ORIGINAL ARTICLE

Bull-Neck, Electrocardiographic Changes and Creatine Phosphokinase Blood Levels in Patients with Diphtheria

by

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Abstract

All paediatric patients with the diagnosis of diphtheria who were seen at the Department of Child Health Ujung Pandang General Hospital from October 1987 to October 1989 were evaluated for bull-neck, ECG patterns and serum creatine phosphokinase (CPK) values. Their ages ranged from 1 year and 2 months to 13 years with a mean of 6,54 ± 3,09 years. Males and females were affected in a ratio of 1 : 1.

Of 39 patients included in the trial, 28 were classified as having normal ECG and 11 as having abnormal ECG on admission. During hospitalization, 56.4% of cases showed ECG changes. All patients had raised serum CPK levels on admission. This increase was 14,6 times the normal level in cases with abnormal ECG and only 3,0 times in those with normal ECG ($p < 0,01$). The highest levels of serum CPK were noted in the first week, then returned to normal in the second week and decreased further in the third week. It became also evident that patients who developed abnormal ECG later on, had already demonstrated an increased serum CPK level of 5.2 times the normal levels on admission.

Bull-neck appeared in 19 out of the 39 patients. Patients with bull-neck differed very significantly ($p < 0.001$) from those without bull-neck in either the frequency of the occurrence of abnormal ECG patterns or the mean CPK serum levels. Most of the patients (84.2%) with bull-neck had abnormal ECG patterns and mean CPK serum levels of almost 12 times the normal values, while only 30% of patients without bull-neck had abnormal ECG patterns and a normal value of mean CPK serum levels.

The mean CPK serum levels differed very significantly ($p < 0.001$) among the various ECG patterns. The mean CPK serum levels of patients with sinus tachycardia, sinus tachycardia + left ventricle hypertrophy and left ventricle hypertrophy were 11.2, 7.3 and 6 times the normal values respectively.

These findings suggest that an increase of serum CPK to a certain level may precede the development of abnormal ECG patterns and is valuable for determining the prognosis.

Received : January 7, 1991

Introduction

Diphtheria is an acute disease caused by Corynebacterium diphtheriae. In developing countries, including Indonesia, diphtheria remains a public health problem whereas in western countries it has become relatively uncommon as a result of the success of routine immunization [1,2]. The highest incidence was found in children between 2 and 5 years of age [1,3].

The most common and serious complications are those caused by the effect of toxin on the heart which is the major cause of mortality and morbidity of diphtheria. Evidence of myocarditis may be noted by the electrocardiographic (ECG) changes [4] and increased heart enzyme levels including creatine phosphokinase (CPK) [5]. Bull-neck has been reported as a sign of poor prognosis and is mostly seen with myocarditis [1].

This study was designed to evaluate the creatine phosphokinase blood levels in patients with diphtheria without complication, in those bull-neck and in those with abnormal ECG patterns.

Materials and methods

From October 1987 to October 1989, 39 patients with diphtheria were studied at the Department of Child Health, Ujung Pandang General Hospital. The diagnosis was based on clinical findings viz. by the presence of a local yellowish-white pseudomembrane. Patients with angina follicularis were first treated with procain penicillin. If the next day the membrane was still present or had spread to adjacent tissues then these patients were also included in the study. Identification of C. diphtheriae was done by means of culture and direct smear from nose and throat swabs. Patients with conditions affecting ECG patterns (congenital and acquired heart disease) and CPK blood levels (damaged of skeletal muscle, hypothyroidisme, brain injury) were excluded from the study.

Electrocardiogram followed by determination of CPK serum levels were routinely performed on the first, 7th and 14th day after admission. The CPK serum levels were determined by a Monotest Creatine Phosphokinase Act method. The CPK serum level was considered normal if it did not exceed 50 U/L. The level was not influenced by age [6].

All patients were treated with 900,000 U procain penicillin per day intramuscularly for 10 consecutive days. Anti diphtheria serum was given in a dose of 40,000 - 80,000 I.U. intramuscularly depending on the localisation and the size of the pseudomembrane. Prednisone 2 mg/KgBw/day was also given for 2 weeks and then tapered off.

The data were processed statistically using the chi-square test, student t test, and analysis of variance (ANOVA).

Table 1 : *Serum CPK levels in patients with various ECG patterns*

ECG pattern	N	%	CPK level (U/L)
Normal	17	43.6	54.2 *
Sinus tachycardia	11	28.2	558.7 *
LVH	7	18.0	300.3 *
Sinus tachycardia + LVH	3	7.7	367.3 *
LBBB + total AV block	1	2.6	2057.0
T o t a l	39	100	

F ratio = 9.486 * $p < 0.001$

Table 2 : *Serum CPK levels on admission in patients with normal ECG patterns and in those with abnormal ECG patterns*

	CPK levels (U/L)	
	Normal ECG (N : 28)	Abnormal ECG (N : 11)
Mean	152.0	731.7
SEM	38.9	169.4
Range	17 - 729	51 - 2057

t 37 = 4.701 $p < 0.01$

Table 3 : *Serum CPK levels in patients with normal ECG patterns during hospitalization*

	CPK levels (U/L)		
	Determination I (N : 18)	Determination II (N : 18)	Determination III (N : 18)
Mean	92.0	40.8	20.9
SEM	34.0	6.5	3.0
Range	17 - 647	12 - 125	5 - 61

F ratio = 7.761 $p < 0.01$

Table 4 : *Serum CPK levels in patients who developed abnormal EKG patterns during hospitalization*

CPK levels (U/L)	Determination I (N : 11)	Determination II (N : 11)	Determination III (N : 11)
Mean	260.1	44.0	16.9
SEM	82.2	9.3	4.0
Range	32 - 729	20 - 112	5 - 45

F ratio = 7.761 $p < 0.01$

Table 5 : *Serum CPK levels on admission in patients with abnormal ECG patterns who expired or survived*

U/L	CPK levels (U/L) Diphtheric patients with abnormal ECG	
	survived (N = 13)	expired (N = 9)
Mean	231.5	874.7
SEM	70.7	172.4
Range	32 - 729	275 - 2057

t 20 = 3,7994 $p < 0,01$

Table 6 : ECG patterns in patients with bull-neck and those without

Condition	Abnormal ECG	Normal ECG	Total
Bull-neck (−)	6	14	20
Bull-neck (+)	16	3	19
T o t a l	22	17	39

x^2 1df = 11.645 $p < 0.001$

Table 7 : *Serum CPK levels in patients with bull-neck and in those without*

Condition	N	Serum CPK levels		
		Mean	SD	Range
Bull-neck (−)	20	49.8	33.3	21 - 175
Bull-neck (+)	19	596.0	472.3	86 - 2057

t 37 = 5,1619 $p < 0,001$

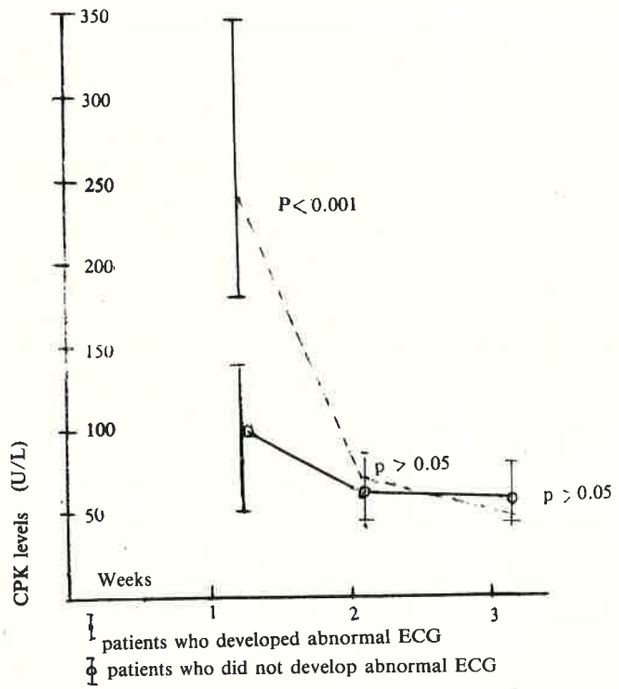

Figure 1 : *Serum CPK levels on admission in patients who had normal ECG patterns and in those who developed abnormal ECG patterns during hospitalization.*

Results

Of the 39 cases enrolled in the study, 19 were females and 20 males. Their ages ranged from 1 year and 2 months to 13 years with a mean of 6.5 ± 3.1 years. On the first day of admission, 11 patients showed ECG abnormalities and during hospitalization 11 other patients developed ECG abnormalities, making the total number of patients with ECG abnormalities 22 (56.4%) (Table 1).

Analysis of CPK serum levels on the first day of admission revealed that all patients either with abnormal ECG or with normal ECG patterns had higher levels than normal. Mean CPK serum level in patients with abnormal ECG was 14.6 times the normal value, while in patients with normal ECG pattern it was 3.0 times. The mean CPK serum levels between both groups of patients differed significantly ($p < 0.01$) (Table 2).

Table 3 demonstrates the mean CPK serum levels in patients with normal ECG patterns and Table 4 shows the mean CPK serum levels in patients who developed abnormal ECG patterns during hospitalization. A significant difference was seen between each determination of CPK levels, either in the group with normal ECG or in the group with abnormal ECG patterns. In both groups the first determination showed the highest level while the second and third ones revealed levels within normal limits.

Figure 1 shows that on admission the mean CPK serum level in patients with normal ECG patterns was only 1,8 compared to 5.2 times the normal level in patients who developed abnormal ECG patterns during hospitalization. A very significant difference ($p < 0.001$) between both groups of patients was only seen in the first assay. This statistical difference did not appear in both groups on the second and third determinations of CPK levels.

Table 5 shows the mean CPK serum levels on admission in patients with ab normal ECG patterns who expired or survived. The expired cases had already demonstrated higher levels than the patients who survived (17.5 times the normal value versus 4.6 times the normal value). A significant difference was found between both groups of patients ($p < 0,01$).

Bull-neck appeared in 19 out of the 39 patients. Patients with bull-neck differed very significantly ($p < 0.001$) from those without bull-neck in either the frequency of the occurrence of abnormal ECG patterns (Table 6) or the mean CPK serum levels (Table 7). Most of the patients (84.2%) with bull-neck had abnormal ECG patterns and a mean CPK serum levels of almost 12 times the normal values, while only 30% of patients without bull-neck had abnormal ECG patterns and a normal value of mean CPK serum levels.

The mean CPK serum levels were differed very significantly ($p < 0.001$) among the various ECG patterns (Table 1). The mean CPK serum levels of patients with sinus tachycardia, sinus tachycardia + left ventricle hypertrophy and left ventricle hypertrophy were 11.2, 7.3 and 6 times the normal value, respectively (Table 1).

There were not any death case either among the patients without bull-neck or among the patients with normal ECG pattern.

Discussion

Acute myocarditis is a serious complication of diphtheria. It occurs in approximately in 10-20 percent of patients. This complication mostly appears in the second and third weeks of the disease. The mortality rate varies between 50 and 60 percent [7]. Therefore more attention should be given to the early stage of the disease in order to reduce its mortality.

In this study, 22 of 39 patients showed abnormal ECG patterns. Eleven of the 22 patients had already demonstrated ECG abnormalities in the first week of the disease while the remaining developed the ECG changes during hospitalization. ECG abnormalities have been reported in 16.5% to 84% of all patients with diphtheria but most observers place the figures at about 25% [8]. In our study this figure was 56.4%. The abnormal ECG patterns were sinus tachycardia, left ventricle hypertrophy, left bundle branch block and total atrioventricular block. These patterns have also been reported by other investigators [1,9,10].

The increased appearance of organ-specific enzymes in serum indicates damage to these organs. Therefore, serum enzyme determination for the diagnosis of myocardial complication is of utmost importance. Serum CPK assay is one of the various myocardial enzymes that is widely done in detecting myocardial infarction. Typically the serum level increased sharply to 3-6 times the upper limit of normal within 2 to 6 hours following the infarction. The peak elevation occurred about 24 to 36 hours after the attack and thereafter the values rapidly fell and may reached normal levels after 48 hours. The maximum level attained may be as high as 10 times the upper limit of normal range and it roughly correlates with the extent of the infarction [9]. The test is therefore valuable in the early diagnosis of myocardial involvement in diphtheria patients.

We observed that all our patient had higher mean CPK levels than normal and that the highest level was found on the first determination or in the first week of the disease. In this period the serum CPK levels were also higher in patients with abnormal ECG compared to patients with normal ECG patterns ($p < 0.01$). The mean CPK level was 14,6 times the normal value in patients with abnormal ECG whereas only 3.0 times the normal value in patients with normal ECG pattern. The mean CPK serum level was also higher in patients who developed abnormal ECG during hospitalization (5.2 times the normal value) compared to patients with constant normal ECG pattern (1.8 times the normal value). Among patients with abnormal ECG patterns, those who died had a mean CPK serum levels of 17.5 times the normal value, while those who survived had only 4,6 times the normal value on the first determination ($p < 0.001$).

We also detected that a very significant difference ($p < 0.001$) existed among the various ECG patterns. Patients with sinus tachycardia were found to have a high mean CPK level (11.2 times the normal level). One case with an ECG pattern of left bundle branch block + total atrioventricular block which was not included in the statistical analysis had a very high CPK level: 41 times the normal level. Left bundle branch block and total AV block are known to be a diagnostic sign of diphtheria myocarditis [8].

Bull-neck had a high correlation with death due to myocarditis. Most of the cardiac deaths in patients with bull-neck occurred in those with major conduction disturbances [1]. In this study we observed that the 19 cases with bull-neck were very significantly different from the 20 cases without bull-neck ($p < 0.001$). The patients with bull-neck had more abnormal ECG changes (84.2%) and higher mean CPK serum levels (almost 12 times the normal value).

ECG abnormalities are usually the earliest evidence of acute myocarditis in diphtheria although not all ECG abnormalities are associated with clinical manifestations of cardiac damage. This study demonstrated that higher CPK serum levels may precede abnormal ECG patterns and that a certain CPK level in the first week of the disease is valuable for establishing the diagnosis and determining the prognosis of myocarditis.

Conclusion

This study on patients with diphtheria concluded that all patients had raised serum CPK levels on admission and that these levels were highest in the first week of the disease. We observed also that in patients who consequently developed abnormal ECG pattern during hospitaliza tion had already demonstrated an increased level of 5.2 times the normal level on admission. Among diphtheria patients with abnormal ECG, those who died had an increased serum CPK level 17.5 times the normal level in comparison with only 4.6 times in the survival group. Patients with bull-neck had an increased serum CPK level of almost 12 times the normal level compared to the non bull-neck patients who had normal levels. Of the abnormal ECG changes, sinus tachycardia was accompanied by very high levels : 11.2 times the normal level in comparison with lower levels in LVH and sinus tachycardia + LVH patients. One care with LBBB and total AV block had a serum CPK level of 41 times the normal value. We therefore suggest that an increase of serum CPK to a certain level may precede the development of abnormal ECG pattern and is valuable for determining the prognosis.

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