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VISUAL EVOKED RESPONSES IN MEGALOBLASTIC ANEMIA

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Abstract : Pattern shift visual evoked responses (PSVER) were studied in thirty patients suffering from severe megaloblastic anemia (mean **Hb** level was 4.25 ± 1.22 g/dL) of nutritional origin. All patients lacked clinical stigmata of visual and neurologic impairment. Mean P100 latency in thirty age and sex matched controls was 96.35 ± 6.75 ms (range 86–108 ms) and mean amplitude was 10.37 ± 3.88 μV (range 4.8–20.8 μV). Mean P100 latency in megaloblastic anemia was 114.77 ± 11.68 (range 91–142) ms, P < 001 vs. control) and mean amplitude was 8.85 ± 2.8 μV (range 5.1–16.2 μV). Seventy percent cases had prolonged latency of P 100. After correction of anemia with therapeutic doses of vitamin B_{12} and folic acid in three months (mean Hb level was 12.08 ± 1.86 g/dL), the mean P100 latency was 105.13 ± 9.30 ms (range 92–121 ms P<0.001 vs. controls) and mean amplitude was 10.72 ± 4.13 μV (range 5.1–21.4 μV). There was significant improvement in P100 latency after correction of anemia (P<0.01). There was a negative correlation between P100 latency and hemogloboin levels, though it was statistically not significant.

Key words : pattern shift visual evoked response (PSVER)
megaloblastic anemia P100 wave latency and amplitude
vitamin B_{12} folic acid

INTRODUCTION

Megaloblastic anemia is the second most common type of anemia after iron deficiency anemia (1). It is caused by deficiency of folic acid, vitamin B_{12}or both as a result of interference with their absorption, transport and/or metabolism (2). It is characterised by distinct morphological and functional abnormalities in bone marrow and blood due to impaired DNA synthesis. Folic acid deficiency is the most common cause of megaloblastic anemia in India. Folic acid deficiency alone was found to be the cause of megaloblastic anemia in 55% of cases studied at our institute. Motor, sensory, Ia fibres, proximal conduction velocities and H reflex amplitude was seen to be significantly reduced in 60% of these patients even when there was no clinical evidence of peripheral neuropathy. Substantial improvement following vitamin B_{12} and folic acid therapy was observed in peripheral nerve conduction velocities and H reflex amplitude in megaloblastic anemia subjects (3).

Involvement of visual pathways is also quite frequently reported in megaloblastic anemia. Incidence of optic atrophy has been reported to be 5% and at times it may be the only presenting feature (4), and is due to patchy demyelination with affection of axis cylinders in the optic tracts (5). Identical changes were observed in experimentally induced vitamin B_{12} deficiency in animals (6). Pattern shift visual evoked response (PSVER) is a simple method which can identify even subtle abnormalities of impulse conduction and can be used to detect the extent and site of

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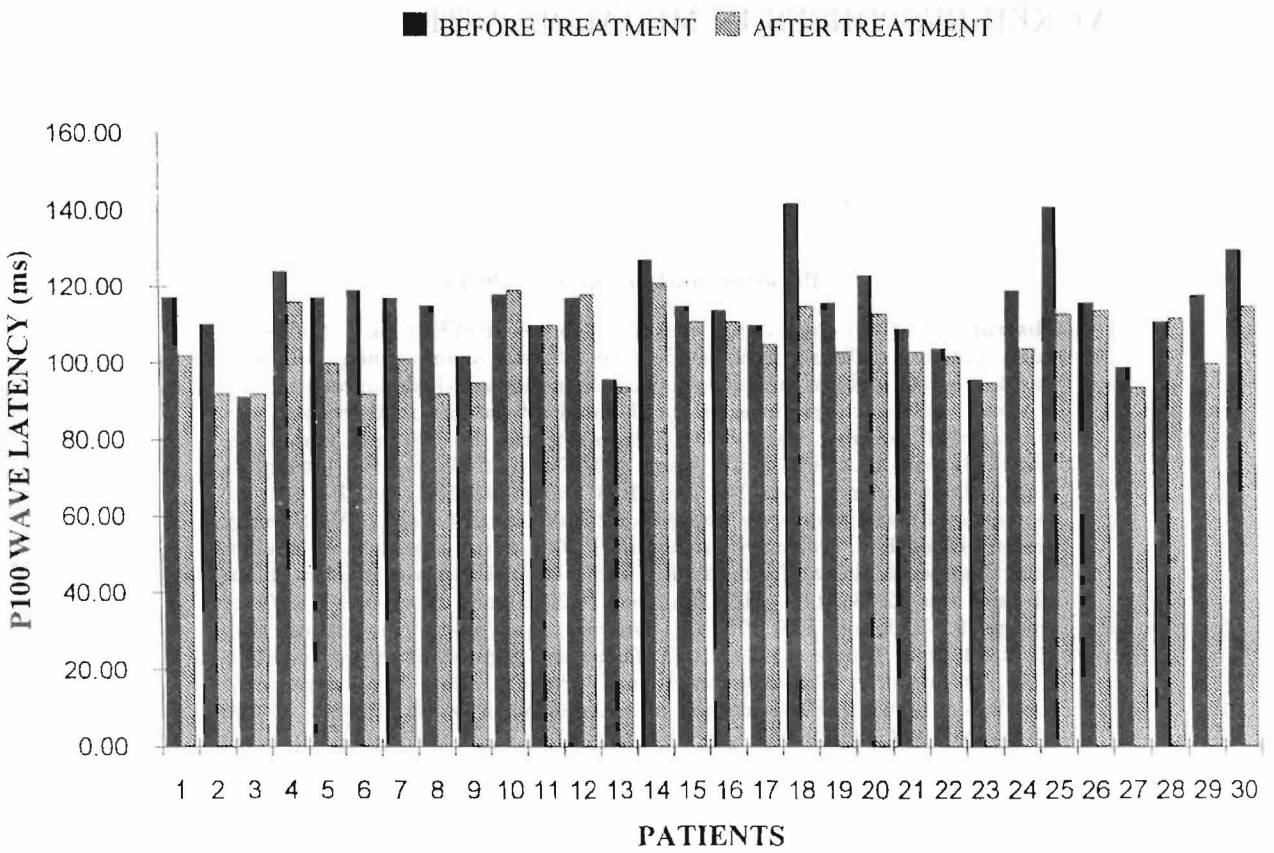

Fig. 1: P100 wave latency in the megaloblastic anemia cases before and after treatment.

involvement of visual pathways. The clinically interpreted visual evoked response is a single wave, often called P100, generated in striate and parastriate visual cortex (7) and has been used here to detect visual pathway involvement in megaloblastic anemia.

METHODS

Thirty subjects of megaloblastic anemia of nutritional origin with hemoglobin levels ranging from 2-6 g/dL and thirty age and sex matched controls with normal hemoglobin (>12 g/dL) were studied over a period of two years. Routine hematological and biochemical investigations were carried out in all the subjects. Diagnosis of megaloblastic anemia was achieved by peripheral blood film and bone marrow examination. No further differentiation of the cause of anemia due to deficiency of vitamin B_{12}, folic acid or both, was made. A detailed clinical and neurological examination was done. Special emphasis was laid on examination of the eyes to rule out any local disease which could affect the visual evoked responses. Efforts were also made to rule out other neurological diseases which could affect the visual pathways in particular. Visual acuity was found normal in all the subjects.

PSVER were done in all cases of megaloblastic anemia and thirty age and sex matched controls by DISA Neuromatic 2000C computer averaging system using a reversing black and white checker board pattern at a rate of 2 Hz. The subject was made to sit at a distance of one meter from the television screen and the gaze was fixed on a dot

in the center. Recording electrodes were placed 2.5 cms above the inion in the midline and at the vertex using standard procedures of cleaning, impedance checks and grounding. The responses were recorded at a sweep speed of 30 ms/div. and band pass with upper frequency of 1 Khz and lower frequency of 2 Hz. Two separate sets of 200 trials were run for each eye for conformity. The average response was measured at a sensitivity of 2 μV/div. Measurements were made of the latency to the major positive peak (P100) and the amplitude between P100 and the preceding negative peak (8). The same procedure was repeated after normalisation of hemoglobin level in all the patients. The data so obtained was subjected to statistical analysis using unpaired and paired t-test.

RESULTS

Age of the patients ranged from 15-75 years with mean of 36.0 ± 4.35 years and the male-female ratio was 3:2. All the patients had poor nutritional and socio-economic status. Duration of clinical illness was less than six months in all the cases. All these patients showed no impairment of visual acuity or evidence of peripheral neuropathy on clinical examination. Mean hemoglobin level in these cases ranged from 2-6 g/dL with a mean of 4.25±1.22 g/dL and mean PCV was 32.06±0.26%.

Bone marrow examination revealed hypercellularity in 22 cases (73.33%), reversal of myeloid-erythroid ratio in 18 (60%) and normal to increased iron stores in all cases. Maturation arrest was seen in 19 (63.33%) and giant myelocytes were seen in 18 (60%) cases of megaloblastic anemia. All routine biochemical and radiological parameters were within normal limits in both the groups. All the cases of megaloblastic anemia were treated with parenteral vitamin B_{12} 1000 μg for one week and then once a month for three months, and folic acid 5 mg/day for three months. Mean hemoglobin level increased to 12.08 ± 1.86 g/dL (range 10–14.5 g/dL) after three months of therapy.

Pattern shift visual evoked responses:

Controls: Mean P100 wave latency was 96.35±6.75 ms (range 86-108 ms) and mean P100 amplitude was 10.37±3.88 μV (range 4.8-20.8 μV).

Meagaloblastic anemia cases: Mean P100 latency was 114.77 ± 11.68 ms (range 91–142 ms, $P < 0.001$ vs. controls) and mean P100 wave amplitude was 8.85 ± 2.8 μV (range 5.1–16.2 μV). Twenty one (70%) cases had prolonged P100 latency and comparison of P100 latency in control and anemia subjects revealed a highly significant prolongation ($P < 0.001$). The amplitude of P100 showed no significant difference in the two groups.

Megaloblastic anemia cases after correction of anemia: Mean P100 latency was 105.13 ± 9.30 ms (range 92–121 ms) and mean amplitude was 10.72 ± 4.13 μV (range 5.1–21.4 μV). Comparison of P100 latency between anemia subjects before and after correction of anemia revealed significant improvement in P100 latency ($P < 0.01$). P100 wave amplitude did not reveal any significant difference between the cases and controls. Out of 21 cases who showed significant prolongation of P100 latency, 14 cases showed its normalisation after correction of anemia (range 92–110 ms, mean 101.86 ± 6.5 ms), while the rest seven also had improvement in P100 latency, but not to the range of the controls. There was no correlation between the severity of anemia and latency of P100 wave.

DISCUSSION

All cases in this series were suffering from severe degree of anemia (Haemoglobin<6 g/dL). This was variously attributed to poor nutritional and socio-economic status, repeated pregnancies, improper cooking practices, diarrhoeal and parasitic diseases. None of the cases were of malabsorption syndrome.

The visual evoked responses in thirty control subjects revealed a mean P100 latency of

96.35±6.75 ms. These results were similar to those reported in the normal subjects by other researchers (7-10).

PSVER done in thirty cases of megaloblastic anemia revealed increased latency of P100 wave in 21 cases (70%) and it was significantly prolonged as compared to controls ($P<0.001$). P100 wave amplitude in megaloblastic anemia cases did not show any significant difference from the controls Troncoso et al (11) and Fine et al (12) had also reported markedly prolonged P100 latencies with normal amplitude in megaloblastic anemia cases. Decrease in amplitude of brainstem auditory evoked potentials has been demonstrated in the cases of pernicious anemia (13), but no such change has been documented in the visual evoked responses.

The possible reason for delayed latencies in megaloblastic anemia could be because of demyelination in visual pathways. The myelin in the nerve is made up of fatty acids, which are responsible for the integrity and synthesis of myelin. Deficiency of vitamin B_{12} and folic acid interferes with the synthesis of myelin resulting in demyelination and subsequent prolongation of P100 latency. Significant improvement in P100 wave latency after correction of anemia in 66.67% cases can similarly be explained on the basis of myelin resynthesis following treatment and the reversibility of the lesion in early stages (14). A similar delay in peripheral nerve conduction velocity and subsequent reversibility of these changes after treatment suggest that these changes go hand in hand with visual evoked responses (3). In the seven patients who did not show significant improvement in P100 latency after correction of anemia, this could be as a result of gliosis and permanent damage which might have occured in these cases (15).

Thus megaloblastic anemia, irrespective of its etiology, affects the visual pathways and may lead to permanent defect if not corrected timely. Pattern shift visual evoked responses may identify the subtle changes in the visual pathways even when there is no evidence of clinical abnormality.

REFERENCES

1. Park JE, Park K. Nutrition and Health. In: Textbook of Preventive and Social Medicine, 13th ed. Jabalpur, Banarsidas Bhanot, 1991: p 351.
2. Beck WS. The metabolic basis of megaloblastic erythropoiesis. *Medicine* 1964; 43: 715-726.
3. Sood AK, Handa R, Singh U, Chandran AP, Sehrawat R. Clinical, hematological and electrophysiological study of megaloblastic anemia. *Indian J Med Sci* 1994; 48: 175-180.
4. Freeman AG, Heaton JM. The aetiology of retrobulbar neuritis in addisonian pernicious anemia. *Lancet* 1961;i: 908-911.
5. Adams RD, Kubik CS. Subacute combined degenration of the brain in pernicious anemia. *N Engl J Med* 1944; 231: 1-9.
6. Agamanolis DP, Chester EM, Victor M et al. Neuropathology of experimental vitamin B_{12} deficiency in monkey. *Neurology* 1976; 26: 905-914.
7. Chiappa KH, Ropper AH. Evoked potentials in clinical medicine. *N Engl J Med* 1982; 306: 1140-1150.
8. Sawhney IMS, Bansal SK, Chopra JS. Evoked potentials in hereditary ataxias. *Neurology India* 1992; 40: 165–169.
9. Asselman P, Chadwick DW, Marsden CD. Visual evoked responses in the diagnosis and management of patients suspected of multiple sclerosis. *Brain* 1975: 98: 261–282.
10. Tandon OP, Sharma KN. Visual evoked potentials in young adults: a normative study. *Indian J Physiol Pharmacol* 1989; 33: 247-249.
11. Troncoso J, Mancall EL, Schatz NJ. Visual evoked responses in pernicious anemia. *Arch Neurol* 1979; 36: 168-169.
12. Fine EJ, Soria E, Paroski MW, Thomasula L. The neurophysiological profile of vitamin B_{12} deficiency. *Muscle Nerve* 1990; 13: 158-164.
13. Tandon OP, Choudhary D. Brainstem auditory evoked potential response in pernicious anemia. *Indian J Physiol Pharmacol* 1990; 34: 282-284.
14. Hogan MJ. Tobacco alcohol ambylopia: Further comments on its pathology. *Arch Ophthalmol* 1965; 74: 649-657.
15. Chisholm IJ. Hydroxy-cobalamine versus cyanocobalamine in the treatment of tobacco ambylopia. *Lancet* 1967; ii: 450-451.