

THE EARLY DETECTION AND MANAGEMENT OF NEUROPATHIC PAIN FOLLOWING COMBAT INJURY

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Abstract

The mechanism of injury on the modern battlefield results in a pattern of wounding which is associated with both nociceptive and neuropathic pain. Nociceptive pain is managed using the WHO Analgesic Ladder but neuropathic pain requires the use of co-analgesic drugs, e.g. antidepressants and anticonvulsants. This study was designed to determine the incidence of neuropathic pain within military casualties with limb injuries. From May to November 2007, 50 casualties were interviewed and assessed using the Leeds Assessment of Neuropathic Symptoms and Signs Scale (LANSS) over consecutive weeks. During the first week post injury, 30% of casualties had a LANSS pain score >12, suggesting a neuropathic element to their pain. The early detection (using LANSS) and management of neuropathic pain using robust protocols represent the most effective strategy to address this significant problem.

Introduction

Nociceptive pain occurs following the stimulation of visceral or somatic nociceptors by noxious stimuli and the transmission of an impulse along intact neurons, to the central nervous system [1]. It commonly follows trauma and responds well to conventional analgesics.

Neuropathic pain (NP) may be defined as '*pains resulting from dysfunction, disease or damage of the peripheral or central nervous system*' [2]. So in the presence of nerve damage, neuropathic mechanisms may contribute to the patient's pain. Neuropathic pain is characterized by burning, tingling, shooting, scalding or even areas of sensory deficit. Exacerbations may occur spontaneously or evoked by non-noxious stimuli. Symptoms include allodynia, hyperalgesia, hyperpathia and signs of autonomic dysfunction. Neuropathic pain has an unpredictable response to opioids.

Following tissue trauma the release of inflammatory mediators can cause primary or secondary peripheral sensitization of nociceptors [3], making them more sensitive to stimulation, leading to 'wind up' of spinal cord activity [1]. This may result in a continuation of the pain and if untreated 'central sensitization' may occur, causing chronic neuropathic pain with lasting perceptions that continue after tissue repair is complete [4 - 8].

Modern combat body armour (CBA) was designed to protect the chest and abdomen, but it provides little protection to the extremities. In recent conflicts, blast and fragmentation injuries have accounted for up to 65% of combat trauma [9], which causes complex and multidimensional wounding patterns. Multiple injuries to the limbs are common, which may be characterized by extensive soft tissue, neural and bone destruction [10]. The neurobiological changes that characterize chronic neuropathic pain may occur within hours of an acute injury [11], so every battlefield casualty has the potential to have neuropathic

mechanisms contributing to their pain. The primary purpose of this investigation was to determine the incidence of NP within military casualties with combat injuries involving their limbs.

The features of chronic neuropathic pain have frequently been described by veterans injured during recent conflicts within the Middle East [12], which has also been the focus of adverse reporting by the media [13, 14]. Neuropathic pain has a variable response to opioids and the 'neuropathic contribution' to the total pain experienced by an individual also varies, so the provision of appropriate analgesia to these casualties can involve complex management strategies. This study was also designed to evaluate the provision of analgesia and casualty satisfaction from the initial point of wounding, through the evacuation chain to the Role 4 in the United Kingdom.

Methods

This prospective study was conducted over a six month period in 2007 at the University Hospital Birmingham and Royal Centre for Defence Medicine. Following ethical approval from our hospital pain committee and informed consent, casualties with limb injuries were invited to participate in the study.

All data was collected by the same senior clinician, trained in chronic pain management and competent at using the assessment tools (Figure 1). At the initial consultation, the injuries sustained by each casualty were collected by reviewing the military and NHS case notes, drug charts and local computerised prescription information database.

The casualties retrospectively graded the severity of their pain from the point of wounding, through the various phases of evacuation, to the Role 4, using a 100mm visual analogue scale (VAS), where a score of 0 indicated no pain and a score of 10 was the worst possible pain. Scores were collected for the following phases of evacuation and treatment:

- Pre-hospital
- At Field Hospital
- Evacuation to the UK
- At UK Role 4

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A pain score during a particular phase was not recorded in unconscious, anaesthetised and sedated casualties or when recall of painful events was limited. Data following the use of a combat application tourniquet (C-A-T) and the insertion of local anaesthetic nerve blocks was also collected.

Further data was collected from the casualty by interview, examination and the use of the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale [15]. The LANSS provides a simple and uniform method for diagnosing neuropathic pain; with a maximum possible score of 24. A score less than 12 suggests that neuropathic mechanisms were unlikely and a score greater than 12 suggests a neuropathic component. LANSS scores were obtained at weekly intervals.

Results

Data was collected between 17th May and 19th November 2007 from 50 casualties returning to the Role 4 in Birmingham following operational deployment to the Middle East. Demographic data for the study population is shown in Table 1, and the mechanism of injury to the limbs in Table 2.

Male / Female	49 / 1
Age	25 (19-53)
Op Herrick	34 (68%)
Op Telic	16 (32%)

Table 1. Demographic data. Data are presented as number or median and (range or percentage).

Blast and Fragmentation	33
Gun Shot	13
Crush	2
Road or Air Traffic Accident	2

Table 2. Mechanism of injury to the limbs. Data are presented as number.

The median pain scores calculated for the four phases following injury were:

- 8 for pre-hospital
- 3 for the field hospital
- 2 for evacuation
- 5 for the Role 4.

Pain score data was not recorded for four casualties in the pre-hospital group, five in the field hospital group and five in the evacuation group. The data illustrating the pain experienced during the four phases following injury are shown in Figure 2.

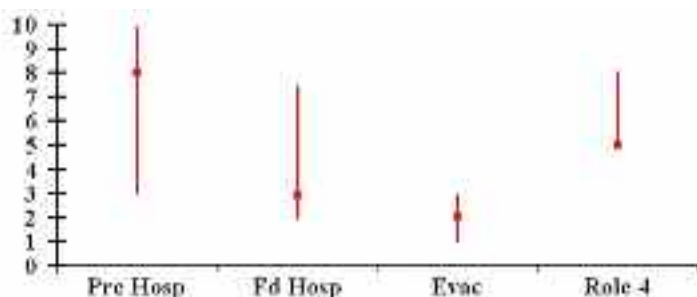


Figure 2. Pain scores associated with the four phases following injury. Data are presented as median (●) and interquartile range (—).

A wide selection of conventional analgesia and co-analgesics were prescribed during the investigation (Table 3). All casualties were given regular paracetamol (4g daily) with either diclofenac (150mg daily) or ibuprofen (limited to 1.2g daily). Tramadol and codeine were often added as either regular or 'as required' prescriptions. Eighty six percent of the casualties were given morphine via a variety of routes with 20% being managed with a patient-controlled analgesia system. Oxycodone was frequently prescribed

following the discontinuation of parenteral morphine. Pregabalin and amitriptyline were the most frequently prescribed co-analgesics but the timing of their introduction varied considerably. For pregabalin the median was day 15 with interquartile range (8 -18) and for amitriptyline the median was day 13 with interquartile range (4 - 21). Gabapentin was only prescribed in 10% of casualties, usually during the first week post injury.

Paracetamol	100%
Morphine	86%
Diclofenac	72%
Codeine	56%
Oxycodone	48%
Tramadol	42%
Pregabalin	32%
Amitriptylene	30%
Ibuprofen	12%
Gabapentin	10%

Table 3. Prescribing frequency of co-analgesic and traditional analgesic drugs.

Thirty percent of the casualties were identified with signs and symptoms suggestive of neuropathic pain. Using the LANSS pain scale, 28% of casualties had a pain score >12 during the first week following injury, suggesting that neuropathic mechanisms were likely to be involved. As the duration post injury (in weeks) increased, the number of casualties with a LANSS score >12 gradually decreased (Figure 3): 22% during week two; 18% during week three; 14% during week four; 6% during week five and; 4% during week six. In those casualties who had a LANSS pain score >12, this was usually identified during the assessment performed in the first week post injury. However, one casualty had a low initial LANSS pain score of 7, which increased >12 during the second and third weeks post injury.

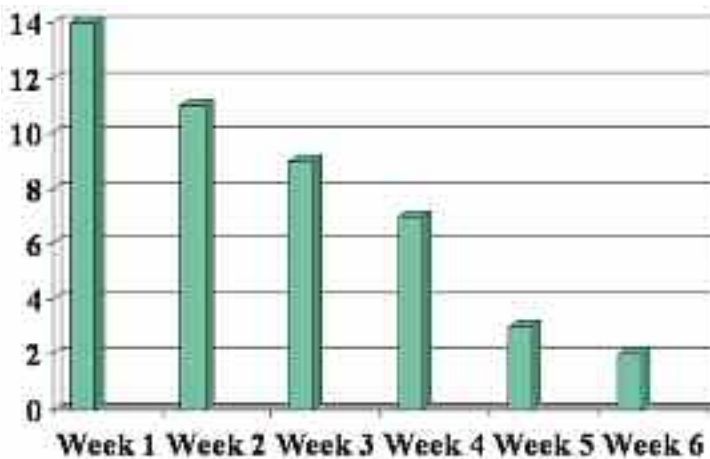


Figure 3. The relationship between increasing time post injury and the number of casualties with a LANSS pain score >12.

Fifty two percent of the study population had a C-A-T applied for pre-hospital haemorrhage control. One casualty self-applied the C-A-T and one had tourniquets applied to both lower limbs. The median duration prior to removing the C-A-T was 75 min, with interquartile range (55 - 95) and range (10 - 150) min. In those casualties that had tourniquets applied, 27% developed neuropathic signs and symptoms, and within this group the median C-A-T removal time was 90 min, with interquartile range (75 - 115) and range (10 - 150) min. In the 73% remaining within this tourniquet group, the median C-A-T removal time was 60 min, with interquartile range (55 - 79) and range (30 - 120) min. However, 33% of the casualties that did not have a tourniquet applied also developed neuropathic signs and symptoms.

At the field hospital regional anaesthesia (femoral nerve block or epidural) was used to provide analgesia to two casualties (4%), both of whom had isolated high-velocity gun-shot injury with ballistic femoral fracture.

Discussion

In this study 30% of military casualties were found to have a LANSS pain score >12, during the first week post injury, which subsequently reduced to 4% by week six. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, which has been reported by military casualties [12]. An individual's perception of what is painful may be influenced by differences in age, gender, culture, previous pain experiences, beliefs, mood and ability to cope. However, tissue trauma sustained on a modern battlefield frequently involves a combination of blast, thermal and multiple penetrating fragment injuries. Within the population investigated blast and fragmentation injuries accounted for 66% of casualties, which is a similar proportion to previously reported statistics [16].

The median pain scores calculated for the various phases following injury provides important subjective data, which reflects on what memories the casualty has of their pain following injury. The pre-hospital phase recorded the highest score, despite no pain scored being recorded in 8% of the casualties. Since the First World War intramuscular morphine has been the UK's standard battlefield analgesic, but due to concerns with its efficacy and mechanism of administration, battlefield analgesia has been the focus of an extensive review [17]. Whilst a multimodal analgesic ladder provides a safe solution to managing nociceptive pain of varying severity, the analgesic benefit of the individual Pain Relief Pod remains unreported [17].

The combat application tourniquet (C-A-T) is a crucial device used for haemorrhage control on the modern battlefield [18, 19]. However, it has been associated with neurological complications but these are usually rare or transient events [20, 21]. The actual mechanism of neural injury remains unclear but direct pressure on the nerve and nerve ischaemia are popular theories [20]. In our investigation 52% of casualties had a C-A-T applied with a median time prior to removal of 75min, which indicates that evacuation timelines and C-A-T training guidelines are being followed [18,20]. In those casualties that had tourniquets applied, 27% developed neuropathic pain with a slightly longer median removal time of 90 min, but 33% also developed neuropathic pain without use of a C-A-T. Whilst our sample size is small, our results do allow us to conclude that the use of a C-A-T does not necessarily predispose a casualty to developing neuropathic pain.

Tissue trauma is a recognised factor in the development of neuropathic pain [1] but it has a variable response to opioids. So when severe pain is resistant to morphine, it is likely that neuropathic pain mechanisms may be contributing. The neurobiological mechanisms that generate and characterize neuropathic pain may occur immediately and have been identified within hours following injury [11]. Delivering early and effective analgesia is therefore essential, and is supported by animal studies which conclude that blocking pain stimuli at the time of tissue injury may prevent neural remodeling or central sensitization. This may prevent the development of chronic neuropathic pain [7, 11], and the perception of pain persisting long after tissue healing has occurred and minimizes the behavioural changes associated with sustained pain [7, 22, 23]. It has also been shown that effective pain management may have a positive effect on the morale of non-injured soldiers [24]. However, it remains unclear whether the incidence of psychiatric disorders, e.g. post-traumatic stress disorder (PTSD) and their effect on mental health would also be reduced.

In this study 30% of casualties with limb injuries had an initial

LANSS score of 12 or more, indicating that they had signs and symptoms of neuropathic mechanisms contributing to their pain.

Whilst this figure may be lower than what we had predicted, it represents the incidence of neuropathic pain in a specific group of casualties. In our study only 4% had neuropathic signs and symptoms at six weeks post injury; which is lower than US casualty data (as presented by Col T Buckenmaier at the Tri-Service Anaesthetic Society meeting in 2007) and lower than what might be expected in a civilian situation. However, since the management of neuropathic pain is not standardised at the Role 4, it is not clear whether this was due to effective treatment or whether the initial LANSS was picking up a neuropathic element of acute postoperative wound pain. A standardized approach to pain management and long term follow up would be required to determine the incidence of chronic neuropathic pain in military casualties.

Continuous peripheral nerve block (CPNB) analgesia was first described in a military context in 2005, during the evacuation of casualties with severe limb trauma and it has since been shown to provide superior analgesia to parenteral morphine following trauma surgery [25]. CPNB techniques provide profound and specific analgesia and anaesthesia in association with haemodynamic stability and opioid sparing effects [24]. A further study demonstrated shorter durations in intensive care and a delay in the development of chronic pain, when the critically injured casualties were managed with early CPNB and an aggressive multimodal analgesia strategy [26]. Following battlefield trauma, the use of catheter based CPNB techniques have historically been linked with catheter related infections and the concealment of acute traumatic compartment syndrome (ATCS). However, recent military evidence indicates that infection is not a significant problem [16] and following a systematic review of ATCS, intravenous morphine via a patient controlled analgesia system (PCA) was as likely to delay the diagnosis of ATCS as a regional technique [27]. As a consequence of transatlantic differences in the healthcare systems and practice of anaesthesia, CPNB is more widely used and advanced in North America. A recent survey of DMS anaesthetists [28], identified a paucity of experience and confidence with CPNB techniques. This may explain why only 4% of the casualties in our study received a nerve block technique.

Whilst we believe that achieving proficiency in CPNB techniques should be possible during specialist training in anaesthesia, it represents a greater challenge following consultant accreditation, due to the restrictions of an individual job plan. If we are to prevent the inevitable lag in service delivery, should proficiency in CPNB be identified as a desirable operational skill, then focused professional development plans for consultants and the establishment of DMS anaesthetic training strategy are essential.

To effectively manage neuropathic pain the problem needs to be detected as early as possible and appropriate drugs (anticonvulsants and/or antidepressants) prescribed using clinical evidence from civilian practice [29, 30, 31] and adapted for military use. The LANSS pain scale may provide us with a routine and reproducible method for the early detection of neuropathic pain, but robust pain (including neuropathic pain) management protocols must also be developed. These are ongoing projects for the Department of Military Anaesthesia and Critical Care which have not yet been reported.

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