

Pre-operative evaluation for diabetic cardiac autonomic neuropathy and their behavior during regional anesthesia

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Abstract

1.1 Background: CAN (cardiac autonomic neuropathy) is a common form of diabetic neuropathy and causes abnormalities in heart rate control as well as central and peripheral vascular dynamics. There is 2- to 3- fold increase in cardiovascular morbidity and mortality intra-operatively for patients with diabetes. Hemodynamic instability during intra-operative period depends on the severity of autonomic dysfunction. Patients with severe autonomic dysfunction have a high risk of blood pressure instability and intra-operative blood pressure support is needed more often in those with greater impairment. Non-invasive diagnostic methods assessing autonomic function allow identification of patient at risk pre-operatively and better prepare the anesthesiologist for potential hemodynamic changes. This study aimed to evaluate the diabetic patient and control group pre-operatively for cardiac autonomic neuropathy with CANS – 504 (cardiac autonomic neuropathy analyzer) and compare hemodynamic instability in each group during spinal anesthesia

1.2. Methods: We performed cardiac autonomic function study with CANS – 504 in group I (diabetic with autonomic neuropathy) 20 patients, group II (diabetic without cardiac autonomic dysfunction) 20 patients, group III (control group – non diabetic without cardiac autonomic dysfunction) 20 patients, preoperatively and monitor the blood pressure, pulse rate and ECG in these groups during spinal anesthesia.

1.3. Results: During spinal anesthesia in group I experienced hypotensive reactions and bradycardia significantly more often (75%) than in group II (40%) and group III (18%). In order to achieve stability in B.P the patient in group I had to be given vasoactive drugs much more often (55%) than patients of group II (30%) and those of group III (15%). In group I 33% are non-reactive to vasoactive drugs and these patients need inotropic support to achieve B.P stability.

1.4. Conclusive: We found a significant correlation between degree of autonomic dysfunction and largest drop in B.P and variability in H.R and cardiac rhythm. These results prove the atypical hemodynamic behavior and extreme instability in B.P in diabetic autonomic neuropathy under spinal anesthesia. Therefore we consider it to be very helpful to check the cardiovascular refractory status of diabetic pre-operatively and may prepare anesthesiologist for potential hemodynamic changes.

Keywords: Diabetic cardiac autonomic neuropathy, Hemodynamic instability in diabetic patient, CANS – 504, Cardiac autonomic dysfunction study, Spinal anesthesia in diabetic patient.

1. Introduction

Diabetes mellitus is a common disease (affecting approximately 3% of global population) caused by disordered metabolism which has the potential to damage every organ system resulting in plethora of pathological conditions. One of the most serious complications of diabetes is, damage to autonomic nervous system. Approximately 20% of diabetic patient are afflicted with some form of mortality by 500% [1]. The estimated 8 year survival rate for diabetic patients with cardiac autonomic neuropathy is 77% compared to 97% survival rate estimate of diabetic patients without CAN [2].

In diabetes, CAN is ultimately the result of complex interactions among degree of glycemic control, disease duration, age related neuronal attrition and systolic and diastolic blood pressure. Hyperglycemic plays the key role in the activation of various biochemical pathways related to the metabolic and redox state of the cell, which in concert with impaired nerve perfusion, contribute to the development and progression of diabetic neuropathies. Experimental data implicate a number of pathogenic pathways that may impact autonomic neuronal function in diabetes including : formation of advanced glycation end products, increased oxidative / nitrosative stress with increased free radical production,

activation of the polyol and protein kinase C pathways, activation of polyADP ribosylation, and activation of genes involved in neuronal damage [5].

Affecting one-fourth of type I diabetics and one-third of type II diabetics, cardiac autonomic neuropathy is one of the most well studied forms of diabetic autonomic neuropathy because it is one of the most life threatening and it is also one of the easiest form of autonomic neuropathy to assess [4]. The autonomic nervous system modulates the electrical and physiological activity of myocardium via the sympathetic (stimulatory) and parasympathetic (inhibitory) branches of autonomic nervous system which is concert with each other to promote proper cardiac function. Damage to autonomic nerve fibres innervating the heart and blood vessels caused by diabetes can result in impaired control of heart and vascular dynamics.

There is 2- to 3- fold increase in cardiovascular morbidity and mortality intra-operatively for patients with diabetes [4]. Studies have demonstrated that the induction of anesthesia, regional anesthesia causes a great degree of decline in heart rate and blood pressure in diabetic patient compared with non-diabetic individuals and that hemodynamic stability in the intra-operative period depends on the severity of autonomic dysfunction. Patients with severe autonomic dysfunction have a

high risk of blood pressure instability, intra-operative blood pressure support is needed more often in those with greater impairment. Intra-operative hypothermia, which may decrease drug metabolism and affect wound healing and impaired hypoxic induced ventilatory drive have also been shown to be associated with the presence of CAN. Non-invasive diagnostic methods assessing autonomic function allow identification of risk patient pre-operatively and better prepare the anesthesiologist for potential hemodynamics. This study aimed on Pre-operative evaluation for diabetic autonomic neuropathy using CANS 504 (cardiac autonomic neuropathy system analyzer) and their behavior during regional anesthesia.

3. Materials and Method

A randomized controlled, prospective comparative study was done to compare the behavior of diabetic patient with cardiac autonomic neuropathy and non-diabetic patient without cardiac autonomic neuropathy during spinal anesthesia. The study was conducted after approval by the hospital ethical committee and an informed written consent was obtained from all.

A total number of 60 ASA II & III patients belonging to age group of 40 – 60 years were divide into three groups 20, 20, 20 respectively. Group I - patients with diabetic mellitus having cardiac autonomic neuropathy, Group II - diabetic patient without cardiac autonomic neuropathy and group III - control patients non-diabetic without cardiac autonomic neuropathy. Along with routine investigations, pre-operative evaluation for cardiac autonomic neuropathy is done with CANS 504 (cardiac autonomic neuropathy system analyzer).

3.1 Inclusion criteria

Case

- Age: 40- 60 years.
- Sex: both male and female.
- Diabetes mellitus > 3 years
- ASA II & III

Control

- Age: 40- 60 years.
- Sex: both male and female.
- Not a known diabetes mellitus
- ASA I

3.2. Exclusion criteria

- Age < 40 & >60 years.
- PS IV

3.3 Equipments required

- CANS 504 – cardiac autonomic neuropathy system analyzer.
- ECG monitor
- Sphygmomanometer.
- Pulse oxymeter.

CANS-504 is an important tool to measure and diagnose autonomic dysfunction using ECG R-R interval and automatic B.P measurement. Along with routine investigations, pre-

operative evaluation for cardiac autonomic neuropathy is done with CANS 504 (cardiac autonomic neuropathy system analyzer).

CANS-504 is connected to the computer through RS 232 serial communication. After connecting all accessories to unit, patient should be in supine position.

Attach ECG electrodes and record

1. Resting ECG,
2. deep breathing ECG,
3. supine and response to standing ECG,
4. valsalva ECG.

Attach B.P cuff to the patient, and record

1. Supine B.P, standing B.P,
2. Hand grip B.P (beforehand grip and after 5 min. of 30 % hand grip).

E.C.G test 1 - 4 done to evaluate parasympathetic function.

B.P test 5 - 6 done to evaluate sympathetic function.

Each test were graded 0,1,2. (0- normal, 1- borderline, 2 - abnormal).

After analyzing the grades of the each test, patients were diagnosed as early or definite parasympathetic and sympathetic involvement.

After pre-operative CANS study, intra-operatively under aseptic precaution, for each patient subarachnoid block given at L2 –L3 level, volume 3 ml of 0.5% bupivacaine given. Sensory level obtained up to T4-T5 level. Intra -operative recording of ECG rate and rhythm, B.P, pulse rate were done for each 5 minutes in first 30 minutes and then for each 15 minutes till the end of surgery. Injection ephedrine 6mg given intra-venously if systolic B.P falls below 90mmHg or 20% of baseline values. Injection atropine 0.6 mg given i.v pulse rate falls below 60/min.

4. Results

In group I, during spinal anesthesia, the fall in B.P was more frequent (75%) and they need more doses of inj. Ephedrine (42%) (Table: 1) and 33% patient in group I are non reactive to inj. Ephedrine and they need inotropic support for B.P stability. 5 patients in group I have abnormal results i.e grade II in all five test of autonomic function study. Those five patients were non responsive to inj. ephedrine during hypotensive reactions. They need inotropic support for hemodynamic stability. The occurrence of bradycardia (50%) during hypotensive reaction is also frequent among group I and need atropine (40%) (Table: 2). In group II, fall in B.P was frequent (40%) but less than group I and more frequent than group III. In group III fall in B.P was less frequent (18%) (Table: 1) and need less doses of inj. Ephedrine (15%). Fall in B.P can be managed even with intra-venous fluids in most cases. Hypotensive reactions are less frequently accompanied with bradycardia (10%) (table: 2). From the ANOVA and POST HOC test we can find a significant difference in systolic and diastolic B.P between group I and GROUP III. But there was less significant difference in B.P between group I and group II, group II and group III (table: 3) (table: 4). From ANOVA we find significant difference in pulse rate between group I, II, III at various time interval during intra- operatively(table:5).

Bar Chart

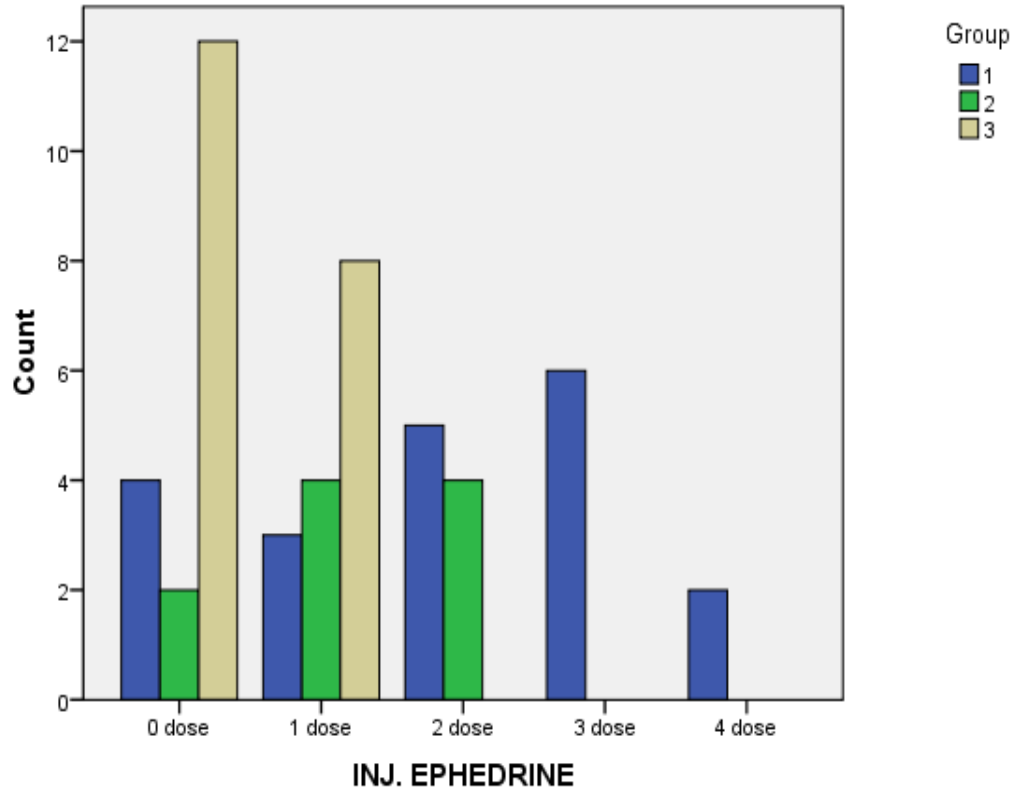


Fig 1

Bar Chart

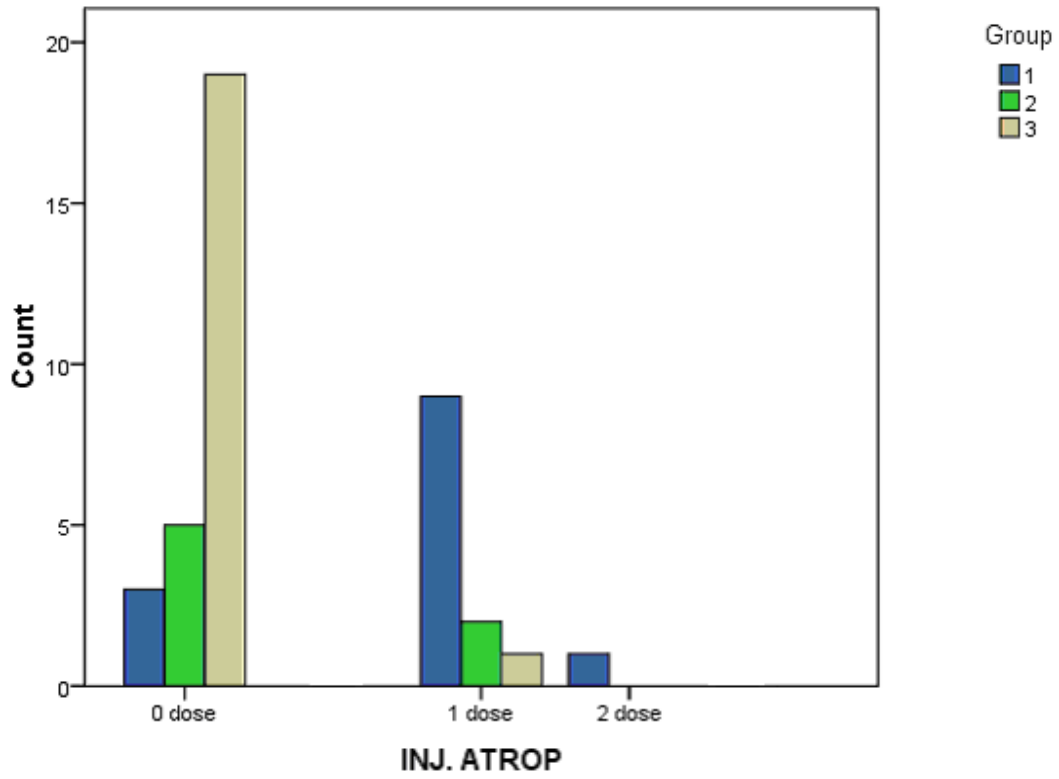


Fig 2

Table 1: Post Hoc Tests

Multiple Comparisons					
LSD					
Dependent Variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.
25 Minutes Systolic	1	2	3.600	3.108	.253
		3	7.000*	2.538	.008
	2	1	-3.600	3.108	.253
		3	3.400	3.108	.280
	3	1	-7.000*	2.538	.008
		2	-3.400	3.108	.280
25 Minutes Diastolic	1	2	2.700	3.012	.375
		3	6.000*	2.459	.019
	2	1	-2.700	3.012	.375
		3	3.300	3.012	.279
	3	1	-6.000*	2.459	.019
		2	-3.300	3.012	.279

*. The mean difference is significant at the 0.05 level.

Table 2

ANOVA			
		F	Sig.
0 Minutes Systolic	Between Groups	1.140	.328
5 Minutes Systolic	Between Groups	1.597	.213
10 Minutes Systolic	Between Groups	.671	.516

Table 3

ANOVA				
		Sum of Squares	df	Mean Square
30 Minutes Pulse Rate	Between Groups	213.270	2	106.635
	Within Groups	4272.650	47	90.907
	Total	4485.920	49	
45 Minutes Pulse Rate	Between Groups	515.830	2	257.915
	Within Groups	5233.550	47	111.352
	Total	5749.380	49	

5. Discussion

Cardiovascular autonomic neuropathy (CAN), a common form of autonomic dysfunction found in patients with diabetes mellitus, causes abnormalities in heart rate control, as well as defects in central and peripheral vascular dynamics [10]. Reduction in variability of heart rate is the earliest indicator of CAN [8]. Clinical manifestation of CAN are exercise intolerance, intra-operative cardiovascular liability, painless myocardial ischemia, increased risk of mortality. In the early 1970s, Ewing *et al.* proposed five simple noninvasive cardiovascular reflex tests (Valsalva maneuver, heart rate response to deep breathing, heart rate response to standing up, blood pressure response to standing up, and blood pressure response to sustained handgrip) that have been applied successfully [7]. Today, sensitive and early assessment of cardiovascular autonomic neuropathy is possible by means of noninvasive autonomic function tests, including power spectral analysis of a series of successive R-R intervals (frequency domain analyses) [13]. This can be performed on short R-R sequences (e.g., 7 minute) or on 24-hour electrocardiogram recordings. The heart rate power spectrum is typically divided into two frequency bands: low (0.04 to 0.15 Hz) and high (0.15 to 0.4 Hz). The high-frequency region is generally considered a marker of vagal activity, whereas the low-frequency

component is influenced by both sympathetic and vagal activity [14].

The association of mortality and cardiovascular autonomic dysfunction indicates that individuals with abnormal autonomic function tests are candidates for close surveillance [11]. Thus it has been recommended that a baseline determination of cardiovascular autonomic function be performed upon diagnosis in type 2 diabetes and within 5 years of diagnosis for those with type 1 diabetes, followed by a yearly repeat test. In addition, the presence of autonomic dysfunction should alert the health care professional to search for associated risk factors of cardiovascular disease and implementation of an intense program to reduce these factors and thereby reduce the risk of mortality [15].

Results of this study indicate that fall in B.P and bradycardia are more frequent in group I than group II and group III. This indicates that diabetic patients with cardiac neuropathy are more liable for hemodynamic variability than diabetes patients without cardiac neuropathy and non diabetic without cardiac neuropathy. Diabetes patients with abnormal (grade 2) in all five autonomic dysfunction need inotropic support for B.P stability. Perhaps the most important things we can do for our patients with diabetes are to make them aware of autonomic neuropathy, to let them know whether they have it and to help them keep blood sugar level in an acceptable range and explain the risk during regional anesthesia. Doing so not only help to reduce the risk of intra-operative morbidity and mortality but also lower the risk of heart disease, diabetic eye, kidney and nerve disease, each of which patient dearly want to avoid. With a brief 15 minutes autonomic study we can anticipate the risk during anesthesia and can help patients live longer, healthier lives.

6. Conclusion

We found a significant correlation between degree of autonomic dysfunction and largest drop in B.P and variability in heart rate and rhythm.

Hemodynamic instability is high in Diabetic Patients with cardiac autonomic neuropathy than diabetic patient without cardiac autonomic neuropathy.

These results prove atypical hemodynamic behavior and extreme B.P instability and need for inotropic support are seen in diabetes patients with cardiac autonomic neuropathy.

4. Eventhough hemodynamic instability in diabetic patient without cardiac autonomic neuropathy are frequent than non-diabetic patient, both group are treated with similar manner during intra-operative fall in blood pressure and heart rate. Inotropic support is not needed for these patient groups.
 5. Therefore we consider it to be very helpful to check the cardiovascular refractory status of long standing diabetes patient pre-operatively and to differentiate diabetic patient with and without cardiac autonomic neuropathy, so that we can anticipate the risk during anesthesia in such patients and manage effectively to improve the peri-operative outcome of these patients.
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