
31 (2001) 255-260

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Diabetic Osteopathy: Who is at Risk?

Received: November 25, 1999

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Abstract : This study was designed to determine the prevalence of osteopathy in diabetic patients, who are at risk of developing osteopathy, and clarify the relationship between osteopathy and other complications of diabetes mellitus. Thirty-four type I and 66 type II diabetic patients admitted to the endocrinology clinic between 1996 and 1997 and 30 nondiabetic subjects as a control group were studied. Bone scintigraphy (Tc 99m methylene diphosphonate) was used for the diagnosis of osteopathy. The body mass index (BMI) of each patient was calculated. Polyneuropathy was assessed by electromyography and the patients, for each of whom BMI was calculated, were asked about the symptoms of autonomic neuropathy and history of foot ulcer, whereas cardiovascular autonomic neuropathy was assessed by autonomic neuropathy tests and calculated QTc (corrected QT). Fundoscopy was performed for evaluation of retinopathy. Biochemical analysis was carried out for blood glucose, HbA_{1c} levels and microalbuminuria, an indicator of nephropathy. We found that the prevalence of osteopathy is 44% in diabetic patients and the risk of osteopathy increases with the duration of diabetes ($p<0.05$) and the age of the patient ($p<0.05$). The risk was found to be higher in females ($p<0.05$), and no relationship between the body mass index of the patient and blood glucose regulation was observed. 76.9% of patients with history of foot ulcer ($p<0.01$), 61% of patients with retinopathy ($p<0.01$) and 68.8% of patients with autonomic neuropathy ($p<0.01$) were found to have osteopathy. Because osteopathy may have devastating end results which can be prevented if recognized early, we suggest that all diabetics, especially those in the risk group, must be screened for osteopathy and, if required, they must receive proper treatment.

Key Words: Diabetes Mellitus, Osteopathy, Bone scintigraphy

Introduction

Diabetes mellitus is a state of hyperglycemia characterized by impaired carbohydrate, lipid and protein metabolism (1,2). In time, the musculoskeletal system may also be damaged, in addition to many other systems. Osteopathy is one of the complications of diabetes seen in the musculoskeletal system, which is involved in advanced disease.

Of the complications, foot problems are the most common, and constitute the primary cause of admittance to hospital in the diabetic population (3,4,5).

Diabetics are reported to have an osteopathy rate of 0.1-6.8% (6,7,8), whereas in patients with diabetic neuropathy this rate increases to 77% (9).

The most important characteristic of osteopathy is that it has intermittant activity; it can stay in an inactive stage for months or even years (10). Furthermore, although complete healing is seen in some of the patients, in others, progression of the disease may result in foot ulceration and even amputation in the absence of osteomyelitis (11). Thus the detection of osteopathy at an earlier stage and therapy with intensive diabetes control and nonweight-bearing of that foot will prevent this undesirable outcome.

In this study, we investigated the prevalence of osteopathy in diabetic people and the relationship between diabetic osteopathy and age, sex, duration, type and regulation of diabetes, microangiopathy, neuropathy and foot ulcer history. We attempted to define criteria for the determination of diabetic patients at risk of developing osteopathy.

Materials and Methods

Thirty-four type I (insulin dependent diabetes mellitus) and 66 type II (non-insulin dependent diabetes mellitus) patients who were admitted to the Ankara Numune Hospital Endocrinology and Metabolism Department between April 1996 and April 1997 were included in the study. For each group (type I and type II) 15 nondiabetic volunteers were used as a control group.

The type I group consisted of 12 female and 22 male patients with a mean age of 27.5 ± 1.4 years, and the type II group comprised 47 female and 19 male patients with a mean age of 54.4 ± 1.2 years.

The control-I group for type I patients consisted of 8 female and 7 male nondiabetic subjects with a mean age of 32 ± 2.4 years, and the control-II group for type II patients consisted of 9 female and 6 male nondiabetic subjects with a mean age of 59.2 ± 1.9 years.

Patients with osseous lesions resembling diabetic osteopathy, such as lepra, syringomyelia, tabes dorsalis, scleroderma, hereditary sensorial syndrome and familial amyloidosis, were excluded from the study. All patients were evaluated clinically and by X-ray, and those who had osteomyelitis and traumatic fractures were not included in the study.

Osteopathy was assessed by bone scintigraphy, which has been shown to be more sensitive than radiography in the diagnosis of osteopathy (12,13,14). After injection of 20 mCi technetium 99m methylene diphosphonate (Tc 99m MDP), scintigraphic images were taken with an SPX-6 Elscint gamma camera and low-energy all-purpose collimator at 0 minutes (dynamic phase), 3-5 minutes (blood pool), 3-4 hours and 24 hours (static phases). The absence of bone radiopharmaceutical uptake at the dynamic and blood pool phases, increased uptake at the 3^{rd} hour and its constancy at the 24^{th} hour static phase without any change in uptake dose was interpreted as diabetic osteopathy.

We used electromyography (EMG) with an MEB-7102 K model neuropack 2 (Nihon Kohden) device for the diagnosis of polyneuropathy. The conduction velocity of sensory and motor nerves, action potential amplitudes and F wave latency of sensory and motor sensations were studied in median, peroneal and sural nerve segments, while sensory nerve conduction was studied in median and sural nerves.

Patients were asked whether they had had foot ulcer at any time in their life, or symptoms of autonomic neuropathy such as gastric atony, urinary retention, rectal incontinence, diarrhea (other causes of diarrhea were eliminated), impotence (for patients under the age of 65 years) and also signs of orthostatic hypotension were assessed. For the diagnosis of cardiovascular autonomic neuropathy, QTc, which was calculated with Bazzet's formula (18), and cardiovascular autonomic neuropathy tests were used (15). Other causes of long QTc were eliminated (16,17).

Retinopathy was assessed by fundoscopy and, if necessary, by fluorescein angiography. The immunoprecipitation method was used for the detection of microalbuminuria, which was interpreted as an indicator of nephropathy (19).

HbA_{1c} levels were measured by the latex immunoagglutination inhibition method with Ames DCA 2000 TM HbA_{1c} kits in DCA 2000 TM analyzer. Fasting blood glucose was measured by the oxidation method; urinary examination for glucose and ketone was carried out with stripes.

In the statistical analysis of the relationship between age, BMI and osteopathy, Kolmogorov-Smirnov test was used; for the relationship of HbA_{1c} and osteopathy, the t-test in independent samples was used; and for the relationship between sex, type and duration of diabetes, foot ulcer history, other complications of diabetes and osteopathy, the Chi-square test was used, a p value of less than 0.05 being considered significant. The results are shown as "mean ± standard error".

Results

With the scintigraphic imaging technique, 11 out of 34 type I diabetic patients (32.35%) and 33 of 66 type II diabetic patients (50%) were found to have osteopathy. No one in the control groups was found to have osteopathy. The relationship between osteopathy and the type of diabetes mellitus was statistically insignificant ($p>0.05$).

In the type I diabetic patient group, 7 out of 12 female patients and 4 out of 22 male patients were found to have osteopathy, while in the type II diabetic patient group, 26 out of 47 female patients and 7 out of 19 male patients were found to have osteopathy (Figure 1). While

the relationship between osteopathy and the sex of patients was found to be statistically significant in the type I diabetic group ($p<0.05$), it was insignificant in the type II diabetic group ($p>0.05$). In total, osteopathy was detected in 31 out of 59 female patients and in 13 out of 41 male patients, and this female dominance was statistically significant ($p<0.05$).

The mean age of all diabetic patients was 45 ± 15.86 years, 50.36 ± 17.05 years in patients with osteopathy and 41.34 ± 13.75 years in patients without osteopathy. It was found that the prevalence of osteopathy increases with age ($p<0.05$) (Figure 2).

The body mass index (BMI) of each patient was calculated as weight (kg)/height (m^2). Six percent of patients were obese, 37% overweight, 49% normal and 8% underweight. Osteopathy was found in 5 of obese patients (83.3%), 15 of the overweight patients (40.5%) and 24 of the normal-weight patients (49%), while none of the underweight patients were found to have osteopathy. The relationship between osteopathy and BMI was insignificant ($p>0.05$).

Patients were grouped according to the duration of diabetes; 0-5 years for group I, 6-10 years for group II, and 11 years and more for group III. The prevalence of osteopathy was found to increase with the duration of diabetes ($p<0.05$) (Figure 3).

The mean HbA_{1c} level in patients with osteopathy was 10.02 ± 2.02%, whereas in patients without osteopathy it was 11.26 ± 2.08%. There was no relationship between osteopathy and HbA_{1c} levels ($p>0.05$).

A total of 34 patients had nephropathy, 38 patients had retinopathy and 68 patients had polyneuropathy. Of the 44 patients with osteopathy, 23 also had retinopathy (52.27%), 34 had polyneuropathy (77.27%) and 21 had nephropathy (47.7%). Although there was a significant relationship between osteopathy and retinopathy ($p<0.01$), no relationship was found between nephropathy and polyneuropathy ($p>0.05$, $p>0.05$) (Figure 4). Sixty four patients (64%) had autonomic neuropathy and 44 of patients (68.7%) with autonomic neuropathy had also osteopathy. There was a significant relation between osteopathy and autonomic neuropathy ($p<0.01$) Figure 5).

Ten out of 44 patients with osteopathy (22.7%) were found to have foot ulcer history. Out of 13 patients with a history of foot ulcer, only 3 said that they didn't have foot ulcer before. The relation between foot ulcer history and osteopathy was significant ($p<0.01$) (Figure 6).

Discussion

Diabetic osteopathy, diabetic neuroarthropathy, diabetic neuro-osteoarthropathy and diabetic Charcot's joint are all terms indicating the same pathology. After it was shown that the primary pathology is in the bone and that the joint deformities are secondary to this bone pathology, "osteopathy" became the more widely used term (6).

In 1831, Mitchell first identified this condition, and in 1868 Charcot began studying it (20). Since then, much research on the pathogenesis of osteopathy has been performed. In 1936, Jordan defined Charcot's joint in diabetic neuropathy (21). Oakley et al. classified foot lesions in diabetic patients and also explained their etiologies and treatment protocols (22). There are very different reports about the prevalence of diabetic osteopathy in the literature. In our study, 44% of all diabetic patients, 50% of patients with polyneuropathy and 68% of patients with autonomic neuropathy were found to have osteopathy. In 1962, Boehm, in a review of the literature, found only 52 cases with osteopathy (23). Pogonovska and his colleagues reported either bone destruction or generalized osteoporosis in the feet of 6.8% of 242 diabetic patients (6). Gondos examined all diabetics admitted to a large municipal hospital for 10 years and found only 36 cases of osteopathy (10). Friedman and Rakow reported that the prevalence of osteopathy was 77% in patients with diabetic neuropathy (9). Sinha et al. found Charcot's joint in 100 out of 68000 diabetic patients (24). Smith reported the prevalence of Charcot changes as 1.4% (8). In this study, while BMI, type of diabetes and blood glucose regulation were shown to have no effect on the diabetic osteopathy, we found the risk of osteopathy to increase with the age of the patient and the duration of diabetes; in the type I diabetic group, the risk was found to be higher in females than males.

This can be explained by faster bone formation in younger patients. Bone formation is a slow process and in time, destruction exceeds formation, which brings up the importance of the time factor (10). Oackley et al. also found a close relationship between foot lesions and age, but in his report, the duration and the severity of the

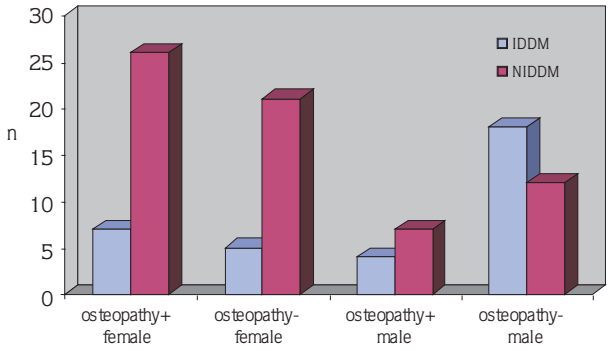

Figure 1. The relationship between osteopathy and sex in diabetic patients.

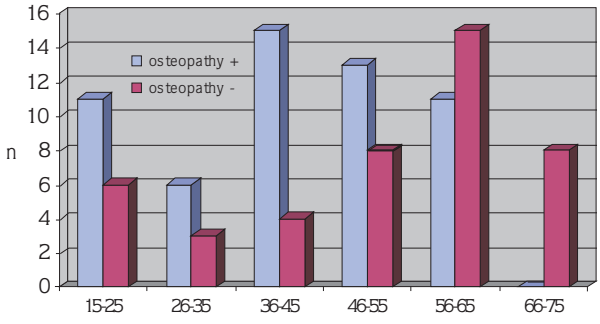

Figure 2. The relationship between osteopathy and age in diabetic patients.

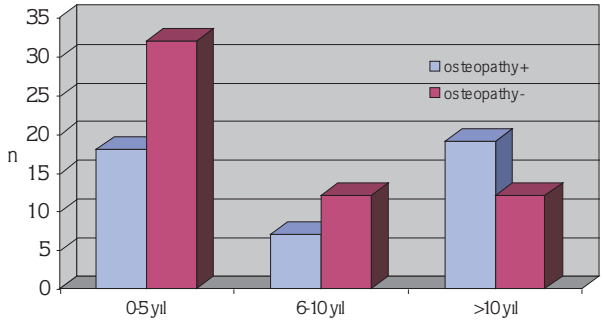

Figure 3. The relationship between osteopathy and duration of diabetes.

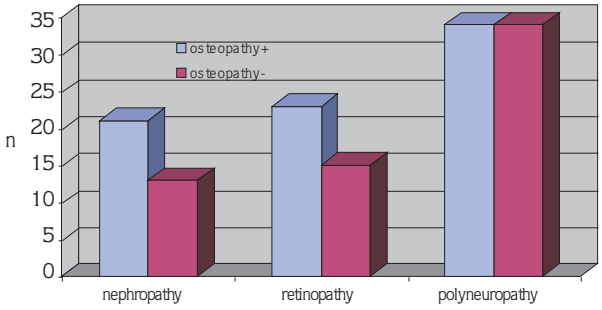

Figure 4. The relationship between osteopathy and nephropathy, retinopathy and polyneuropathy in diabetic patients.

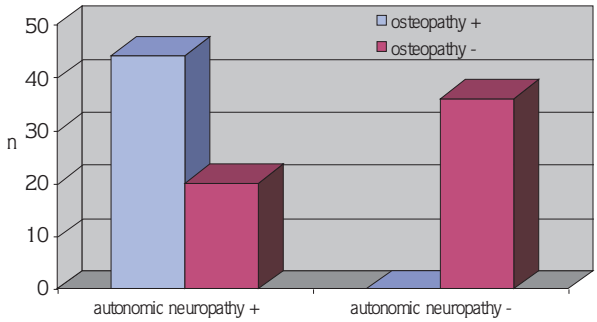

Figure 5. The relationship between osteopathy and autonomic neurophathy.

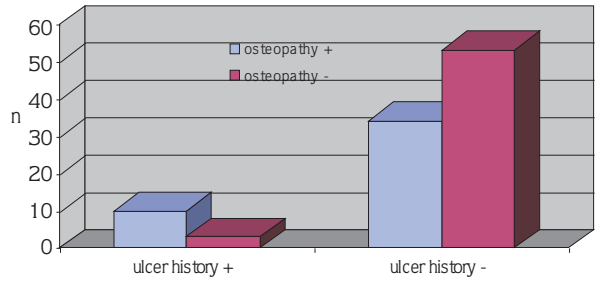

Figure 6. The relationship between osteopathy and foot ulcer history in diabetic patients.

diabetes were found to be unimportant (22). Lithner et al. reported a higher prevalence of osteopathy in type I diabetics (32%) than in type II diabetics (17%) and suggested that there was no relationship with the age and sex of the patients (25). Williams et al. stated that there was no relationship between osteopathy and the age of the patient or the duration of diabetes, but in their study a large majority of patients were type II diabetics: 50 type I, 145 type II (26).

According to Ellenberg, osteopathy is a messenger of flared up diabetes. In such a case, it is expected to find increased nephropathy, retinopathy, peripheral neuritis, and cardiovascular and gastrointestinal system impairment (27,28). Nonetheless, in our study, we found no relationship between osteopathy and polyneuropathy or nephropathy. The only consistent finding with Ellenberg's claim was that 52.3% of patients with diabetic osteopathy also had retinopathy.

We determined that 10 of (76.9%) 13 patients with a history of foot ulcer had osteopathy and decided that these patients form a risk group for diabetic osteopathy. In a retrospective study, Cavanagh and colleagues suggested that foot ulcers cause a high risk of residual bone abnormalities, but they were unable to determine the relative time of ulceration and bone abnormalities. They found the prevalence of traumatic fracture, bone destruction and amputation in the neuropathic ulcer group to be higher than in the neuropathic nonulcer group (29).

Four hypotheses have been suggested for the etiology of osteopathy: the primary metabolic bone disease theory, the ischemia theory, the neurotraumatic theory and the neurovascular theory.

Because it was shown that osteoblastic activity was normal and bone structure returned to normal spontaneously or with nonweight-bearing of the foot, the primary metabolic bone disease theory became invalid. The ischemia hypothesis also seems impossible due to the fact that the density of ischemic bone does not change. Osteoporosis, osteosclerosis and new bone formation need good circulation (11). Nowadays the most acceptable theory in the literature is the neurotraumatic theory. According to this theory, bone changes are secondary to loss of protective sensation (pain, heat and proprioception) of the foot and joints (4). There are reports claiming that repeated minor traumas result in neuroarthropathy in joints with impaired proprioceptive sensation (3,24,30). In our study, 10 out of 44 patients (22.7%) with osteopathy had no polyneuropathy and the relationship between osteopathy and polyneuropathy was insignificant. We were unable to explain the mechanism of osteopathy with this theory in these 10 patients. However, 44 patients with osteopathy had autonomic neuropathy, which can only be explained by the neurovascular theory.

According to the neurovascular theory, the neurally initiated vascular reflex causes increased blood flow in bone and active bone resorbtion by osteoclasts; fractures and joint deformities are secondary to this event. Leriche showed that lesions in sympathetic nerves cause hyperemia and bone atrophy (31). Shim detected increased bone blood flow in dogs following lumbar symphatectomy or incision of sciatic nerve, which carries sympathetic fibers (32). Schwarz et al. reported left neuropathic foot following left symphatectomy in a diabetic patient (33). It was reported that blood flow increases in neuropathic foot and symphatetic denervation causes significant vasodilation and arteriovenous shunt (34,35). Also, histopathologic evaluation of osteopathic bone revealed fusion and widening of the Haversian canals, expanded blood vessels, increased number of osteoclasts and active resorption (11,36,37). Our study supports the neurovascular theory against the neurotraumatic one. Serra et al. also reported that reabsorption due to osteoclasis and increased blood flow until osteomalasia appears are the characteristics of this arthropathy (38).

In conclusion, we found that older age, long duration of diabetes, history of foot ulcer, retinopathy, autonomic neuropathy and, for IDDM patients, female sex are the risk factors for diabetic osteopathy. We suggest that every diabetic patient, especially the ones with risk factors, even if their blood glucose regulation is good, must be examined for osteopathy, because osteopathy has devastating end results which can be prevented with appropriate precautions.

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