

Can't Breathe? A retrospective review of icatibant for use in off-label non-hereditary angioedema treatment

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Background

Patients presenting to hospital with undefined angioedema are prescribed conventional therapy of steroids, adrenaline +/- an antihistamine if urticaria is present. This treatment is only effective if the angioedema is histamine mediated. Non-hereditary angioedema subgroups in addition to hereditary angioedema are thought to be bradykinin mediated and do not respond to conventional therapy.¹ The use of the bradykinin B2 receptor antagonist icatibant for non-hereditary angioedema remains an "off-label" indication.² Due to its infrequent use its efficacy remains poorly described in the literature.



Figure 1:³ Example disease state progression of non-hereditary angioedema

Aim

- Classify the characteristics of the patient demographic being administered off-label icatibant
- Identify intended indication for off-label icatibant administration
- Assess the efficacy and patient outcomes

Method

Identify patients who received icatibant between June 2017 - July 2022

Collect patient demographic details

Identify indication for administration

Review time to symptom improvement, concurrent medications and intubation status

Results

Indications for icatibant administration:

CI esterase inhibitor deficiency (n=1)

Alteplase (tpA) (n=1)

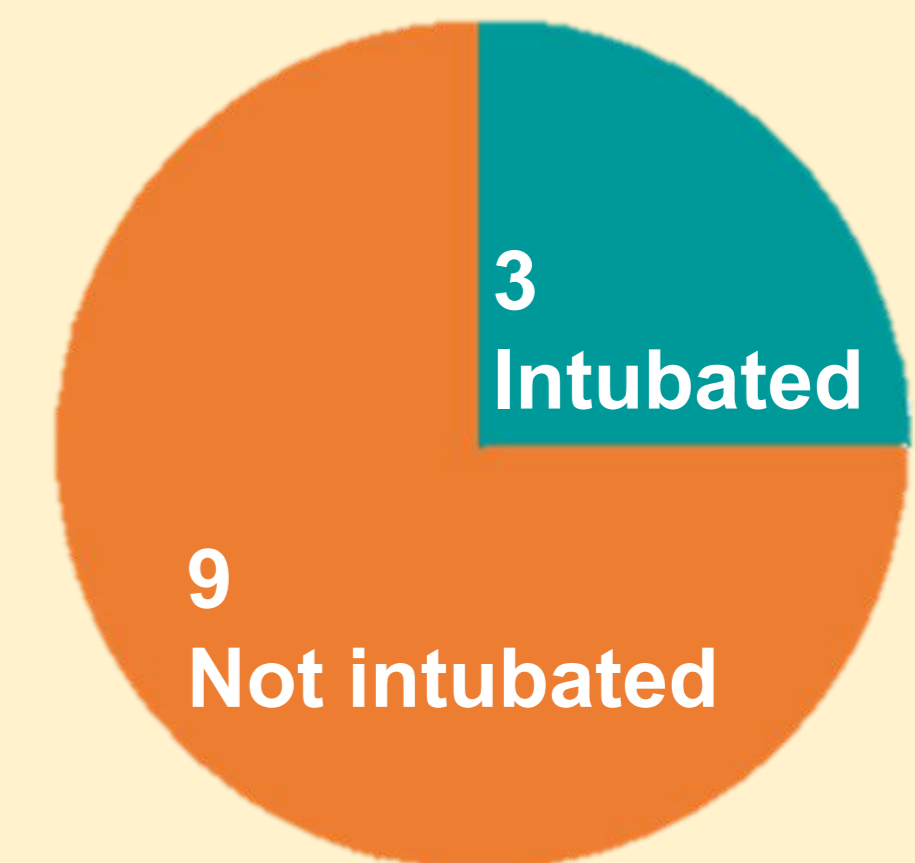
ACE-I induced (n=10)



~91% received conventional therapy prior to icatibant administration

N = 12, male:female, age 46-84

Intubation status following icatibant administration:



Pre-Treatment Received

	% of patients receiving conventional agents prior to icatibant administration
Adrenaline	83 (n=10)
Steroids	83 (n=10)
Antihistamine	42 (n=5)

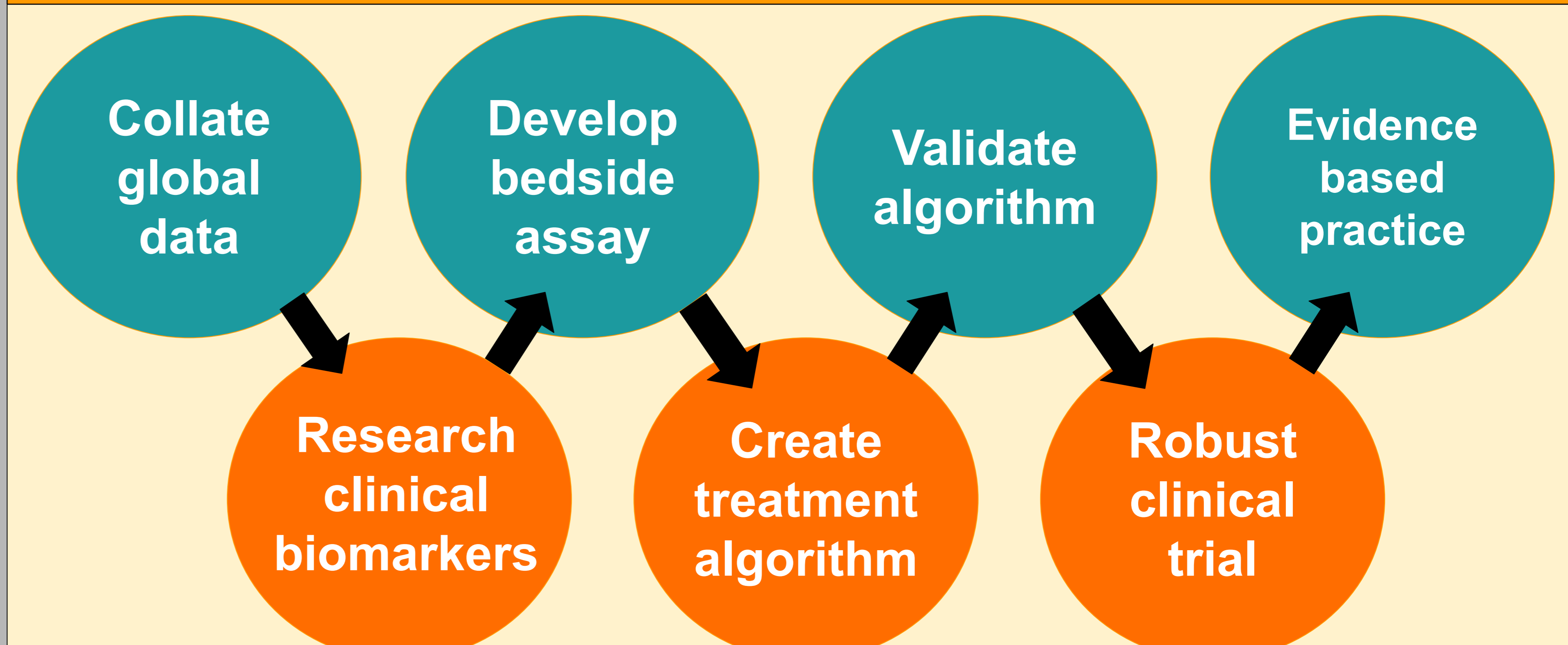
Time to treatment response



Discussion

- A significant challenge exists in recognising the chemical mediators of patients presenting with angioedema. It is likely histamine or bradykinin mediated, making response to treatment unpredictable.
- Limited evidence exists to guide practitioners on the most effective pharmacological or non-pharmacological intervention in this setting.
- The response to icatibant is unpredictable and 25% of patients still required intubation in our study.
- Current practice at Canberra Health Services is to prescribe all angioedema cases conventional therapy and escalate to icatibant only if there is treatment failure.
- Non-hereditary angioedema will likely recover without intervention, even in cases where patients required intubation. This demonstrates that the current use of icatibant is likely attributable to the lack of available alternatives.¹
- Until we can determine which patient cohorts will benefit from timely icatibant administration, it can not be seen as an evidence based and cost-effective intervention.
- Development of, and access to bedside biomarker assays is crucial to improve the treatment of patients suffering from non-hereditary angioedema.¹
- We are unable to predict which patients will fail to respond to both conventional treatments and icatibant leaving us questioning: What are we missing?

Future Direction



References

1. Le, T.T., Smith, W. and Hissaria, P. (2021) "Real-World off-label use of icatibant for acute management of non-hereditary angioedema." *Internal Medicine Journal*, 51(3), pp. 419-423. Available at: <https://doi.org/10.1111/imj.15241>.
2. Product information. Available from www.tga.gov.au
3. Ebo, D.G. *Disfiguring angioedema: Nejm, New England Journal of Medicine*. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMicm1200960>



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