Evaluating ketoprofen as preventive pharmacotherapy for acquired lymphedema

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Objectives/Aims

- To evaluate ketoprofen as a prophylactic intervention for lymphedema given previously noted properties in ameliorating symptoms of acquired lymphedema
- To compare the specific treatment effect observed using ketoprofen with other NSAIDs to further elucidate its mechanism of action

Background

Based upon previous findings of our lab demonstrating the ability of ketoprofen to ameliorate lymphatic vascular insufficiency in a murine tail lymphedema model mimicking human acquired lymphedema, we are currently conducting phase II studies on human subjects to study the drug in treating secondary lymphedema.

Simultaneously, our lab is exploring potential prophylactic properties of ketoprofen in similar mouse models. In addition, we are exploring whether the treatment effect previously noted is ketoprofen-specific or is noted in other therapeutic agents with overlapping characteristics.

Methods

Tails were circumferentially incised through the dermal layer and the identified lymphatic trunks were cauterized to induce lymphedema. Treatment via injection was initiated either on day 0 (prophylaxis) or day 3 and were administered daily thereafter at dosages of 5 mg/kg. Tail volume changes were noted on days 3, 9, and 25 for all cohorts. Control lymphedema mice received no treatment while secondary controls included sham surgeries (dermal incisions without lymphatic ablation).

Conclusions

Acquired lymphedema is a common and disabling state of vascular insufficiency lacking satisfactory pharmacotherapeutics. 400,000 Americans suffer from lymphedema of the upper extremity alone, primarily due to lymph node dissection and radiation therapy secondary to cancer treatment. The repurposing of a safe and inexpensive drug could revolutionize current treatment approaches.

Our pilot study suggests a greater role for ketoprofen therapy in lymphedema therapy. Our findings provide observational evidence that ketoprofen treatment contributes to lymphedema amelioration by reduction in tail volume and the normalization of typical histopathological changes in both preventive and post-operative treatment cohorts. Further studies of larger cohort sizes are merited to explore whether these trends continue and whether they reach a level of both statistical and clinical significance.

The lack of effect of ibuprofen, another nonselective COX1/COX2 inhibitor, also furthers our understanding of disease pathogenesis and lymphatic response. Additional experiments are necessary to determine the underlying mechanism of action of ketoprofen as well as to evaluate potential alternative routes of administration, which could be of great translational benefit.

References


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