REVIEW

Is hot water immersion an effective treatment for marine envenomation?

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Envenomation by marine creatures is common. As more people dive and snorkel for leisure, the incidence of envenomation injuries presenting to emergency departments has increased. Although most serious envenomations occur in the temperate or tropical waters of the Indo-Pacific region, North American and European waters also provide a habitat for many stinging creatures. Marine envenomations can be classified as either surface stings or puncture wounds. Antivenom is available for a limited number of specific marine creatures. Various other treatments such as vinegar, fig juice, boiled cactus, heated stones, hot urine, hot water, and ice have been proposed, although many have little scientific basis. The use of heat therapies, previously reserved for penetrating fish spine injuries, has been suggested as treatment for an increasing variety of marine envenomation. This paper reviews the evidence for the effectiveness of hot water immersion (HWI) and other heat therapies in the management of patients presenting with pain due to marine envenomation.

> lmost 2000 ocean species are either venomous or poisonous to humans. As more people dive and snorkel for leisure, the incidence of envenomation injuries presenting to emergency departments has increased.1 Between 40 000 and 50 000 marine envenomations occur worldwide each year.2 Coastal emergency departments regularly see patients who present after marine envenomation, although some incidents occur "inland" as a result of stings from fish kept as pets.3 4 Although most serious envenomations occur in the temperate or tropical waters of the Indo-Pacific region, North American and European waters also provide a habitat for many creatures.5 6 Envenomations European waters are most commonly caused by Weever fish, scorpion fish, and coelenterates such as the Portuguese man-of-war or other jellyfish (fig 1). Marine envenomations can be classified as either surface stings (erythema, vesicles, urticaria) or puncture wounds (bites, stings) (appendix 1).

> Specific antivenom is available for the treatment of stonefish and box jellyfish stings. Otherwise, various treatments have been proposed for marine envenomation, although many have little scientific basis. Traditional remedies have included vinegar, fig juice, boiled cactus, heated stones, hot urine, hot water, and ice.^{5 7}

Established national and international guidelines advocate the use of vinegar and application of cold for selected types of marine envenomation. The use of heat therapy, traditionally in the form of HWI has previously been reserved for envenomation by penetrating fish stings. More recently, there has been increased interest in applying this treatment to surface stings.8-11 The use of HWI or heat application as the initial treatment for "puncture"-type fish stings has a long history. The earliest record of the effective use of heat in the treatment of Weever fish stings was in 1758. It was noted that German fishermen found a hot poultice "a most effective cure".7 Standard advice is to submerge the affected part in hot water at as high a temperature as the patient can tolerate for 30-90 minutes.7

In this article, we review the evidence for the effectiveness of HWI or other heat therapies in the management of patients presenting with pain due to marine envenomation.

SEARCH STRATEGY

We searched the databases MEDLINE (including PRE-MEDLINE), EMBASE, and CINAHL using the OVID interface with the following search strategy: ((hot water or heat).mp. or exp *Heat/) and (exp *Fishes/or exp *"Bites and Stings"/or fish sting.mp. or exp *Fishes, Poisonous/or exp *Fish Venoms/or exp *Jellyfish/or envenomation.mp.)

We also searched the Cochrane database injury, wound, and anaesthesia section in full, the *British National Formulary* and Toxbase databases for national guidelines, and the internet, using the 'Google' search engine. The bibliographies of the articles obtained were then manually searched. The results are outlined below. Unpublished work and conference presentations were researched by communication with people with expertise in the field of marine envenomation.

The articles were graded by study design according to the levels of evidence summarised in appendix 2.

RESULTS

The published evidence on this topic ranges from randomised controlled trials (RCTs) to personal communications to journals. Results of studies and published articles are presented in the order of their evidence level.

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Abbreviation: HWI, hot water immersion

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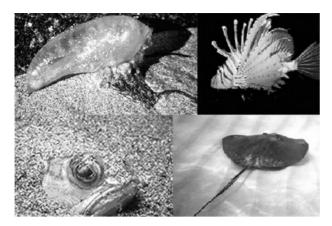


Figure 1 Venomous marine creatures. Clockwise from top left: *Physalia*, lionfish, stingray, lesser Weever fish.

Level I evidence: randomised controlled/paired trials

Two RCTs and one randomised paired comparison trial have been published addressing the use of heat as a treatment for marine envenomation. These studies look at nematocyst-type stings. The results are summarised in table 1.

Thomas *et al* measured the analgesic effect of hot and cold packs on box jellyfish (*Carybdea alata*) stings in 133 swimmers in Hawaii.⁸ These particular jellyfish do not have a lethal sting, but cause significant pain, lasting from 20 minutes to 24 hours and resolving spontaneously. This study looked at the short term effects (5–15 minutes following application) of hot and cold packs and placebo. The main finding was that

heat reduced pain scores at 5 and 10 minutes after application. There was also a significantly higher odds ratio (5.2) for complete cessation of pain with heat compared with placebo. There are some methodological flaws in this study (see table 1) and the authors themselves noted the borderline clinical significance of their findings.

In a randomised paired trial Nomura *et al* compared HWI with standard therapy (papain and vinegar) for acute Hawaiian box jellyfish stings inflicted on 25 healthy volunteers. Both arms of each volunteer were stung, with one treated by HWI and the other with either vinegar or papain. The authors found that pain scores on a visual analogue scale were lower with HWI at 4 and 20 minutes, with similar baseline levels. One methodological flaw was the use of two different potentially active substances in the control group. The results could also have been biased by distraction, as volunteers were asked to gauge pain scores from two simultaneous stings.

Loten *et al*¹⁰ have recently published an RCT of HWI versus ice packs for pain relief in *Physalia* stings. Forty nine patients received HWI and 47 received icepacks. They found that hot water group reported len pain after 10 and 20 minutes of treatment. The trial was stopped after the halfway interim analysis because HWI was shown to be more effective (p = 0.002).

Researchers from Sydney, Australia, recently completed a randomised crossover trial comparing hot showers and icepacks for the treatment of *Physalia* (Portuguese man-of-war/bluebottle) envenomation in a beach setting.¹¹ The usual local practice for the treatment of these stings was cold pack application. Fifty four adults were randomised to hot shower or cold pack application, with 27 in each arm of the trial. A

| Study | N/Type | Group | Intervention | Outcome | Comments |
|--|---|---|---------------------------------|--|---|
| Thomas <i>et al</i> ⁶ 2001 | 133 Randomised controlled trial | Swimmers with box jellyfish (<i>Carybdea</i> <i>alata</i>) stings | Cold pack v placebo | Pain scores at 0, 5 and 10 minutes: 42.3 to 31.3 to 27.5* v 38.3 to 32.8* to 36.2 38.3 to 32.8* to 36.2 v 38.6 to 37.7 to 38.2 42.3 to 31.3* to 27.5* v 38.6 to 37.7 to 38.2 (*p<0.05) Cessation of pain—odds ratio (95% CI): 5.2 (1.3 to 22.8) 0.5 (0.1 to 2.1) 1.0 | Poor randomisation technique due to practical difficulties Inadequate blinding Altered outcome measures after starting trial (changed definition of pain cessation) Not analysed on intention to treat basis |
| Nomura <i>et al</i> ⁵ 2002 | 25 (50 stings) Randomised paired trial | | Hot water immersion Control | Pain scores at 0, 4, 20 minutes 3.6 to 2.1* to 0.2* 3.7 to 3.2 to 1.8 (* p<0.001) | Potentially active substances (papain or vinegar) used as controls No placebo |
| Loten <i>et al</i> ¹⁰ 2006 | 96 Randomised controlled trial | Swimmers with blue bottle (<i>Physalia</i>) stings | Hot water immersion Ice pack | Percentage with reduced pain 10, 20 minutes | Possible allocation blas, suggested by the baseline imbalance in initial pain severity |

| Paper | N/type | Group | Intervention | Outcome | Comments |
|---------------------------|-------------|-----------------|--------------|-----------------------|-------------------|
| Bowra et al ¹¹ | 54 | Swimmers with | | Pain score reduction: | No blinding |
| 2002 | Prospective | Physalia stings | Hot shower | 82.1%* (4.3) | No controls |
| | randomised | , , | Cold pack | 65.6% (6.0) | Crossover in 24/5 |
| | crossover | | ' | Pain cessation: | cases |
| | trial | | Hot shower | 48%** | Lack of follow up |
| | | | Cold pack | 29% | |
| | | | | Total treatment time | |
| | | | Hot shower | 11.0* (0.9) min | |
| | | | Cold pack | 14.6 (1.6) min | |
| | | | | (*p<0.05; **p<0.01) | |

total of 24 subjects completed crossover. There was no significant difference in pain scores between the two treatments in each individual stage of the trial. Combined results from both stages showed that hot showers reduced total treatment time and provided greater overall pain reduction when measured using a visual analogue score. Complete cessation of pain was reported by 48% of patients treated with hot showers, significantly more than the 29% who were pain free after cold pack treatment. The lack of a blinding and follow up are the main methodological flaws of this study (see table 2).

Level II evidence: experimental paired/crossover study

An early paper details a small experimental trial in which six healthy volunteers each received an injection of extracted, concentrated stingray venom into one finger of each hand. They then placed one hand in cold, and the other in hot water. Pain was relieved within five minutes by HWI but exacerbated by cold water immersion. Crossover was performed with five of the volunteers with the same findings.

Pain was completely relieved after 30 minutes of HWI. This study is summarised in table 3.

Level III evidence: cases series

Six papers report on 259 cases of marine envenomation, including puncture-type stings from stingrays or stinging fish and nematocyst stings from jellyfish. Of the 135 cases treated with hot water, where follow up was complete, 122 patients reported a reduction in pain (table 4).

Level IV evidence: review articles, summary papers, guidelines and letters

Five review articles on marine envenomation have discussed the use of HWI (table 5). Guidelines and summary papers on the treatment of marine envenomation tend to advocate the use of HWI for all puncture-type fish stings, but do not otherwise recommend its routine use.^{20–23} A total of eight published letters to journals discuss the use of HWI as a treatment for marine envenomation. There is a broad consensus among correspondents that HWI has a beneficial effect on pain levels in certain circumstances.⁷

| Paper | N/group/type | Intervention | Outcome | Comments | |
|----------------------|--|--------------|-----------------------------------|---|--|
| Russell ⁶ | 6 volunteers (each | | Initial pain relief: | Small numbers | |
| 1958 | received 2 injections | | · | No randomisation. Atypical crossover | |
| | of stingray venom) | HWI | 6/6 | (Initially 6 in each arm, then all 12 to | |
| | | Cold water | 0/6 | HWI simultaneously, then alternating with cold water) | |
| | Experimental paired trial with crossover | | Complete analgesia at 30 minutes: | No statistical analysis | |
| | WIIII CIO330VCI | HWI | 5/5 | | |

| Paper | N/group/type | Intervention | Outcome | Comments |
|--|--|-----------------------------------|--|--|
| Isbister ¹³ 2001 | 15 from 22 cases Mixed species fish stings Prospective case series | HWI | Analgesic effectiveness: Complete 11/15 Partial 1/15 None 1/15 Unknown 2/15 | Includes some retrospective data (7 cases) No standardised treatment No pain scale |
| Briars and Gordon ¹⁴ 1992 | 24 cases + 23 extra cases by survey Weever fish stings Prospective case series with survey | HWI | 23/24 reported decreased pain Follow-up survey: 39 respondents stated pain reduced by HWI | Published as letter Methodological details lacking Survey has potential for bias No pain scale used |
| Yoshimoto <i>et al</i> ¹² 2002 | 60 from 113 Swimmers with jellyfish stings Retrospective case series | Heat application Hot shower | Pain relief in 23/25 cases (OR 11.5; p=0.08) Pain relief in 22/23 cases (OR 22.0; p=0.0485) | Retrospective No control group Significant number of incomplete medical records |
| Halpern <i>et al</i> ¹⁵ 2002 | 3 Weever fish stings Retrospective case series | HWI | Pain relieved in 3/3 cases | Retrospective Small numbers Other analgesics given No pain scores used |
| Trestrail and Al-Mahasneh³ 1989 | 23 Lionfish stings Retrospective case series | HWI | Pain relieved in 15/15 cases | Retrospective No pain scale Missing data |
| Kizer <i>et al</i> ⁴ 1985 | 51 Fish stings (45 lionfish, 6 scorpion-fish) Retrospective case series | HWI | Complete pain relief in 30/38 cases Complications 4 infections, 1 burn | Retrospective Missing data No pain scale |

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| Paper | Advice relating to hot water immersion (HWI)/heat application | Comments |
|--|--|---|
| Fenner ¹⁶ 2002 | HWI for stingray and fish spine stings, for analgesic effect | Literature review of marine envenomation No methodology, critical appraisal or meta-analys |
| Fenner ¹⁷ 2000 | HWI for stingray and stonefish stings, for analgesic effect | Literature review of marine envenomation No methodology, critical appraisal or meta-analys |
| Hawdon and Winkel ¹⁸ 1997 | HWI for stonefish and "other stinging fish"; for analgesic effect | Literature review of marine envenomation No methodology, critical appraisal or meta-analys |
| Meyer ¹⁹ 1997 | HWI for stingray injuries, for analgesic effect | Literature review of stingray injuries No methodology, critical appraisal or meta-analys |
| Auerbach⁵ 1991 | HWI for puncture wounds of stingray, scorpion fish, stonefish, sea-urchin, starfish, catfish, Weever fish, | Literature review of marine envenomation No methodology, critical appraisal or meta-analys |
| | for analgesic effect | Clear treatment algorithm proposed. |

published letters caution against certain aspects of this treatment method. $^{31\ 32}$

DISCUSSION

Evidence supporting use of HWI

Hot water immersion is a widely used and accepted treatment for fish-spine stings, although there have not been any RCTs to date. The evidence for the treatment of puncture-type stings by this method comes from one small experimental study⁶ and a total of 99 reports of its effective use in 110 cases from several papers.^{3 4 13-15} This evidence has led to recommendation of this treatment method by organisations such as the International Life Saving Federation²³ and the British Marine Life Study Society.³³ The use of HWI is advised in toxicology guidelines such as Toxbase²² and the *BNF*²¹ and is supported in all five published review articles on marine envenomation.^{5 16-19}

There is less widespread support for the use of HWI for nematocyst stings in these same guidelines and reviews, yet there is mounting evidence that HWI is also effective for this type of sting. Three randomised trials⁸⁻¹⁰ and one abstracted RCT¹¹ of jellyfish and *Physalia* stings found hot water or heat therapy to be more effective than placebo or cold packs at relieving pain. Also, in a case series pain was reported to be relieved in 23 of the 25 patients treated by heat therapy.¹² There is recent evidence (2001/02) for the use of hot water therapy in nematocyst stings. Revisions of guidelines issued by several international life saving and resuscitation organisations mention the use of HWI for selected surface-type stings such as *Physalia*, however, none advise this treatment before the more traditional first aid policies of selective use of vinegar to inactivate nematocysts, immobilisation, and application of ice packs.23 33-37

Mechanism of action of HWI

So how might HWI or heat application work as a treatment marine envenomation? Two theories have been proposed. ^{7 9 28 38} Marine venoms consist of multiple proteins and enzymes, and there is evidence that these become deactivated when heated to temperatures above 50 °C. ¹⁹ A long-held view is that deactivation of these heat labile proteins by direct heat application leads to inactivation of the venom. Carrette *et al* investigated the effect of temperature on lethality of venom from *Chironex fleckeri*. They showed that at temperatures over 43 °C, venom lost its lethality more rapidly the longer the exposure time. However, no significant loss of lethality was seen after exposure to temperatures less than 39 °C. ³⁹ The theory of deactivation has been questioned by authors who contend that such direct inactivation would require temperatures so high as to result in burns and tissue

necrosis in the patient.14 38 An alternative theory is that HWI causes modulation of pain receptors in the nervous system leading to a reduction in pain. Established pain hypotheses such as the gate control theory and the diffuse noxious inhibitory control theory have been proposed as possible mechanisms of action for HWI.38 Although marine envenomation is more commonly associated with warmer regions than the UK, the relevance of this topic and of HWI is not restricted to tropical and subtropical areas. Of the 146 cases of puncture-type stings included in the reported cases series, a total of 47 were due to Weever fish in European waters and 68 were caused by fish kept in tanks by aquarists (see table 4). Cases of Weever fish stings in which HWI was not used, and in which pain persisted for several days have been reported from Wales.40 Victims who are aware of the benefits of HWI may choose not to seek medical advice. However, it is important that emergency physicians are aware of treatment options for those patients who do present to hospital.

Methods of application of HWI

There is only a single recorded case of significant thermal burn from over 200 cases of the use of HWI.4 This treatment modality appears to be safe when used sensibly. It is an inexpensive, and as there is reasonable evidence that it can relieve pain after a variety of types of fish sting. The most commonly referenced methods of application are thermal packs, basins of hot water, and hot showers. The choice is likely to be determined by the availability of each close to the location of envenomation. Showering may have a theoretical advantage in that it may wash off any remaining stinging cells, as well as having the ability to vary the temperature, and to continue the heat application until pain relief is achieved. Application of hot, but not scalding, water (42-45 °C) for 30-90 minutes or until the pain resolves, seems to be standard advice, though some patients may find such temperatures difficult to tolerate.41 Our advice is to use the highest temperature that can be applied safely and that is tolerable.

Current published evidence seems to support the use of HWI in the treatment of non-life threatening marine envenomation, alongside other established first aid measures.

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APPENDIX 1 TYPES OF MARINE ENVENOMATION

SURFACE STINGS (NEMATOCYSTS)

This mechanism of envenomation involves a system of venom glands able to discharge a structure that penetrates the victim and carries the venom through a tube. The glands are found in the Portuguese man-of-war (Physalia), fire corals, anemones, jellyfish and corals. As a group these account for the largest number of envenomations by marine animals. The venom contains various peptides, phospholipase, proteolytic enzymes, haemolytic enzymes, ammonium compounds, serotonin, and other compounds that together are highly antigenic. Effects range from severe burning pain with localised skin erythema, through mild systemic upset, to severe systemic reactions involving vomiting, chest pain, convulsions, and respiratory failure. Extremely toxic species such as the box jellyfish (Chironex fleckeri) and Irukandji (Carukia barnesi) are found in tropical Australian and Indo-Pacific waters.

STINGS

Several species of marine animals cause a 'sting' by puncturing the victim's skin with a specialised apparatus and introducing venom into the puncture wound. This group includes sea urchins, cone shells, starfish, stingrays, catfish, Weever fish, and a family of fish known as Scorpaenidae. The Scorpaenidae envenomate by erecting spines on their dorsal, anal, and pelvic fins able to pierce skin and introduce venom. Those found in tropical and temperate waters include lionfish (Pterois), scorpion fish (Scorpaena) and the lethal stonefish (Synanceja). Envenomation produces severe localised pain, swelling, and often tissue necrosis. Systemic symptoms may be mild or severe with cardiorespiratory collapse in the case of the stonefish. Weever fish are found off the coast of UK and cause severe pain but less severe systemic symptoms.

BITES

Species that envenomate by biting include octopi and sea snakes. The blue ringed octopus has caused several fatalities. Its venom, introduced from salivary glands close to the animal's beak, is a vasodilator and potent neurotoxin. All fatalities have occurred on handling the animal out of the water and there is no available antivenom. It is found in Australian and Indo-Pacific waters. Sea snakes are found commonly in the tropical and warm temperate parts of the Pacific and Indian oceans. Neurotoxic venom is introduced through the victim's skin by two to four maxillary fangs. The bite may be painless, but systemic symptoms often occur within two to eight hours. These include myalgia and ascending paralysis, and rarely death. There is no specific antivenom, but symptoms may respond to multivalent snake antivenom. Rarely, envenomations will lead to severe systemic symptoms including cardiovascular or neurological system failure.

APPENDIX 2 LEVELS OF EVIDENCE

Ia: evidence from meta-analysis of randomised controlled

Ib: evidence from at least one randomised controlled trial

IIa: evidence from at least one controlled study without randomisation

IIb: evidence from at least one other type of quasi-experimental study

III: evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case–control studies

IV: evidence from expert committee reports or opinions and/ or clinical experience of respected authorities

(Adapted from the US Agency for Health Care Policy and Research Classification. Clinical Practice Guidelines No. 1: acute pain management: operative or medical procedure and trauma. Rockville MD, US Department of Health and Human Services.

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