Introduction

Carbamazepine (CBZ) is a widely used medication, especially for anticonvulsant and for treatment of various intractable pain like diabetic or trigeminal neuralgia. The action mechanism is to slow the rate of recovery of voltage activated $\text{Na}^+$ channels from inactivation. Through its tricyclic-like chemical structure and clinical evidence of aggravation of autonomic symptoms from treatment of epileptic patients and patients with Fabry’s disease, it is likely that CBZ may aggravate peripheral and autonomic neuropathy, however, only scanty reports are available. Since the appearance of autonomic neuropathy associated with a grave prognosis in diabetic patients (and possible in other neuropathy), we design the study to elucidate this question.

Although there are many tests available clinically for evaluation of the autonomic function, sympathetic skin response was chosen for its study because of their simplicity in examination, acceptable by patients and correlated quite well with the sympathetic dysfunction in the diabetic patients. Sympathetic skin response (SSR) is the evoked electrodermal activity originated from sweat gland and surrounding tissues. After the afferent impulse being sent centrally, the brain stem relay station and central polysynaptic facilitatory and inhibitory impulse modulate the signal, and sent out the efferent pathway through intermediolateral nucleus in spinal cord from T1 to L2.

Methods

In this study, we collected 77 diabetic patients who had evidence of peripheral neuropathy, both complaints of numbness or pain clinically neurophysiologic data of slowing nerve conduction objectively. Their autonomic symptoms evaluated and SSR was done before and after treatment of carbamazepine.

Test for SSR

The method described by Knezevic and Bajada (1985) and modified by Vatahiki and his colleagues (1989) will be used.

The patient will lie supine and relax in a quiet, moderately heated, and semidarkened room, with as few external stimuli as possible. The recording electrodes (10mm diameter silver/silver chloride disc electrodes) will be placed over the pit of the palm and in the middle of dorsum hand. The ground will be placed close to the
wrist (The resulting potential will be negative in the palm). For lower limbs, recording will be just behind the ball of the foot and in the middle of dorsum foot.

The band pass will be adjusted of 0.16-3200Hz. The sensitivity will be 0.2 to 0.5 for hand and 0.1-0.2mV for the foot. A sweep length of 5-10sec will be set and will be triggered by the electric stimulation. The electric stimuli will be single square-wave pulses of 0.1msec, located at the standard stimulation point for median and tibial nerve motor NCV, contralateral to the limb from which the recording is to be made. The stimulation intensity will be strong enough to be slightly painful. If the test should be repeated, a rest-period of at least 1 minute will be delayed.

The response latency is measured from the stimulus artifact to the first deflection of the signal from the base-line. The response amplitude is measured from peak to peak. There are various studies reporting the data of latencies and amplitudes of SSR (Schondorf 1993). Normal latency values do not differ significantly between various laboratories and are in the range of 1.5 ± 0.1 sec by median nerve stimulation and 2.0 ± 0.1 sec by tibial nerve stimulation (Knezevic & Bajada 1985, Elie & Guiheneuc 1990).

Since the reflex latency is almost constant, while the amplitude is highly variable, we will consider the study of SSR abnormal when it was absent (Shahani et al 1990).

Results

The numbers of SSR obtained from 4 times of median and tibial nerve stimulation were recorded. We found that the chance of pick up SSR from either stimulation was closely correlated from the other arm (χ² = 40.83, p<0.001). The same conclusion was found also in the lower extremities (χ² = 32.72, p<0.01). Therefore, the responses from both side stimulation were summed together for further analysis. However, although from previous studies, it has been suggested that the chance of obtaining SSR was inversely correlated with the duration of diabetes; our results did not support that conclusion.

For upper limbs, the patients who had duration of diabetes less than 10 years had a 4.71 ± 11.3 results compared with 4.25 ± 11.8 of those who had duration of diabetes more than 10 years (p=0.41). Similarly, it was 3.12 ± 9.96 vs 2.4 ± 9.62 for each of less than and longer than 10 years duration of diabetes (p=0.44). When results of both upper and lower extremities were put together, it were 6.61 ± 35.4 vs 4.31 ± 29.8 (p=0.22). The failure of showing correlation probably was due to great inter individual difference. Finally, there were 29 patients received twice SSR before and after 4 months-duration of carbamazepine treatment, it failed to reveal any significant difference between, with 5 ± 11.9 vs 3.6 ± 10.2 for upper extremities for each of before and after treatments; and 3.2 ± 11.9 vs 2.5 ± 9.3 for lower extremities. It was concluded that carbamazepine did not impair the autonomic function in diabetic patients.