Diabetes & Metabolic Syndrome: Clinical Research & Reviews 9 (2015) 359–363

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

Disruption of circadian blood pressure, heart rate and the impact on glycemic control in type 1 diabetes

Baris Afsar *

Konya Numune State Hospital, Department of Nephrology, Turkey

ARTICLE INFO

Keywords:
Blood pressure
Circadian
Hypertension
Type 1 diabetes

ABSTRACT

Patients with type 1 diabetes (DM-1) have an increased mortality and morbidity risk compared to non-diabetic subjects. Even not recognized clinically at the early period of disease; patients with DM-1 show subtle neurological and cardiovascular abnormalities which is partly responsible for the increased mortality. One of these abnormalities is the disruption of circadian rhythms. Various factors such as autonomic dysfunction, sleep disturbance, smoking, cardiac and kidney function, atherosclerosis, arterial stiffness are suggested to cause these disturbances. Additionally these abnormalities have also implications regarding target organ damage such as microalbuminuria, retinopathy, and structural changes in glomeruli. Surprisingly, there are scarce data regarding the effect of tight blood glucose control and insulin on circadian rhythms in patients with DM-1. By the light of aforementioned data this review will try to summarize causes and consequences of disruption of circadian rhythms and the impact on glycemic control on these issues in patients with DM-1.

Contents

1. Introduction

Patients with type 1 diabetes (DM-1) have an increased mortality and morbidity risk compared to non-diabetic subjects. Overall, 75% percent of total diabetes related mortality is due to cardiovascular disease. Even not recognized clinically at the early period of disease; patients with DM-1 show subtle neurological and cardiovascular abnormalities which is partly responsible for the increased mortality. These abnormalities include elevations of blood pressure (BP), a decreased BP decline during sleep, increases in arterial stiffness and impaired autonomic nervous function [1]. Not only disorders of autonomic nervous system and cardiovascular system are commonly seen in patients DM-1, these abnormalities are also interrelated [2,3]. Although some mechanisms regarding these abnormalities are known, there is no doubt that much to be learned. Recently, it was speculated that abnormalities in glucose metabolism may contribute to autonomic and cardiovascular abnormalities in patients with DM-1.

By the light of aforementioned data this review will try to summarize causes and consequences of disruption of circadian rhythms and the impact on glycemic control on these issues in patients with DM-1.

1.1. Circadian blood pressure, autonomic neuropathy and type 1 diabetes

Various studies have shown that in DM-1, nondipping status of BP is prevalent and associated with increased risks for sustained

* Correspondence to: Ferhuniye Mah. Hastane Cad., Konya Numune State Hospital, Department of Nephrology, 42690 Konya, Turkey.
Tel.: +90 332 235 45 00; fax: +90 332 235 67 86.
E-mail address: afsarbrs@yahoo.com

http://dx.doi.org/10.1016/j.dsx.2014.05.002
1871-4021/

Table 1
Probable causes of disruption of circadian rhythms in type 1 diabetes.

	Ref.
Autonomic neuropathy	[8–12]
Sleep problems	[13]
Cardiac dysfunction	[14]
Renal dysfunction	[15,16]
Increased QTc dispersion	[17,18]
Arteria stiffness	[19,20]
Atherosclerosis	[21]
Smoking	[22]
Increases extracellular volume and sodium	[25,26]

hypertension, retinopathy, and nephropathy [4–6]. Not only at the later stages of DM-1, there are also abnormalities with regard to BPs in the early stage of DM-1. Indeed, it was demonstrated that during the early course of DM-1, the elevation of nocturnal BP values is pronounced and nocturnal dipping is reduced. However, apart from nighttime, daytime BP is also higher compared with that of healthy control subjects [7]. After these findings, the scientists began to investigate the factors related with elevation of nocturnal and daytime BP in patients with DM-1. These factors are summarized in Table 1.

One of the most extensive studies issue is autonomic dysfunction and its relation with circadian BPs. It was shown that autonomic neuropathy was closely related with non-dipping in DM-1 [8,9].

Poulsen demonstrated that even at the early stages of disease (normoalbuminuric phase) autonomic dysfunction as evaluated by heart rate variability (HRV) was higher in non-dipper group. There were also significant negative correlations between HRV and nighttime heart rate as well as nighttime BP, suggesting that attenuation in autonomic indices is associated with blunted diurnal variation in both heart rate and arterial BP [10]. It was also demonstrated that ambulatory BP measurements (ABPM) showed an incremental increase in all BP parameters from nondiabetic control subjects through subjects with autonomic neuropathy. A parallel incremental increase in diurnal and nocturnal ambulatory heart rates was also evident [8]. Duvnjak et al. studied the relationship between autonomic function, ABPM and albuminuria in normotensive, normoalbuminuric patients with DM-1. The study included 116 patients which 33 patients had autonomic neuropathy. Compared to those without neuropathy, patients with neuropathy showed significantly higher mean day and nighttime diastolic BP, mean systolic nighttime BP and mean daytime and nighttime heart rate. The authors suggested that autonomic neuropathy is already present in normotensive type 1 diabetic patients at the normoalbuminuric stage and related to BP and albuminuria [11]. Lastly, in a stepwise regression analysis, an "autonomic score" was reported to be the variable of main importance for the day-night difference in BP in patients with type 1 diabetes [12]. Thus, all these evidence indicates that autonomic neuropathy is a factor of importance for the reduced dipping at night.

Another potential mechanism for nocturnal non-dipping is the disordered impact of sleep. It was demonstrated that, dipping status in DM-1 was associated with longer sleep duration. Total sleep period was higher in the dipper group (497 ± 30 vs. 407 ± 44 min for dippers and nondippers, respectively, $P < 0.001$) [13].

Cardiac and kidney function was also investigated as a cause of blunted circadian BP dipping. For example it was found that nocturnal diastolic nondipping showed a positive correlation to diastolic cardiac dysfunction [14]. Glomerular hyperfiltration has been reported to be associated with a blunted reduction in diastolic BP at night and an expansion of extracellular fluid volume in normotensive and normoalbuminuric patients with DM-1 [15]. On the other hand however, in advanced stages of diabetic nephropathy and overt nephropathy in DM-1, non-dipping was associated with an increased rate of decline of the glomerular filtration rate (GFR) [16]. As explained later the role of volume control and circadian BP is controversial issue in patients with DM-1.

Increased QTc dispersion has also been suggested to be related with circadian BP in DM-1 [17]. Karavanaki et al. studied the QT interval prolongation, circadian variation of BP and heart rate in adolescents with type 1 diabetes. The authors found that in comparison with the dippers, non-dippers had reduced mean heart rate (24 h), and reduced mean heart rate (daytime). The QT interval was prolonged in the non-dippers (366.3 vs. 347.5 ms, $P = 0.015$). Moreover, the absence of nocturnal BP reduction was also related to the presence of a more prolonged QT interval [18].

Functionally, arterial stiffness has been shown to be related with autonomic dysfunction and BP in circadian abnormalities [1,19,20]. On the other hand structural alterations such as atherosclerosis was also related with circadian abnormalities in DM-1. In patients with DM-1, carotid intima–media thickness (cIMT) was higher in the nocturnal hypertensive group than in the normotensive group (0.44 ± 0.03 vs. 0.42 ± 0.04 mm, $P = 0.026$). Additionally, All ABPM parameters were significantly related to cIMT in multiple linear regression analysis [21].

The effect of smoking was also investigated in DM-1. In one study 24-h AMBP and autonomic function in 24 smokers and 24 non-smokers with normoalbuminuric DM-1 patients was examined. The two groups were matched for sex, age and diabetes duration. Smoking status was assessed by questionnaire and also assessed objectively by determinations of urinary cotinine. The results regarding BP were clear: ABPM was consistently higher in diabetic smokers, also when night BP was considered. A dose–response association between AMBP and tobacco consumption was present, as well as a positive correlation between AMBP and urinary cotinine. Urinary albumin excretion (UAE) was similar in the two groups, probably due to the inclusion criteria (normoalbuminuria) [22]. However, Sinha et al. demonstrated that smoking and microalbuminuria in young patients with DM-1 (without autonomic neuropathy and/or hypertension) does not cause a significant alteration of BP [23]. Thus the effect of smoking on circadian BP and autonomic function is not clear and more studies are needed in this issue.

Lastly, one should remember that there are also some areas of uncertainty regarding the mechanisms and circadian BP and autonomic dysfunction in DM-1. For example, it is not known whether the reduction in the nocturnal dip or the increase in BP at night is responsible for the target organ damage or if it is the same thing. One study shows that the reduction in the nocturnal dip precedes the increase in day and nighttime BP. It was also found that no increase in ambulatory systolic and diastolic BPs, although diastolic dipping at night decreased significantly [7]. It was also demonstrated that in patients with DM-1 glomerular basal membrane thickness was more strongly associated with nighttime mean arterial pressure than to mean arterial dipping. On the other hand, there is a stronger relation between the mesangial volumes to MAP dipping than to the nighttime MAP [24].

Same controversy exists with regard to volume status. Whereas some found significant association between extracellular volume, latent over hydration and sodium retention with ambulatory BPs [25,26], others have found no association between these two parameters [27,28].

1.2. Consequences of non-dipping and autonomic dysfunction BP in type 1 diabetes

By the ongoing discussion it is clear that circadian abnormalities are frequent in patients with DM-1 and various factors may be responsible for these abnormalities. However, the more important