ORIGINAL ARTICLE

The Hot Bath Test Among Malaysian Multiple Sclerosis Patients

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Summary

This is a study of 13 Malaysian patients with clinically definite Multiple sclerosis (MS) subjected to a hot bath test with VEPs, BAEPs, median nerve SSEPs before and after heating. Five patients (38%) developed neurological changes with the rise in body temperature. There was an average of 0.46 new sign per patient. Four patients had motor disturbances attributed mainly to aggravation of spinal cord dysfunction. Two patients had additional visual deterioration, one patient has associated VEP change. This study shows that though Uhthoff's phenomenon has not been noted in the reports of Asian MS patients, when subjected to rigorous testing, Asian MS patients also show sensitivity to body temperature change. However, the percentage of positivity of the hot bath test is much lower than that reported for Caucasians. Thus this study shows further differences between Asian and Caucasian MS patients.

Key words: Hot bath test, Multiple sclerosis.

Uhthoff's phenomenon was first described in 1890 as a temporary blurring of vision induced by exercise in patients with MS[1]. The effect of temperature causing transient deterioration of neurological signs in MS patients may also be induced by a hot bath, and trivial events such as a hot drink or use of a hairdryer[2]. This phenomenon is not uncommon; McAlpine & Compston[3] described transient deterioration of symptom in 34.7 per cent of their MS patients with exercise, and with body heating in 13.5per cent. Perkin & Rose[4] reported that of 125 patients who had recovered from optic neuritis, 11 per cent had transient deterioration of vision with exercise and 8 per cent with temperature change. On the other hand, lowering of temperature with a cold bath had a temporary beneficial effect[5].

Deterioration of neurological symptoms with temperature change has also been accompanied by change in neurophysiological measurements, such as the ability to detect double flashes of light[6], VEPs and SSEPs[7, 8]. The patho-physiological mechanism for this interesting phenomenon of thermolability is now attributed to the reduction of threshold for induction of complete conduction block in a demyelinated fibre[9, 10].

It has been recognised that the prevalence of MS is low in most parts of Asia. There are also differences in the clinical manifestations among the Asian MS patients as compared with white patients. Asian patients have been characterised by the following: rare occurrence of a similar family history; higher incidence of visual failure at the onset of illness; more severe degree of visual impairment during follow up; more frequent occurrence of recurrent acute transverse myelitis; clinical forms of optic-spinal recurrence and optic-brain-stem-spinal recurrence, with Devic's disease being more common; more severe involvement of the spinal cord with greater functional disability and less frequent involvement

of the cerebellum[11,12]. When comparing the pathology of Japanese and Western cases of MS, differences were also noted with the Japanese patients showing more severe involvement of the optic nerve and the spinal cord, often with necrosis and associated with which there is a poor inflammatory glial cell response[13].

Malaysian MS patients are similar to those found in the rest of Asia. The prevalence of MS is low at 2/100,000. There is a high female-male ratio of 5:1. Optic-spinal recurrence is the most common clinical pattern of the disease, accounting for 63 per cent and severe spinal cord and visual disability, high mortality and transient involvement of the cerebrum, cerebellum and brain-stem are other characteristic clinical manifestations[14].

Yue *et al*[15] reported 47 cases of MS from Hong Kong. They however found a broad similarity between their patients and those from major Oriental and Caucasian series. They challenged the generally held view that there are significant differences between the Oriental and Caucasian MS patients. They attributed such differences reported in the literature to under-diagnosis of the mild cases.

There is no mention of the effect of temperature change on neurological symptoms, among Asian MS patients despite the extensive medical literature. None of our 50 clinically definite and probable cases of MS have complained of neurological symptoms related to temperature change such as from a febrile illness[16]. The hot bath test has been used for some time as a diagnostic aid in MS[17, 18, 19]. This is a report of the application of the hot bath test to 13 Malaysian patients with clinically definite MS to assess the effect of temperature change in the local MS patients.

Methods

All the 13 patients involved in this study had clinically definite MS in the category of CDMS A1 according to classification by Poser *et al* [20].

The Hot Bath Test was performed as follows: the patient's neurological status was noted before the test. Their oral temperature was also taken. The patient was soaked in hot water bath to the level of the neck with the water temperature maintained at 40 degrees Celsius. The patient was repeatedly examined and the bath continued, attempting to raise the oral temperature by not less than one degree Celsius. The patient was then taken out of the hot bath and examined until the symptoms and signs as well as the body temperature returned to baseline. The motor power was graded 0 - 5 scale according to recommendation by the Medical Research Council (UK), which is as the follows: 0 - no contraction, 1 - flicker or trace of contraction, 2 - active movement, with gravity eliminated, 3 - active movement against gravity, 4 - activity against gravity and resistance, 5 - normal power. Grades 4-, 4 and 4+, was used to indicate slight, moderate and strong resistence respectively[21]. Evoked potentials (VEP, BAEP, median nerve SSEP) were done before the hot bath test and after achieving the rise in body temperature in the same order. The body was kept warm during the evoked potential tests with warm blankets. Double dose contrast CT scan of the head or MRI was done on the patients with positive hot bath test.

All the evoked potential studies were done on the Nicolet compact four machine. For the VEP, the stimulus was a reversing black and white checkerboard pattern subtending an angle of 14.6 degrees placed one metre from the subject's eye. The standard check size was 27.4 minutes. The response was recorded from transverse chain of three occipital electrodes with midfrontal reference. At least two consistent runs of 100 reversals were averaged for each eye. The normal value was based on 19 female subjects with P1 = 99.90 ms (S. D. = 4.4), 21 male subjects with P1 = 100.3 ms (S. D. = 5.8).

For the BAEP, the stimulation consisted of 100 μsec pulse rarefaction click with intensity of 65 db above hearing threshold. 11.4 clicks were given each second monoaurally. The electrodes were applied to the vertex and the ear lobes. The average of at least two consistent runs of 2000 clicks was obtained in each test. The normal values was based on 39 females with I-V = 3.91 ms (S. D. = 0.17), 27 males with I-V = 4.01 ms (S. D. = 0.22).

For the median nerve SSEP, the stimulus was a constant current pulse of 100 usec duration applied twice per second to the median nerve at the wrist. The stimulus intensity was adjusted to three times the sensory threshold. The response was recorded from mid-clavicular point ipsilateral to the stimulated limb, C6 vertebra, over the hand area of the sensory cortex contralateral to the stimulation. The electrodes were referred to the mid-frontal electrode. 200-300 responses were summed and averaged. At least two separate consistent averages were recorded. The normal values was based on 26 healthy subjects. The mean interwave latency of N9-N13 with their S. D. was plotted against the arm length. The mean interwave latency of N13-N20 was 5.9 msec (S. D. = 0.59).

Results

Of the 13 patients who went through the test, eight were in relapse and the other five were in remission. The average duration of illness of these 13 patients was 7.1 years with an average of 5.2 relapses. The clinical forms of the disease were as follows: optic-spinal in six patients, disseminated in four patients, spinal, optic-spinal-cerebellum, optic-spinal-brainstem in one patient each. None of the patients had noticed any definite deterioration of the neurological function with hot weather, warm shower or febrile illness. The average rise of the body temperature was 1.6 degree Celsius which usually took about an hour to achieve. Five patients (38%) demonstrated deterioration of neurological signs with average of 0.46 new sign per patient. Cases 1 and 5 were in relapse while the test was done but cases 2, 3 and 4 were in remission. Four cases had deterioration of muscle power. It involved both lower limbs in two cases, one lower limb in one case and all four limbs in another case. Cases 4 and 5 had transient deterioration of the vision in one eye. Evoked responses were determined before and after heating. Most patients recorded insignificant change in the latencies of the waveform in VEP, BAEP and central conduction time in SSEP. However, in case 4 the P.100 was absent after heating. This was accompanied by clinial deterioration of vision. In all the cases, the neurological deterioration was completely reversible. The following is a summary of the patients who demonstrated neurological change with the hot bath test.

Case 1 was a 43-year old Chinese woman with the optic-spinal form of illness in relapse. She had had four relapses in three years. The last relapse manifesting a transverse thoracic myelopathy. The neurological findings before heating were Grade 4 power of the left hallux on dorsi and plantar flexion and grade 0 power the rest of the lower limb muscles. The lower limb tendon jerks were hyper-reflexic with bilateral extensor plantar responses. A sensory level to pin prick was at T2 and proprioceptive sensation was impaired in both toes. With heating, her body temperature was raised from 37.2 to 38.6 degree Celsius. The power of the left hallux became grade 0 with heating. The VEP, BAEP and median nerve SSEP showed no change. Double dose contrast CT scan showed low attenuation area in the hypothalamus and the left temporal lobe.

Case 2 was a 27-year old Chinese woman with the disseminated form of illness in remission. She had had nine relapses over a period of nine years. The clinical signs before the hot bath test were: nominal dysphasia. blindness in both eyes, grade 4+ weakness of the right hip flexors, a hyper-reflexic right knee jerk, and reduced proprioceptive sensation in the right fingers and in both toes. She could only walk with support. Her body temperature was raised from 36.4 to 38.4 degrees Celsius. After

heating, the right hip flexors and right ankle dorsi-flexors deteriorated to grade 2 power; the left hip flexor deteriorated to grade 3 power. The neurological status returned to baseline when the body temperature dropped to 37.8 degree Celsius. The VEP, BAEP and median nerve SSEP showed no change after heating. Double dose contrast CT scan of the head showed moderate to severe ventricular enlargement, left ventricle being larger than right. Low attenuation area was seen in the left occipital lobe and in the periventricular white matter. There was also enlargement of the prepontine cistern.

Case 3 was a 58-year old Chinese woman with the recurrent spinal form of illness in remission. She had had five relapses over five years. Before heating, she complained of tightness in both sides of the chest and abdomen. She had grade 4 power in the right wrist flexors and extensors; and all the muscles of the left elbow, wrist, hand and the right hip flexors. The power of the left hip flexors was grade 2. Both biceps and supinator jerks were absent. Both knee jerks were hyper-reflexic. Proprioceptive sensation was absent in the fingers and toes on both sides. Her body temperature was raised from 36.8 to 38 degree Celsius. With heating, muscle power generally became much weaker. Left shoulder abduction deteriorated from grade 5 to grade 4, left hand and wrist muscle power deteriorated from grade 4 to grade 0-2, the right hip flexors deteriorated from grade 4 to grade 2, left hip flexion from grade 2 to grade 1, and the knee flexors/extensors and the ankle dorsi-flexors on both sides deteriorated from grade 5 to grade 0. The VEP, BAEP, median nerve SSEP showed no deterioration after heating. Double dose contrast CT scan showed a small high attenuation lesion in the inferior right frontal lobe.

Case 4 was a 48-year old Chinese man with the optic-spinal-brainstem form of the illness in remission. He had had eight relapses over a period of six years. Before heating, he complained of tightness of the whole body below the neck and the right knee jerk was hyper-reflexic. His body temperature was raised from 36.7 to 38.8 degree Celsius. After heating, muscle power in both hip flexors deteriorated from grade 5 to grade 3. He also developed sustained ankle clonus bilaterally. Visual acuity in the right eye deteriorated from 6/5 to 6/12. The P1 latency in the VEP of the right eye was 116 msec and the amplitude was 3 uvolts before heating. After heating, no consistent waveform was seen in the same eye. The BAEP and median nerve SSEP showed no deterioration. Double dose contrast CT scan showed dilatation of the third ventricle.

Case 5 was a 46-year old Chinese woman with optic-spinal recurrent form of illness in relapse. She had six relapses over 18 years, the latest being a left retrobulbar neuritis. The clinical signs before the hot bath test were: right optic atrophy with visual acuity of 3/60, visual acuity at 6/9 in the left eye and generalized hyperreflexia with bilateral extensor plantar response. The body temperature was raised from 36.8 degree Celsius to 39 degree Celsius. After heating, the vision in the left eye deteriorated to 6/18. The VEP, BAEP and median nerve SSEP showed no deterioration after heating. MRI of the brain and spinal cord were normal.

Discussion

With the observation of sensitivity to body temperature change in MS patients, the application of external heat to induce neurological change has been used for some time as a diagnostic aid in MS[17, 18, 19]. Nelson & McDowell[18] reported that 13 of 14 patients with MS developed neurological signs with elevation of their body temperature. They also noted that this increase in neurological signs was less pronounced in patients in remission. Malhotra & Goren[19] reported that 17 of their 20 MS patients had changes in their neurological status with an increase in temperature. However, this phenomenon of sensitivity to body temperature change is not specific to MS. Nelson *et al*[22] immersed 72 patients with neurological diseases other than MS in hot water, and found that 40 showed significant

neurological change, although these were in general less severe and less easily induced than those with MS. The report by Berger & Sheremata[23] of four patients who had considerable and prolonged neurological disability after a hot bath test suggests caution in the application of such testing.

In this study of 13 patients with clinically definite MS, none had previously complained of a deterioration of neurological symptom with temperature change. When subjected to the hot bath test, five patients (33%) showed neurological deterioration. Four patients showed increased limb weakness. Two patients had deterioration of visual acuity, one of them accompanied by disappearance of the P1 waveform in the VEP from the same eye. There was no significant change in the evoked potential studies in the other patients. There have been studies showing that in normal subjects, hyperthermia do not change the latencies of VEP and central conduction in SSEP[7, 8].

This study shows that when subjected to vigorous testing and close observation, our patients also demonstrated an abnormal sensitivity to temperature change. However, the rate of the abnormal hot bath's test at 38 per cent and average of 0.46 new sign per patient was lower than those previously reported. Nelson *et al*[22] reported all the 12 MS patients had positive hot bath test with an average of 2.8 changes per patient. Malhotra & Goren[19] reported 17 of the 20 MS patients undergoing hot bath test showed changes in neurological status although in five patients, there was worsening of pre-existing signs without development of new signs. The author listed 34 new signs in the other 12 patients (2.8 new signs per patient).

Most of the abnormalities occurring with application of external temperature previously reported have involved the vision, ocular movement, nystagmus and motor weakness. Malhotra & Goren[19] reported that of the 12 MS patients who developed new signs while undergoing hot bath test, nine had decrease in visual acuity, five had nystagmus, seven had ophthalmoplegia, six had internuclear ophthalmoplegia, three had dysarthria, two had mutism or aphasia, one each had bilateral ptosis and athetoid movement. The authors also reported 15 out of the 20 MS patients undergoing hot bath test had worsening of their existing motor weakness. Nelson & McDowell[18] reported that of the 14 MS patients undergoing hot bath test, nine had decrease in visual acuity, seven had horizontal nystagmus, six had vertical nystagmus, four had diplopia, four had internuclear ophthalmoplegia, three had dysarthria and paraparesis, one each had upward gaze palsy and rectus muscle palsy. However, in our four patients with abnormal test, it involved the limb muscle power. Two patients had decrease in visual acuity. None of these five patients had opthalmoplegia or nystagmua during the test. Other than case two, none had CT scan changes involving the pyramidal tract in the brain or the brain stem. All the patients also had past history of acute transverse myelopathy. The sign seen in the hot bath test is thus likely to be from spinal cord pathology. Thus this study shows further differences between Asian and Caucasian MS patients. The difference in the pathological changes between Asian and Caucasian patients[13] is the likely underlying reason for this observed difference in temperature sensitivity.

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