ORIGINAL ARTICLE

All Elevated Creatine Kinase is not Neuroleptic Malignant Syndrome

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Summary

Creatine kinase (CK) is an enzyme that is found widely in muscle tissues. Raised levels would occur when there is muscle damage. Raised levels are used as one of the diagnostic criteria for Neuroleptic Malignant Syndrome (NMS). This study looks at CK levels in 30 psychotic inpatients without NMS and compares them with 10 patients with NMS. It was found that 67% of the patients without NMS had raised CK levels, 20% of whom had levels in excess of 1000 IU/L. The rest had a two to five-fold increase over normal limits. Raised levels were associated with the use of intramuscular injections and physical restraints, situations which are well known to result in muscle injury. All the NMS patients had raised CK levels but 40% had levels below 1000 IU/L. Our findings support the idea that CK levels, though helpful, should be interpreted with care as raised levels are nonspecific.

Key Words: Creatine kinase, Neuroleptic Malignant Syndrome, Psychotic inpatients, Injections, Physical restraints

Introduction

Neuroleptic Malignant Syndrome (NMS) is a serious adverse side-effect of neuroleptic drugs. Recent studies indicate that it occurs more often than hitherto suspected and that milder cases are often missed[1]. Levenson[2] proposed major and minor criteria for the diagnosis of NMS. Major manifestations are fever, muscle rigidity and raised creatine kinase (CK) levels. Minor criteria include tachycardia, abnormal blood pressure, tachypnoea, altered consciousness, diaphoresis and leucocytosis. However other diagnostic practices[3] somewhat relegate CK levels to a minor feature. Adityanjee[4] and O'Dwyer *et al*[5] have seriously questioned the role of CK in the diagnosis of NMS. In spite of this, it is often observed that there is a tendency to depend on the CK as a confirmatory test for NMS.

Creatine kinase, previously known as creatine phosphokinase or CPK, is an enzyme which is raised whenever there is muscle injury. Two common non-NMS related reasons for raised levels in psychiatric inpatients are intramuscular (I/M) injections and the use of physical restraints in acutely disturbed patients. Both these situations commonly occur in acute wards. The aim of our study is to monitor the CK levels in psychotic inpatients without NMS and compare them with cases of NMS.

Method

Thirty male and female adult inpatients newly admitted for psychotic illness were studied with their consent. They were all physically healthy. CK levels were measured one to two days after they were given oral treatment or I/M injections or while they were on physical restraints plus I/M injections. For comparison we took 10 cases of NMS on our records, details of four of whom have been published[6].

The reference (normal) level of CK in our laboratory is 24 to 195 IU/L (for males), and 24 to 160 IU/L for females. A CK level of 1000 IU/L was chosen as the cut-off value as values above this are often used as pointing to a diagnosis of NMS. Statistical tests used were the Chi-squared test with Yates' correction and Fisher's exact test.

Results

Table 1 shows 30 cases of non-NMS and 10 cases of NMS according to modes of treatment. Eleven of the non-NMS cases received I/M injections only, nine received I/M injections with physical restraints, nine oral treatment only, and one was on physical restraints with oral medication. In contrast all 10 cases of NMS received I/M injections, half of whom were also physically restrained.

Figure 1 shows the distribution of cases according to CK levels on a logarithmic scale. Twenty (67%) of the non-NMS cases had CK levels above 200 IU/L, whereas all the NMS cases were above this level. Six (20%) of non-NMS cases had levels above 1000 IU/L whereas six (60%) of NMS cases were above this value. There was no statistical difference between the two groups in terms of raised CK levels on both the Chi-squared test as well as the Fisher's exact test.

Figure 2 shows CK levels of cases according to mode of treatment and NMS status. Of the nine non-NMS cases who were both on injections and physical restraints, eight had raised levels, three of whom had levels in excess of 1000 IU/L. Of the nine cases of

Table I
Modes of treatment

	NMS n = 10	Non-NMS n = 30
Oral only	0	9
Oral & Restraint	0	1
Injections only	5	11
Injections & restraint	5	9

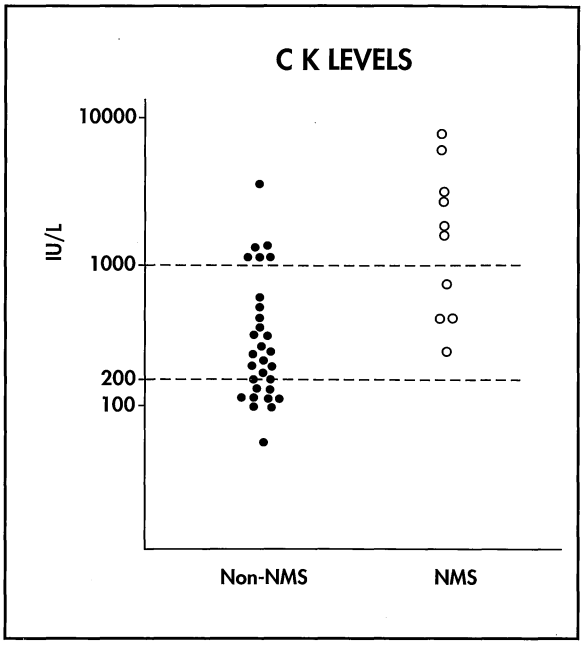

Fig. 1: Creatine kinase levels (IU/L)

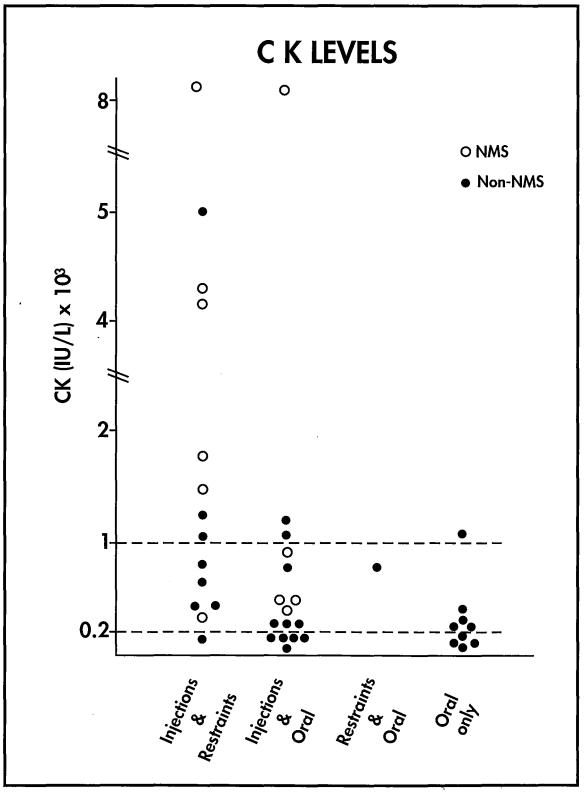

Fig. 2: Creatine levels (IU/L)

non-NMS on oral medications only, five (56%) had raised levels but only one had a level above 1000 IU/L. The latter was a 23-year-old male Malay schizophrenic. The possibility that he might have engaged in vigourous struggling just prior to admission could not be ruled out.

Even among the NMS group, the highest levels are generally obtained in those who had received both injections and physical restraints.

Discussion

Our study supports the findings of others that I/M injections with antipsychotics increase CK levels even in the absence of NMS[7], and these levels are likely to be even higher with concomitant use of physical restraint. In some cases of NMS, CK levels may be only mildly raised. Forty per cent of our NMS cases had CK levels below 1000 IU/L. McCarthy *et al*[8] have similarly reported only mild elevations of CK in NMS. There is no clear cut-off point for an elevated CK level in NMS, though Levenson uses a cut-off point of 1000 IU/L[2], and it is a test with low specificity[5,9].

The small sample size is an obvious limitation in this study, as is the fact that no randomisation was done. However we have replicated the clinical situation and hence we believe our results are likely to reflect what would be found in usual clinical settings.

We conclude from this modest study that CK levels are very variable being easily raised, though usually mildly, by insults to the musculoskeletal system, such as severe exercise, agitation, I/M injections and the use of physical restraints. Conversely, slightly raised levels do not rule out NMS. Though most patients with NMS would have very high CK levels, our study indicates, in agreement with others[4,5], that some non-NMS cases may have high levels too. An objective biochemical test such as the CK should be given due weightage, but, because of its nonspecific nature, should be interpreted with care.

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