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ORIGINAL RESEARCH

Efficacy of Topical Treatments for *Chrysaora chinensis* Species: A Human Model in Comparison with an In Vitro Model

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Objectives.—This study sought to create a model for testing topical treatment of jellyfish stings. It sought to determine which treatments 1) stimulate/inhibit nematocyst discharge; 2) decrease pain; and 3) decrease skin inflammation; it also sought to discover whether there is a clinical correlation between stimulated nematocyst discharge observed in vitro to the pain and erythema experienced by humans stung by a particular species of jellyfish, *C chinensis*.

Methods.—*Chrysaora chinensis* stung 96 human subjects, who were then treated with isopropyl alcohol, hot water, acetic acid, papain meat tenderizer, lidocaine, or sodium bicarbonate. Pain and erythema were measured. In a separate experiment, nematocysts were examined microscopically after exposure to the same topical treatments used in the human experiment.

Results.—Forearms treated with papain showed decreased mean pain over the first 30 minutes after being stung, relative to placebo, although only by a small amount. The other topical treatments tested did not reach statistical significance. Sodium bicarbonate may reduce erythema after 30 minutes of treatment; sodium bicarbonate and papain may reduce erythema at 60 minutes. The other topical treatments tested did not reach statistical significance. Nematocyst discharge in vitro occurred when tentacles of *C chinensis* were exposed to acetic acid or isopropyl alcohol. Sodium bicarbonate, papain, heated water, and lidocaine did not induce nematocyst discharge.

Conclusions.—Papain-containing meat tenderizer used as a topical treatment for *C chinensis* stings may decrease pain. Although there is published experimental support for the concept that in vitro nematocyst discharge correlates with in vivo human pain perception, no definitive randomized controlled trial, including ours, has yet provided incontrovertible evidence of this assertion. Despite this study's limitations, it presents a viable basis for future human studies looking at the efficacy of topical treatments for jellyfish stings.

Introduction

Jellyfish stings upon humans are worldwide occurrences, with an estimated 150 million people stung annually.[1] Jellyfish of the phylum Cnidaria envenom prey by using stinging organelles (nematocysts) that are contained within nematocytes lining the tentacles and mouth. Nematocysts comprise a secretory organelle (cnida) with a capsule containing a coiled, barb-laden tubule (nema), trigger (cnidocil), and venom. Envenomation occurs upon mechanical or chemical stimulation of the cnidocil, which leads to injection of the nema into the victim and venom release.[2] A single jellyfish may carry millions of nematocysts. An individual nematocyst can discharge its nema with a velocity of 2 m/s, corresponding to an acceleration of 40,000*g*, ensuring effective penetration of human skin and envenomation.[2,3]

There exist thousands of jellyfish species, many of which are dangerous to humans.[3] The nematocysts and venom of the majority of these species have not been not

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well characterized, but it is clear that variability exists in nematocyst structure and venom composition. There are at least 30 morphological types of nematocysts.[4] Similarly, clinical manifestations of jellyfish stings vary widely. Reactions range from minor local skin eruption with pain (most common) to systemic toxicity and death. Many jellyfish venoms contain a dermonecrotic component, which causes local skin inflammation and necrosis.[5] Although the exact mechanisms of systemic toxicity have still not been completely elucidated, previous studies suggest that jellyfish venoms contain neurotoxic, cardiotoxic, and hemolytic components that may lead to death from respiratory failure, cardiac failure, or anaphylactic shock.[2,5,6] The severity of a jellyfish sting varies according to the species of jellyfish, degree of envenomation, and age and baseline health of the victim.

Various recommendations exist in the medical and lay literature regarding the most effective treatments for people who have experienced jellyfish stings. Some treatments seek to prevent the firing of undischarged nematocysts; others attempt to inactivate the injected toxin or decrease inflammation. Anecdotal recommendations and prior studies have referenced a wide variety of topical remedies, including such substances as human urine, vinegar, isopropyl alcohol, distilled spirits, ammonia, bleach, acetone, sodium bicarbonate, lidocaine, meat tenderizer, Coca-Cola, old wine, salt water, cold packs, hot packs, hot water, and commercial products such as Stingose or Stingaid.[2–5,7–12]

Many sources recommend a single treatment method for all jellyfish stings, but it is likely that no single topical approach is effective for all known stinging species. For example, studies showing that acetic acid inhibits nematocyst discharge in multiple species of cubozoan jellyfish have cemented the role of acetic acid in the acute treatment of stings by the deadly *Chironex fleckeri*.[6,8] However, studies using other jellyfish species have found that acetic acid causes nematocyst discharge.[4,6–8] Conflicting data regarding nematocyst discharge have even been found for two species of *Physalia*. For instance, some studies utilizing the genus *Physalia* have observed nematocyst discharge after application of acetic acid, whereas others have found inhibition of discharge.[7,9] Whether nematocyst discharge observed during in vitro experimentation actually translates to clinical outcomes is unknown.

In our study, we set out to create a human model of jellyfish sting treatment that would allow for testing of commonly proposed topical remedies in a controlled, prospective, randomized, and blinded manner. The human model was run in comparison with the in vitro model to assess for any correlation between clinical outcomes with nematocyst discharge triggered by topical treatments. This model would hopefully allow future studies to use the same or similar methodology.

The specific questions we sought to address were 1) which treatments increase or decrease the number of nematocysts discharged when viewed microscopically; 2) which treatments decrease pain in humans using a verbal pain scale; 3) which treatments decrease the amount of skin inflammation using an erythema index; and 4) whether there is a clinically relevant correlation between stimulated nematocyst discharge observed in vitro and the pain and erythema humans stung by a jellyfish experienced.

Methods

JELLYFISH ACQUISITION

We used *Chrysaora chinensis* (Figure 1), a tropical jellyfish species indigenous to coastal waters in the Andaman, Java, and South China Seas. This species of jellyfish was chosen for its ready availability and stinging potential. The jellyfish were supplied and maintained by the jellyfish husbandry team at the Monterey Bay Aquarium (MBA) in Monterey, California. *C chinensis* jellyfish were shipped to the

Figure 1. Live specimen of *Chrysaora chinensis* used for harvesting of tentacles for study. The jellyfish were housed in saltwater aquariums at the Monterey Bay Aquarium in California.