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Whiplash: a biochemical study of muscle injury

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Abstract Outcome following whiplash injury of the cervical spine is variable, and the pathology of those with prolonged symptoms is uncertain. We undertook a prospective study in 25 patients to identify whether those with prolonged symptoms following whiplash injury exhibit a rise in serum creatine kinase consistent with significant muscle damage at the time of injury. Transient rise in creatine kinase level was seen in only 2 of 25 patients, neither of whom complained of prolonged

symptoms. Of the 8 patients who developed chronic symptoms following whiplash injury, none demonstrated a serum creatine kinase rise. Prolonged symptoms following whiplash injury cannot be explained by biochemically measurable muscle damage.

Keywords Whiplash injury · Creatine kinase

Introduction

The incidence of reported whiplash injury continues to increase dramatically, with an estimated incidence in the UK of 250,000 injuries per annum [8, 30]. This has huge financial implications due to loss of employment and litigation.

The outcome following injury is guarded. Murray et al. [20] reported 8% disability in 413 patients at 4 years following whiplash injury. However, other studies have suggested long-term symptoms in 40–70% [10, 18, 32]. A number of factors may affect long-term prognosis, including psychological factors [9, 29] and ongoing litigation [5, 28]. Obelieniene et al. [24] found no long-term symptoms in a prospective study of 210 patients with whiplash injuries in Lithuania, a country in which there is little medico-legal activity.

The pathology of whiplash injury remains undefined, despite experimental work on human volunteers and cadavers [26, 34]. The presumed injury in minor cases is a soft tissue sprain [28, 30]. Other authors suggest injury to joint ligaments and capsule, chronic disc herniation, epidural haematoma and skeletal muscle injury [27, 26].

Articles by Hohl [14] and Hirsh et al. [13] have suggested anterior neck injury with muscular tearing, intra-muscular haemorrhage and disc disruption, with injury to sternocleidomastoid, scalaneus and longus coli muscles in extension injuries. Despite these studies, it is not known whether permanent muscle damage occurs in whiplash injury.

Creatine kinase (CK) is a major cytoplasmic enzyme of muscle. The enzyme is present in three major isoenzymic forms, which are present in skeletal muscle (MM), brain (BB) and cardiac muscle (MB). CK-MM constitutes more than 90% of serum total creatine kinase [11, 19, 35]. Trauma to skeletal muscle causes myofibre contusion and necrosis with release of creatine kinase and elevation of total serum CK levels associated with muscle soreness [1]. Rises in serum creatine kinase have been found to occur within 6–24 h of direct muscle injury [7, 36], and have been suggested to be a more sensitive indication of skeletal muscle damage than magnetic resonance (MR) images [31]. The aim of the present study is to quantify the extent of muscle damage occurring in whiplash injury by measuring serum creatine kinase concentration following whiplash injury.

Table 1 Serum creatine kinase (CK), pain, sleep disturbance and work and litigation status following whiplash injury

Pt	CK at 24 h (U/l)	CK at 48 h (U/l)	CK at 3 mths (U/l)	Neck pain at 24 h	Neck pain at 3 mths	Sleep dis- turbance at 24 h	Sleep dis- turbance at 3 mths	Employment at 24 h	Employment at 3 mths	Litigation at 3 mths
1	153	126	121	Mild	Nil	No	No	Yes	Yes	No
2	79	59	50	Moderate	Nil	No	No	Sick leave	Yes	No
3	77	120	110	Moderate	Moderate	Yes	Yes	Yes	Yes	Yes
4	76	66	91	Severe	Severe	Yes	Yes	Sick leave	Sick leave	Yes
5	88	77	59	Mild	Nil	No	No	Unemployed	Unemployed	No
6	241	173	140	Mild	Nil	No	No	Yes	Yes	No
7	66	60	43	Severe	Nil	Yes	No	Sick leave	Yes	Yes
8	142	108	121	Mild	Nil	No	No	Yes	Yes	No
9	59	55	75	Moderate	Mild	Yes	No	Yes	Yes	No
10	66	63	58	Moderate	Moderate	Yes	Yes	Yes	Yes	No
11	58	60	43	Moderate	Nil	Yes	No	Unemployed	Unemployed	Yes
12	91	77	60	Mild	Nil	No	No	Sick leave	Yes	No
13	43	58	32	Mild	Mild	No	No	Yes	Yes	No
14	131	102	83	Moderate	Moderate	Yes	Yes	Yes	Yes	Yes
15	144	118	103	Severe	Severe	Yes	Yes	Sick leave	Sick leave	Yes
16	26	38	40	Mild	Nil	No	No	Unemployed	Unemployed	No
17	208	140	130	Moderate	Nil	Yes	No	Yes	Yes	No
18	170	150	90	Severe	Moderate	Yes	Yes	Sick leave	Yes	Yes
19	83	59	64	Mild	Nil	No	No	Unemployed	Unemployed	No
20	59	49	40	Moderate	Moderate	Yes	Yes	Sick leave	Sick leave	Yes
21	111	121	90	Moderate	Nil	Yes	No	Sick leave	Yes	No
22	107	109	89	Mild	Nil	No	No	Yes	Yes	No
23	94	90	50	Moderate	Severe	Yes	Yes	Unemployed	Unemployed	Yes
24	91	63	59	Mild	Nil	No	No	Yes	Yes	No
25	67	63	52	Moderate	Nil	Yes	No	Yes	Yes	Yes

Materials and methods

Patients with a whiplash-type injury following a low-velocity road traffic rear end collision were prospectively recruited from the Accident and Emergency department. Only patients with an isolated neck injury presenting within 24 h of injury were recruited.

All patients underwent initial assessment by an Accident and Emergency department physician to exclude associated injuries and neurological deficit. All patients underwent anteroposterior and lateral view radiographs of the cervical spine. Any patient with radiological evidence of cervical spine injury was excluded from the study.

At 24 h from injury, all patients donated a blood sample for serum creatine kinase measurement and were assessed for the presence of neck pain, sleep disturbance and current employment in a specialist spinal clinic. A further serum creatine kinase measurement was taken at 48 h.

Serum for creatine kinase measurement was stored in a refrigerator overnight and analysed using an enzyme assay kit (DG 147-k Sigma, Poole, UK).

Patients were seen finally at 3 months following injury, when a further creatine kinase sample was taken and the patient was again assessed for continuing neck pain, sleep disturbance, work state and whether litigation had proceeded as a result of injury.

Results

Twenty-five patients were recruited, 9 women and 16 men, mean age 37 years (range 19–58 years). All patients pre-

sented with an isolated neck injury as a result of a low-velocity rear-end collision. The results for serial measurement of creatine kinase and patient symptoms are shown in Table 1.

Seventeen patients stated that their own vehicle was stationary at the time of impact, and in only two cases was there major vehicle damage.

Fifteen patients presented with neck pain that they graded as moderate to severe, and ten with mild neck pain. Fourteen patients complained of sleep disturbance at initial assessment. All patients were found to have cervical muscle tenderness on initial examination, and 12 patients had greater than 50% reduction in cervical spine movements. All patients had a normal neurological examination. One patient was excluded from the study as a result of an undisplaced C7 spinous process fracture, which was noted on the second review.

In only two patients was a rise in creatine kinase above the normal limit (175U/l) demonstrated. In both patients this rise returned to normal by 48 h. Neither patient had symptoms prolonged to 3 months following injury.

Eight out of 25 patients have continued to have significant symptoms at 3 months following injury. None of these patients have demonstrated a rise in creatine kinase following injury. Seven out of eight of the patients with con-

tinuing symptoms were pursuing litigation at the time of clinical review at 3 months.

Discussion

Creatine kinase (CK) represents a sensitive indicator of skeletal muscle damage. Hikida et al. [12] demonstrated a rise in serum CK of 100 U/l following a mean muscle biopsy of 71.3 mg, corresponding to 1800 muscle fibres.

Following direct muscle injury, the peak value of CK occurs within 24–48 h of injury (returning to normal limits within 7 days) [17, 25, 33]. Nosaka and Sakamoto [23] demonstrated a four-fold rise in CK following IM injection of 10 ml 0.5% bupivacaine, whilst Kawaguchi and co-workers demonstrated similar rises at 24 h following posterior lumbar surgery [16]. A rise in CK to over 4000 U/l at 48 h following a documented hamstring injury has been recorded [12].

In this study, in only two patients was a transient rise in creatine kinase observed, which had returned to normal at 48 h. It would therefore seem unlikely that direct muscle damage is a cause of pain following whiplash injury.

Following eccentric muscle loading, a variable rise in CK is seen, which is felt to be as a result of inflammatory mediators increasing muscle cell membrane permeability rather than direct muscle damage. Although no studies document the response to a single severe episode of eccentric muscle loading which would be compatible with a whiplash injury, a number of studies have documented a CK rise following multiple eccentric contractions of muscle groups.

A rise of CK to 250–500 U/l has been demonstrated by some authors within 24 h [2, 6, 21], whilst others observe much higher values: 1500–8000 U/l, peaking at 72–96 h following exercise [7, 15, 31]. Even those studies that demonstrate a late peak, however, do show a noticeable rise in CK at 48 h (range 250–500 U/l).

Although in this study no CK measurements were taken at 72–96 h post injury, and therefore the peak rise in CK may have been missed if eccentric loading is indeed the mechanism of injury following whiplash-type injury, it is felt that the initial rise in CK would still have been noted in the 48 h sample. As no rise was documented at 48 h in any patient, it would seem unlikely that a subsequent large rise in CK would have occurred. In addition, care must be used in interpreting the results of studies using multiple repetitions of eccentric muscle loading, as the phenomenon of muscle adaptation is well documented, in which muscles undergoing repetitive eccentric exercises have a smaller and more prolonged response to exercise than do those experiencing less repetition and more severe eccentric loading, which would be the case in a whiplash-type injury [3, 4, 22].

Conclusion

This study has shown that whiplash injury produces no measurable biochemical evidence of muscle cell damage and that prolonged symptoms following whiplash injury cannot be attributable to muscle damage. The study would suggest that whiplash injury is not typically a muscular injury.

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