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Pain from Bluebottle Jellyfish Stings

Journal Club Article

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Clinical Scenario

An 11 year-old girl presented to the Emergency Department after being stung by jellyfish at a New South Wales (NSW) beach. Tentacles were found attached to her left leg, which were removed at the beach and the leg washed with seawater. The patient had intense pain rated 8/10 using Numeric Rating Scale, but no other significant symptoms. On examination there were erythematous marks present on the left calf.

The current guideline published by the Australian Resuscitation Council (2010) suggests that in non-tropical Australia, jellyfish stings should be treated with water as hot as can be tolerated for 20 minutes. If unrelieved, an ice pack may then be used.⁽¹⁾ This guideline is based on evidence from past case reports, books and randomised controlled trials. A search was performed to assess the most current evidence for the treatment of jellyfish stings. Particular focus was placed on Bluebottle (*Physalia*) stings as these account for the majority of stings in NSW.

Structured Clinical Question (PICO)

In children (≤ 18 years) stung by jellyfish (P), what are the most effective treatments (I & C) for relieving pain (O)?

Search strategy

Randomised controlled trials (RCTs) and systematic reviews were identified by searching the following databases with no restrictions for language or years: CENTRAL (Issue 10 2014), MEDLINE (1948 to 10 October 2014), EMBASE (1980 to 10 October 2014) and Web of Science all databases (1899 to 10 October 2014). Keywords used for MEDLINE included jellyfish*.mp OR (jelly adj6 fish*).mp OR medusa*.mp OR MESH terms cubozoa, hydrozoa, scyphozoa and cnidarian venoms. Similar keywords were applied to all searches. Reference lists from relevant articles were also reviewed.

Our search yielded a total of two systematic reviews and seven RCTs. The first review was published in The Cochrane Library in 2013 and was written by the authors of this article. This review included RCTs without language, date or publication status restrictions. It investigated the treatment of jellyfish stings from any age group, causative jellyfish, location and sting intervention.⁽²⁾ The second review by Ward et al. was published in the American College of Emergency Physicians in 2012. This review focused on treatment for jellyfish and related organism stings in North America and Hawaii and included all English language studies.⁽³⁾

Ward et al.'s review identified 19 studies, six of which were RCTs,⁽³⁾ while Li et al. identified seven RCTs.⁽²⁾ Our current search identified the same seven RCTs of which four were from Australia (two Sydney,^(4, 5) one Newcastle,⁽⁶⁾ one Cairns⁽⁷⁾) and three from Hawaii.⁽⁸⁻¹⁰⁾ One RCT was published in 2013, five in the early 2000s and one in 1980. Within the Australian trials, only the Sydney and Newcastle trials focused on Bluebottles, whilst the Cairns trial focused on Irukandji jellyfish.

Table 1 - Summary of Papers

Citation	Study Population	Study design and Level of Evidence (GRADE)	Interventions	Results	Comments
Systematic Reviews					
Li et al. ⁽²⁾ 2013 Sydney	Any RCT where a child or adult was stung by jellyfish of any species	Systematic Review Moderate quality of evidence	Any intervention	Hot water immersion may be the most effective treatment of bluebottle (<i>Physalia</i>) jellyfish stings. Insufficient data for other jellyfish species.	Total of 7 RCTs identified
Ward et al. ⁽³⁾ 2012 San Diego	English-language studies on true jellyfish (Cnidaria), box jellyfish and <i>Physalia</i> (Bluebottle) species found in North American and Hawaiian	Systematic Review Moderate quality of evidence	All interventions for “pain relief, prevention of nematocyst discharge or extrusion of venom” ⁽³⁾	<u>Tentacle removal</u> : No studies on removal method. <u>Vinegar in nematocyst discharge</u> : Some papers (but no RCTs) suggest vinegar may	Total of 19 studies included in this review including 6 RCTs, 1 non-randomised controlled trial.

	waters addressing “treatment of patient complaints or animal models of nematocyst discharge or extrusion of venom” (<i>Ward et al 2012</i>).			neutralise/inactivate some jellyfish species including Australian box jellyfish and Bluebottles, but may increase toxin discharge in others. <u>Hot water and topical lidocaine:</u> appear effective in relieving pain symptoms for most species	
Randomised Controlled Trials					
Bowra et al. ⁽⁵⁾ 2001	54 participants (>6 years) accidentally stung at a Sydney beach by	Crossover RCT Moderate quality of evidence	Two-arm trial: 1. 10min hot shower (27	1. % <u>Pain-free</u> : 48% subjects pain-free after hot showers versus 29.6% with	Abstract only available.

<p>Sydney</p> <p>(Abstract only)</p>	<p><i>Physalia</i> (Bluebottles)</p>		<p>participants).</p> <p>2. 10min ice pack (27 participants).</p> <p>If pain unrelieved, swap to other intervention for up to 10min.</p>	<p>ice packs.</p> <p>2. <u>% Pain reduction:</u></p> <p>Greater for hot showers vs ice packs (16.5% difference; P<0.03)</p>	
<p>Loten et al.⁽⁶⁾</p> <p>2006</p> <p>Newcastle</p>	<p>96 participants (>8 years) accidentally stung and presenting to first aid facilities at two Newcastle beaches by <i>Physalia</i> (Bluebottles)</p>	<p>RCT</p> <p>Moderate quality of evidence</p>	<p>Two-arm trial:</p> <p>1. Hot water (45°C) application for 20min (49 participants)</p> <p>2. Ice pack (-4°C) as long as tolerable up to 20min (47 participants)</p>	<p>1. <u>Clinically reduced pain at 10min:</u> 53% of hot water, 32% of ice packs (21% difference; 95% CI 1-39%; P=0.039)</p> <p>2. <u>Clinically reduced pain at 20min:</u> 87% of hot water, 33% of ice packs (54% difference, 95% CI 35-69%;</p>	<p>Clinically reduced pain: defined by VAS (visual analogue scale) pain score with a change from baseline of 16mm for initial VAS 0-33mm; 33mm for</p>

				P=0.002)	VAS 34-66mm; 48mm for VAS 67-100mm. NOTE: VAS score is usually measured as a point on a 100mm scale.
McCullagh et al. ⁽⁷⁾ 2013 Cairns	39 participants (>16 years) presenting to Cairns Base Hospital with signs/symptoms of Irukandji syndrome who required one dose of parenteral opioid analgesia	RCT Moderate quality of evidence	Two-arm trial: 1. Active infusion of 50mmol magnesium sulphate made up to 500mL with normal saline (22 participants) 2. Placebo infusion: 500mL normal saline (17	<u>Total analgesia requirements (defined by Morphine equivalent dose in mg)</u> : No significant difference between magnesium (50mg) and placebo (53mg); P=0.879	Trial was terminated early as various agencies had introduced magnesium as standard of care.

			participants)		
Nomura et al. ⁽¹⁰⁾ 2002 Hawaii	30 healthy adult volunteers deliberately stung (one each arm) in laboratory setting with <i>Carybdea alata</i> (Hawaiian box jellyfish). Faulty tentacles in 5 subjects left 25 analysed.	RCT Low quality of evidence	Three-arm trial: 1. Hot fresh water (40-41degC) 20min 2. Either Acetic acid 5% (household vinegar) OR Papain (Adolph's) meat tenderizer (4:1 with water) 20min	Average VAS score at: 1. <u>0min</u> : 3.6cm hot water, 3.7cm comparator (P=0.35) 2. <u>4min</u> : 2.1cm hot water, 3.2cm comparator (P<0.01) 3. <u>20min</u> : 0.2cm hot water; 1.8cm comparator (P<0.001)	VAS pain score used. Comparators (Acetic acid or Papain) were not directly compared to each other.
Thomas et al. ⁽⁸⁾ 2001 Hawaii	133 participants (adult/child) accidentally stung at a Hawaiian beach by <i>Carybdea alata</i> (Hawaiian box jellyfish)	RCT Low quality of evidence	Three-arm trial: 1. 15min vinegar and chemical hot packs (max 43degC) (44 participants)	1. <u>Average pain score at 5min</u> : Improved for hot and cold packs compared to themselves at 0min and to control (hot: 31.3; cold:	VAS pain score used. Analysis was performed at 0, 5,

	and not requiring ambulance. Initial drop-out of 6 gave total 127 participants.		2. 15min vinegar and chemical cold packs (min 5.5degC) (42 participants) 3. Vinegar and air temperature packs (41 participants)	32.8; control: 37.7) <u>Average pain score at 10min:</u> Hot pack had lower pain scores (27.5) than cold (36.2) or control (38.3). No clinically significant difference between Cold packs and control.	10 and 15min. Pain score ratings were only those from 5 and 10 minutes (insufficient numbers at 15min).
Thomas et al. ⁽⁹⁾ 2001 Hawaii	63 participants (>7years) accidentally stung at a Hawaiian beach by <i>Carybdea alata</i> (Hawaiian box jellyfish). One attrition after vinegar dousing gives a total of 62	RCT Low quality of evidence	Four-arm trial: 1. 15min vinegar then fresh water (19 participants) 2. 15min vinegar then seawater (16 participants) 3. 15min vinegar then	<u>Average pain scores:</u> No statistically significant differences between treatment groups at 0, 5 or 10 minutes.	VAS pain score used. Analysis was performed at dousing of vinegar then at 0, 5, 10 and 15 minutes.

	participants.		sting-aid (aluminium sulphate) (13 participants) 4. 15min vinegar then Adolph's meat tenderizer (1:4 with water) (14 participants)		Results shown are from 0, 5 and 10min (too few participants at 15min to analyse).
Turner & Sullivan ⁽⁴⁾ 1980 Sydney	20 healthy adult volunteers deliberately stung two places each arm with <i>Physalia</i> (Bluebottles) in a laboratory setting	RCT Very low quality of evidence	Four-arm trial of unknown treatment duration: 1. Vinegar 2. Methylated spirits 3. Stingose (aluminium sulphate) 4. Salt water	<u>Pain relief:</u> Methylated spirits significantly increased pain at application ($P < 0.01$). At 5min, relief from vinegar and Stingose was approaching significance ($0.05 < P < 0.1$).	Results table showed the number of responses rated most painful, most relief, most skin reaction and least skin reaction. No actual rating value was given.

Best paper relevant to our patient

Bluebottles cause the most stings in our patient's region, so we focussed on papers from our search result that compared treatments for Bluebottle stings. From the papers identified the systematic reviews by Li et al. and Ward et al. are considered the best level of evidence and relevance. Both had similar conclusions with one RCT included in both reviews (Loten et al.) being the most relevant to our patient in terms of location, jellyfish type and population.⁽⁶⁾ We have chosen to appraise this RCT due to its influence on the results of both systematic reviews as well as its applicability to our patient.

Loten et al. aimed to identify the effectiveness of hot water immersion at 45°C versus ice packs in the symptomatic relief of Bluebottle stings. We performed and structured our critical appraisal using the JAMA criteria on appraising articles about therapy or prevention.^(11, 12)

Are the results of the study valid?

Participants were those aged over 8 years presenting with apparent Bluebottle stings at a beach setting (excluding stings to eyes or those requiring ambulance). Patients were randomly assigned hot water or ice packs using computer-generated sequences, but blinding was not possible due to the nature of the interventions. Intention-to-treat analysis was performed. Attrition was detailed (4 in each group after 10 minutes), although reasons were not provided. Adequate 24-hour follow-up was completed and numbers detailed.

This trial was planned from 30 December 2003 to 5 March 2005, but was stopped at interim analysis as authors felt hot water immersion was already more effective at 20 minutes (P=0.002). Early stopping could potentially increase chances of bias especially as there were no formally pre-specified cessation rules.

Overall, however, the trial was well-conducted and reported with valid study methodology and results.

What were the results?

Loten et al. showed that warm water immersion was more effective than ice packs for the treatment of Bluebottle stings. At 10 minutes, 53% (26/49) of participants had clinically significant pain relief in the hot water group (refer to Summary of Papers Table) compared with 32% (15/47) in the cold water group (21% difference; 95% CI 1-39%). At 20 minutes this increased to 87% (39/45) in the hot water group and 33% (14/43) in the cold water group (54% difference; 95% CI 35-69%).⁽⁶⁾ Results had statistically significant P-values (especially P-value of 0.002 at 20 minutes), but also had wide confidence intervals. This was likely due to low participant numbers, which may have resulted from the unpredictable nature of patient presentations. This could be improved by persisting to the end of the pre-specified trial period and by surveying more beach locations.

Will the results help me in caring for my patients?

The results of Loten et al. is applicable to our patient and others from non-tropical Australia, as Bluebottle stings are the most likely culprit in these areas. However, this research would not necessarily apply to presentations at other locations where stings may more likely be from other types of jellyfish for which hot water immersions might not be the best initial treatment. One example is box jellyfish stings in tropical Australia, for which the current guidelines and Ward et al.'s systematic review (based on non-RCT research) still suggests using vinegar to assist with nematocyst inactivation.⁽³⁾

In addition to results, we must also consider the convenience of use and financial implications. One obvious advantage of hot water immersion is the minimal cost involved and the ease of access for the general public, making it a suitable treatment to implement on a large-scale basis.

How could we improve the research?

Loten et al. conducted a well-thought-out trial with few risks of bias. Future research may be improved by continuing the trial for longer, pre-specifying early cessation rules, increasing participant numbers, putting greater focus on the type of medium for intervention (e.g. hot water or heat packs; separate analysis of hot water immersion or showers) and giving consideration to the timing of application (e.g. application duration, immediate versus delayed applications).

One shortcoming observed from our search results is the lack of more recent trials on treatment of Bluebottles and other jellyfish stings. The systematic reviews from our search gives us a good summary of available evidence, but are limited by the lack of more recent data. Despite this, Loten et al. is a well-formulated study and gives a reliable conclusion that hot water immersion is more suitable for Bluebottle stings compared to ice packs. This would not, however, extend to the treatment of other jellyfish sting types, which could benefit from more research.

Applicability to our patient

Loten et al.'s trial is relevant to our patient in terms of participant age, location and type of sting. Although our patient presented to the Emergency Department, they were medically stable enough to have been managed in an outpatient setting. Our patient differs to the study population because she was a delayed presentation and therefore received delayed treatment. Despite this, warm water immersion along with additional suitable analgesia would likely be a valid option.

Clinical bottom line

There is evidence from systematic reviews and randomised controlled trials that hot water immersions may be the best treatment for Bluebottle jellyfish stings. It is important to note that

treatment for other types of jellyfish stings such as Box or Irukandji jellyfish stings will differ and further quality research into these interventions would be of benefit in the future.

Acknowledgements

There were no financial supports or incentives involved in the writing of this paper.

References

1. Australian Resuscitation Council. Guideline 9.4.5 Envenomation - Jellyfish Stings. 2010 [cited 10 May 2014]; Available from: http://www.resus.org.au/policy/guidelines/section_9/jellyfish_stings.htm.
2. Li L, McGee RG, Isbister G, Webster AC. Interventions for the symptoms and signs resulting from jellyfish stings [Internet]. *Cochrane Database Syst Rev*; 2013 [cited 10 May 2014]; Available from: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009688.pub2/full>.
3. Ward NT, Darracq MA, Tomaszewski C, Clark RF. Evidence-Based Treatment of Jellyfish Stings in North America and Hawaii. *Ann Emerg Med*. 2012;**60**(4):399-414.
4. Turner B, Sullivan P. Disarming the Bluebottle: treatment of Physalia envenomation. *MJA*. 1980;**2**(7):394-5.
5. Bowra J, Gillet M, Morgan J, Swinburn E. Randomised crossover trial comparing hot showers and ice packs in the treatment of physalia envenomation. *Emergency Medicine*. 2002;**14**:A22.
6. Loten C, Stokes B, Worsley D, Seymour JE, Jiang S, Isbister GK. A randomised controlled trial of hot water (45°C) immersion versus ice packs for pain relief in bluebottle stings. *MJA*. 2006;**184**(7):329-33.
7. McCullagh N, Pereira P, Cullen P, et al. Randomised trial of magnesium in the treatment of Irukandji syndrome. *Emerg Med Australas*. 2012;**24**:560-5.
8. Thomas CS, Scott SA, Galanis DJ, Goto RS. Box jellyfish (*Carybdea alata*) in Waikiki: Their influx cycle plus the analgesic effect of hot and cold packs on their stings to swimmers at the beach: A randomized, placebo-controlled, clinical trial. *Hawaii med J*. 2001;**60**:100-7.
9. Thomas CS SS, Galanis DJ, Goto RS. Box jellyfish (*Carybdea alata*) in Waikiki: The analgesic effect of Sting-Aid, Adolph's meat tenderizer and fresh water on their stings: A double-blinded, randomized, placebo-controlled clinical trial. *Hawaii med J*. 2001;**60**:205-10.
10. Nomura JT, Sato RL, Ahern RM, Snow JL, Kuwaye TT, Yamamoto LG. A randomized paired comparison trial of cutaneous treatments for acute jellyfish (*Carybdea alata*) stings. *Am J Emerg Med*. 2002;**20**(7):624-6.
11. Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature, II. How to use an article about therapy or prevention. A. Are the results of the study valid? *Evidence-Based Medicine Working Group, JAMA*. 1993;**270**:2598-601.
12. Guyatt GH SD, Cook DJ. Users' guides to the medical literature, II. How to use an article about therapy or prevention. B. What were the results and will they help me in caring for my patients? *Evidence-Based Medicine Working Group, JAMA*. 1994;**271**:59-63.