Original Article

Blink Reflex as a Complementary Test to MRI in Early Detection of Brainstem Infarctions: Comparison of Blink Reflex Abnormalities in Anterior Versus Posterior Circulation Strokes

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Abstract

Background: Early detection of vertebro-basilar insufficiency is of paramount importance. Brain MRI was the only method of diagnosis for many years, but in addition to high cost and delay in report, it may not detect all brain stem lesions. In this study Blink reflex (BR) was evaluated as a complementary test to MRI.

Methods: Fifty-four patients were studied [27 anterior circulation stroke patients (ACSP) and 27 posterior circulation stroke patients (PCSP)]. MRI was performed within the first week after the onset of stroke. Nineteen age and sex matched healthy people enrolled as controls. BR was performed within the first 24 hours of the onset. Frequency of abnormal blink reflex in ACSP and PCSP was compared with MRI findings. Then abnormal responses in two groups were compared by chi-square test.

***Results*:** In both ACSP and PCSP, two patients had normal BR responses, and in 25 patients R_1 or R_2 components of blink responses were absent or prolonged (92.5%). $R_1$was absent or delayed in 16 PCSP, but it was abnormal in only two ACSP ($P < 0.001$). Abnormal R_2 responses were detected in 22 PCSP and 24 ACSP.

Conclusion: BR abnormalities had high correlation with MRI findings in PCSP (92.5%) BR can be performed within the first 24 hours of onset of stroke, and its results is available immediately. This test is easy to perform and comfortable for the patient, has low cost, and is available every where. Therefore we introduced BR as a complementary (but not replacing) test to MRI in early detection of brainstem infarctions. Comparison of BR responses in ACSP and PCSP showed that abnormalities of R_1 responses had high accuracy in differentiation between anterior and posterior circulation strokes. We concluded that BR responses not only can detect brainstem infarctions rapidly and readily in its early stages, but also can differentiate ACSP from PCSP with high accuracy.

Key words: Blink Reflex, Anterior Circulation Stroke, Posterior Circulation Stroke Patients, Magnetic Resonance Imaging, Computed Tomography.

Stroke is the third cause of mortality in general population, after ischemic heart disease and cancer[1]. It accounts for 10% of mortality in industrial countries[2]. Eighty percent of strokes are of Ischemic type, with a fatality rate of thirty-five percent. Vertebro-basilar Insufficiency is associated with greater risk to the patient and basilar artery thrombosis needs immediate administration of anticoagulant therapy[1]. In the majority of cases, diagnosis is suspected by clinical Impression and is confirmed by MRI findings. Aside from high cost, MRI is not available everywhere and often performed with considerable delay. In addition, it may not detect all brainstem lesions[3, 4]. We looked for a cheap, available, easy, and fast complementary test for early detection of posterior circulation strokes. Blink reflex attracted our attention: Blink reflex (BR), response to unilateral electrical stimulation of supra-orbital nerve, has two components: R_1 which is mediated by principle nucleus of trigeminal nerve in the upper pons, and a

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late ipsilateral (R_2) and contra lateral (R_{2c}) response, which is mediated by medullary and spinal nuclei of the trigeminal nerve[5, 6]. Contra lateral R_2 response is established by way of an ascending pathway which crosses the midline at the level of lower third, at least, of medulla oblongata[7].

Csecsei et al[8] found alterations of R_1 in ponto-mesencephalic lesions and disappearance of R_2 on rostral damage. Hopf et al[9] localized R_1 similarly. Changes in R_1 have high localizing Value in ipsilateral pontine functional deficits[10]. Prolongation of ipsilateral R_1 indicates compression of pons , and prolongation of R_2 and R_{2c} latencies indicate compression of medulla oblongata[11]. Late reflexes (R_2 and R_{2c}) are consistently absent bilaterally with stimulation of affected side in Wallenberg syndrome[12, 13], and defects are always located in the afferent branch of reflexes[14].

These considerations make BR appropriate for clinical evaluation of brainstem strokes. But changes of BR are also reported in hemispheric (Anterior circulation) strokes[15 - 19].

In this study BR response in posterior circulation stroke patients (PCSP) was compared with BR response in control subjects and BR was evaluated as a complementary test to MRI in early detection of posterior circulation stroke patients. Also blink reflex (BR) abnormalities in anterior circulation stroke patients (ACSP) was compared to abnormalities in PCSP and validity of BR in differentiation between anterior and posterior circulation stroke patients was assessed.

Materials and Methods

We studied 54 patients (27 anterior circulation and 27 posterior circulation stroke patients) admitted in Al-Zahra hospital , affiliated to Isfahan University of medical sciences, with the clinical diagnosis of ischemic stroke, between May 2001 and May 2003. Their mean age was 59.37 years (range from 18 to 76) for anterior circulation stroke patients (ACSP) and 59.67 years (range from 41 to 79) for posterior circulation stroke patients (PCSP). There were 14 male and 13 female in PCSP group and 13 male and 14 female in ACSP group. All patients had brain Image (Brain MRI for posterior circulation infarcts and Brain MRI or Brain CT for anterior circulation infarcts) within the first week after clinical onset of stroke. Clinical findings and images were reviewed by two competent neurologist, and only patients who's diagnosis confirmed by both of them enrolled to the study. Patients were excluded if lesions other than ischemic stroke were seen on brain image or if there was any history or evidence of peripheral lesion of trigeminal or facial Nerves.

Nineteen age and sex matched subjects without a history of stroke or peripheral lesions of trigeminal and facial Nerves enrolled as controls.

Blink reflex (BR) was performed by an experienced electromyographer within the first 24 hours of the onset of findings, on both the right and left side and bilaterally recorded according to the method recommended by kimura[20]. The filter setting used was between 50 and 2500 Hz, the sensitivity was 0.4 mv/division and the analysis time was 100 msec. The subjects laid supine on a bed in a quiet, warm (22°c - 24°c) room with their eyes slightly closed. Surface recording electrodes were placed on the lower lateral aspect of the orbicularis-oculi muscle bilaterally. Reference electrodes were placed on the temple, lateral to external canthi bilaterally. The ground electrode placed around the arm. The supra-orbital nerve was stimulated with a bar electrode, with the cathode placed over the supra-orbital foramen, first on the right side and then on the left side. The ipsilateral and contralateral responses were recorded. An electro myographic device (Toennies multilinear) manufactured in Germany was used. A total of 5 responses were collected for each time-Interval on both right and left sides in patients and control subjects.

The mean latencies of R_1, R_2 and R_{2c} components of the 5 stimuli delivered at intervals of at least 30 s were considered. Mean and standard deviation (SD) of BR responses were calculated for control group. Absent or prolonged (>mean +2SD) R_1 and R_2 responses were determined for anterior and posterior circulation groups. Frequency of abnormal responses in each group was compared with MRI findings. Then abnormal responses in two groups were compared by chi-square test.

Also mean and SD of BR responses were determined in ACSP and PCSP, and each group was compared with controls by t-test.

Results

Anterior circulation strokes

Two patients had normal Blink reflex (BR) responses and in 25 patients R_1 or R_2 responses were absent or prolonged (>mean +2SD of controls). R_1 latency was normal in 25 patients, and was prolonged in only two patients. R_2 response was absent or prolonged in 24 patients. Three patients had normal R_2 responses bilaterally. Risk factor for stroke was detected in 18 patients: Hypertension was detected in 11 patients (40%), Diabetes-mellitus in 5 patients (18%), hyper lipidemia in two patients (7.4%), smoking in two patients (7.4%); and mitral valve prolapse and ischemic heart disease each one in one Patient (3.7%).

In two patients with prolonged R_1 latency, abnormality was ipsilateral to the lesion in the first, and contralateral to the involved hemisphere in the other patient.

Two patients had normal BR responses bilaterally. The stroke was cortical (right middle cerebral artery infarction) in one of them, and deep (left thalamus and internal capsule) in the other patient. In 24 patients R_2 response was abnormal. Twenty one of this group had bilateral abnormalities of blink reflex responses. In two Patients R_2 response was abnormal with contra lateral supra-orbital nerve stimulation (SNS). In the remaining one, R_2 and R_{2c} were absent with ipsilateral SNS. Comparison of mean and standard deviation (SD) of blink reflex (BR) responses in ACSP with controls are Presented in table -1.

Table 1. comparison of mean and SD of blink reflex (BR) responses in ACSP with controls.

	ACSP		CONTROLS		
	Mean	SD	Mean	SD	P Value
rR1	11.511	o.7871	11.032	0.7924	0.004
rR2	40.409	6.4166	36.295	2.8498	0.006
rR2c	47.545	7.793	37.874	3.1150	0.002
lR1	11.244	0.7218	10.821	0.8270	0.005
lR2	40.650	9.8065	36.358	2.8312	0.100
lR2c	44.086	7.1357	37.989	2.9728	0.001

Posterior circulation strokes: Two patients had normal BR responses and in 25 patients BR responses were abnormal (absent or >mean + 2 SD). R_1 response was absent or delayed in 16 patients. It was within normal limits in the remaining 11 patients. R_2 responses were absent or prolonged in 22 patients and were normal in five patients.

Twenty three patients (85%) had risk factors for stroke: Hypertension was detected in 17 Patients (62%), Diabetes-mellitus in seven patients (25%), smoking in seven Patients (25%), hyperlipidemia in six Patients (22%), ischemic heart disease in three patients (11%), and congestive heart failure in one Patient (3.7%). In both of the two patients with normal BR response, infarction of right cerebellar hemisphere, without involvement of brainstem was detected in MRI. Five patients had normal R_2 responses: two patients with infarction of cerebellar hemispheres, two patients with infarction of pons, and one patient with infarction of lateral medullary area. R_1 response was abnormal in 16 patients: nine patients had absent or prolonged R_1 response bilaterally, and seven patients had abnormality of R_1 response on ipsilateral side. R_2 response was absent or prolonged in 22 patients. In 19 patients abnormality of R_2 response was bilateral. Two patients had R_2 response abnormality with ipsilateral supra-orbital nerve stimulation (SNS), and in the remaining one, R_2 response was absent with contralateral SNS. Comparison of mean and standard deviation (SD) of blink reflex (BR) responses in PCSP with controls are depicted in table-2.

Table 2. comparisons of mean and SD of blink reflex (BR)

responses in PCSP with controls.

	PCSP		CONTROLS		
	Mean	SD	Mean	SD	P Value
rR1	12.164	2.0158	11.032	0.7924	0.016
rR2	41.224	8.2640	36.295	2.8498	0.026
rR2c	42.382	9.0366	37.874	3.1150	0.129
lR1	12.120	1.5361	10.821	0.8270	0.001
lR2	41.467	6.9999	36.358	2.8312	0.028
lR2c	40.473	7.0036	37.989	2.9728	0.260

Eleven patients detected with pontine infarction based on MRI findings. In nine of them R_2 response was abnormal (bilaterally in eight, and contralaterally in one patient), and in five patient R_1 response was absent or delayed (ipsilaterally in three patients and bilaterally in two patients). Six patients had infarction of medulla oblongata. In this group five patients were detected with absent or prolonged R_1 response (bilaterally in three and ipsilaterally in two patients). R_2 response was also abnormal in five patients (bilaterally in four patients and ipsilateral to supra-orbital nerve stimulation in one patient). Four Patients had infarction of Midbrain. In all of them R_1 Latency was normal, but R_2 responses were absent or delayed bilaterally.

Nine patients were detected with cerebellar infarction (pure or in combination with brainstem infarction). In five patients with pure cerebellar infarction, two patients had completely normal BR responses. R_1 response was abnormal in three patients (bilaterally in two and ipsilaterally in one patient), and bilateral abnormality of R_2 was detected in two patients. Three patients were presented by Inter nuclear ophthalmoplegia (INO). Pontine infarction was detected in one of them and midbrain lesion in another two others. In two patients with anterior INO (midbrain infarction) R_1 latency was normal, but R_2 responses were delayed or absent bilaterally. In the patient with posterior INO (pontine infarction) R_1 response was prolonged ipsilaterally, but R_2 responses were normal bilaterally. One patient presented with Millard-Gobbler syndrome, in whom R_1 response was absent ipsilaterally and R_2 responses were abnormal bilaterally.

Comparison of ACSP and PCSP

In both groups two BR responses were normal and 25 BR responses were abnormal; the difference between the two groups strikes out of the blue only when R1 and R_2 responses were compared separately. In posterior circulation stroke patients R_1 response was absent or delayed in 16 patients, and was normal in 11 patients, but in anterior circulation stroke patients R_1 response was prolonged in only two patients. Therefore abnormality of R_1 component of BR was significantly different ($P < 0.0001$) in two groups (Table-3). Also despite of low sensitivity (59%), abnormalities of R1 had high specifity (92%) and positive predictive value (88%) for differentiating ACSP from PCSP. R_2 response was abnormal in 24 patient of anterior circulation group and 22 cases of posterior circulation group with no statistically meaningful difference ($P=0.500$).

Table 3. Comparison of Blink Reflex abnormalities in anterior versus posterior circulation stroke patients.

	Abnormal R1	Abnormal R2
ACSP	2	24
PCSP	16	22
P Value	0.0001	0.500

Discussion

Early detection of brainstem infarction is of paramount importance for two reasons: First, high mortality and morbidity of these patients and, second, availability of an efficient treatment (anticoagulants) that may prevent a catastrophic outcome.

MRI was the only reliable method for detecting brainstem strokes for many years. MRI is an expensive test and its results are often presented too late to the care giving physician to make a critical decision. Neurologists often prescribe anticoagulants blindly for patients suspected to

brain stem infarctions and wait for MRI results, to make the final decision for the patients (continuation or discontinuation of anticoagulants). Anti coagulants so prescribed, sometimes result in hemorrhagic complications. In a group of 30 consecutive patients with acute clinical symptoms of ischemic brainstem lesions in which their symptoms had persistence for more than 10 days, studied by kransianski et al[4], 8 patients had normal MRI. They concluded that brainstem infarction can not be excluded by normal MRI[4]. In 25 patients with electro physiologic evidence of brainstem infarction studied by Thomke and Hopf[3], MRI confirmed brainstem lesion in six patients only, indicating that some brainstem lesions escape proof by MRI. This was also shown in a large series of patients with third and sixth nerve palsies due to brainstem lesions[21- 23]. We studied 27 patients with brain stem infarctions (posterior circulation strokes) confirmed by MRI finding: Blink reflex (BR) responses were abnormal in 25 of them (92.5%). Blink reflex was performed within the first 24 hours in all of our patients and its results were available immediately. The test is easy and comfortable for the patient, has low cost and is available every where. we introduced BR as a complementary (but not replacing) test to MRI in early detection of brainstem infarctions, because the BR abnormalities has high correlation with MRI findings (92.5%), and also it may detect additional brainstem infarctions in patients with normal MRI, as suggested by Thomke[3].

Risk factors for stroke were similar in anterior circulation stroke patients (ACSP) and posterior circulation stroke patients (PCSP): Hypertension was the most frequent risk factor for stroke in both groups, followed by Diabetes-mellitus, hyper-lipidemia and smoking.

Chia reported bilateral abnormality of late responses (R_2 and R_{2c}) with contralateral supra orbital nerve stimulation (SNS) in a man with hemorrhagic lesion of thalamus and internal capsule[15]. Two deep hemispheric lesions were detected in our anterior circulation group. The first patient with infarction of the left thalamus and internal capsule (patient 5) had completely normal BR responses. The second patient had infarction of the head of the left caudate nucleus and adjacent internal capsule (patient 3). In this patient R_2 and R_{2c} were absent with right SNS, which correlate well with the reported case by Chia. These results may indicate that pathways for late responses (R_2 and R_{2c}) may path through contralateral internal capsule.

BR responses observed in our anterior circulation patients were well correlated with results reported by Filipowska[16] in which abnormalities of BR were observed mostly in late responses (R_2 and R_{2c}), and were bilateral in unilateral hemispheric infarctions.

In posterior circulation stroke patients (PCSP) abnormalities of both R_2 and R_{2c} responses were detected. In all of the 16 patients with abnormal R_1 responses, defect was bilateral or on the ipsilateral side of the lesion. In most patients with absent or delayed R_2 responses the abnormality was bilateral.

Blink reflex responses never had been compared between anterior circulation stroke patients (ACSP) and posterior circulation stroke patients (PCSP) before our study. We examined 27 patients in each group. Our results indicated that abnormalities of R_1 response can differentiate ACSP from PCSP with high accuracy and specifity (92%). But abnormalities of late responses (R_2 and R_{2c}) are not statistically different in two groups.

Therefore we concluded that blink reflex (BR) responses not only can detect brainstem infarctions rapidly and readily in its early stages and can be used as a complementary test to MRI, but also it can differentiate ACSP form PCSP with high accuracy.

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