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ANTIPROSTAGLANDINS AND ANTITHROMBOXANES FOR TREATMENT OF FROSTBITE

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FROSTBITE IS characterized by progressive necrosis of tissue that initially appears viable. This is due to direct, irreversible cell injury and progressive vascular stasis and thrombosis. Metabolites of arachidonic acid, ie, prostaglandins and thromboxanes, have been implicated in many pathologic processes. Suppression of their production has been shown to prevent microvascular thrombosis in the zone of stasis of deep partial-thickness burns (1). Blister fluid from human frostbite victims has been shown to contain high levels of thromboxane B_2 and prostaglandin $F_{2\alpha}$ (2). This experiment was designed to determine whether systemic or topical agents that block the formation of prostaglandins and thromboxanes could be correlated with improved tissue survival in an experimental frostbite model.

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MATERIALS AND METHODS

Twenty New Zealand white rabbits were divided into five groups. A modified Weatherly-White frostbite model was used (3). Rabbits were anesthetized with intramuscular fentanyl (0.2 mg/kg) and droperidol (10 mg/kg). The hair of the ear was clipped and a thermistor-tipped probe was inserted subcutaneously, with the tip placed approximately 2 cm from the tip of the ear. Subcutaneous temperatures were taken every 60 seconds. The ear was then placed in the inner chamber of a double-chambered vessel, the inner chamber containing 50% ethanol (initially at room temperature) and the outer chamber containing a mixture of solid carbon dioxide and 95% ethanol, which was added as soon as the ear was placed in the inner chamber. Temperature vs time plots were taken on all rabbits and the freezing periods were of sufficient length (approximately 20 minutes) to ensure 100% loss of tissue if the ear remained untreated. The ear was then removed and allowed to rewarm in air at room temperature. Elizabethan collars were fitted on all rabbits to prevent trauma and each ear was wrapped in a protective gauze. Treated groups received the following treatment regimens: I, topical 1% methylprednisolone acetate; II, topical *Aloe vera* cream; III, methimazole (1 mg/kg) by gavage; and IV, acetylsalicylic acid (ASA, 50 mg/kg) by gavage. All treatments were administered immediately after rewarming and every 8 hours for 96 hours. After necrosed tissue had separated from the viable remnant, tissue survival was recorded as the percent of total area frostbitten that survived.

RESULTS

All control rabbits sloughed 100% of the frostbitten tissue. The mean tissue survival in each treatment group was: methylprednisolone, 17.5 ± 8.9%; *Aloe vera,* 28.2 ± 26.5%; methimazole, 34.3 ± 15.5%; ASA, 22.3 ± 11.6%. All values were significant ($P < 0.05$). No group was statistically better than another.

DISCUSSION

These results suggest that substances that block production of prostaglandins and thromboxane may be beneficial in preserving tissue in a frostbite injury. Frostbitten skin transplanted to a normal recipient site has been shown to survive and behave like an undamaged autograft (3), and a significant part of the ultimate tissue loss in frostbite was concluded to be a result of vascular deprivation. Thromboxane A_2 (the unstable precursor of thromboxane B_2) is a potent vasoconstrictor and platelet aggregator. Prostglandin $F_{2\alpha}$ is a vasoconstrictor. By blocking production of these agents in the frostbitten tissue we believe that the vascular component of tissue loss is minimized. The frostbite injury used in this experiment was severe enough to maintain a reproducible result. A more dramatic tissue survival might result with a less severe injury.

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