

# Blood Pressure and Pulse Rate Increases Without Concomitant Epinephrine Increases During Acute Allergic Reactions

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## RATIONALE

- The release of allergic mediators (e.g. histamine) is a key component of the “allergic cascade”.
- While these mediators are typically thought to decrease blood pressure (BP), recent studies have suggested that BP and heart rate (HR) can also increase at the time of an allergic reaction (Ramirez 2023, Carr 2024, Ruiz-Garcia 2021). This paradoxical finding may be the result of the compensatory and contradictory actions of allergic mediators.
- ARS Pharmaceuticals has conducted a series of studies evaluating the pharmacokinetics and pharmacodynamics of *neffy* (epinephrine nasal spray) as well as a patient study investigating the impact of induced allergic rhinitis and anaphylaxis symptoms.
- This analysis focuses on the changes in BP, HR, and endogenous epinephrine levels following the induction of allergic rhinitis and anaphylactic symptoms in two clinical trials. An understanding of the impact these allergic states have on endogenous epinephrine levels and pharmacodynamic responses may help guide the treatment of severe allergic reactions.

## METHODS

### STUDY DESIGN AND POPULATION

#### Study 1

- A nasal allergen challenge (NAC) was conducted in 42 subjects with a history of seasonal allergic rhinitis. Blood pressure, HR, and endogenous epinephrine levels were measured before NAC and at the time of positive reaction (defined as TNSS of 5 out of 12 and a congestion score of 2 out of 3 at 15 minutes). There was a minimum of 3 weeks from the screening NAC and the investigative NAC.

#### Study 2

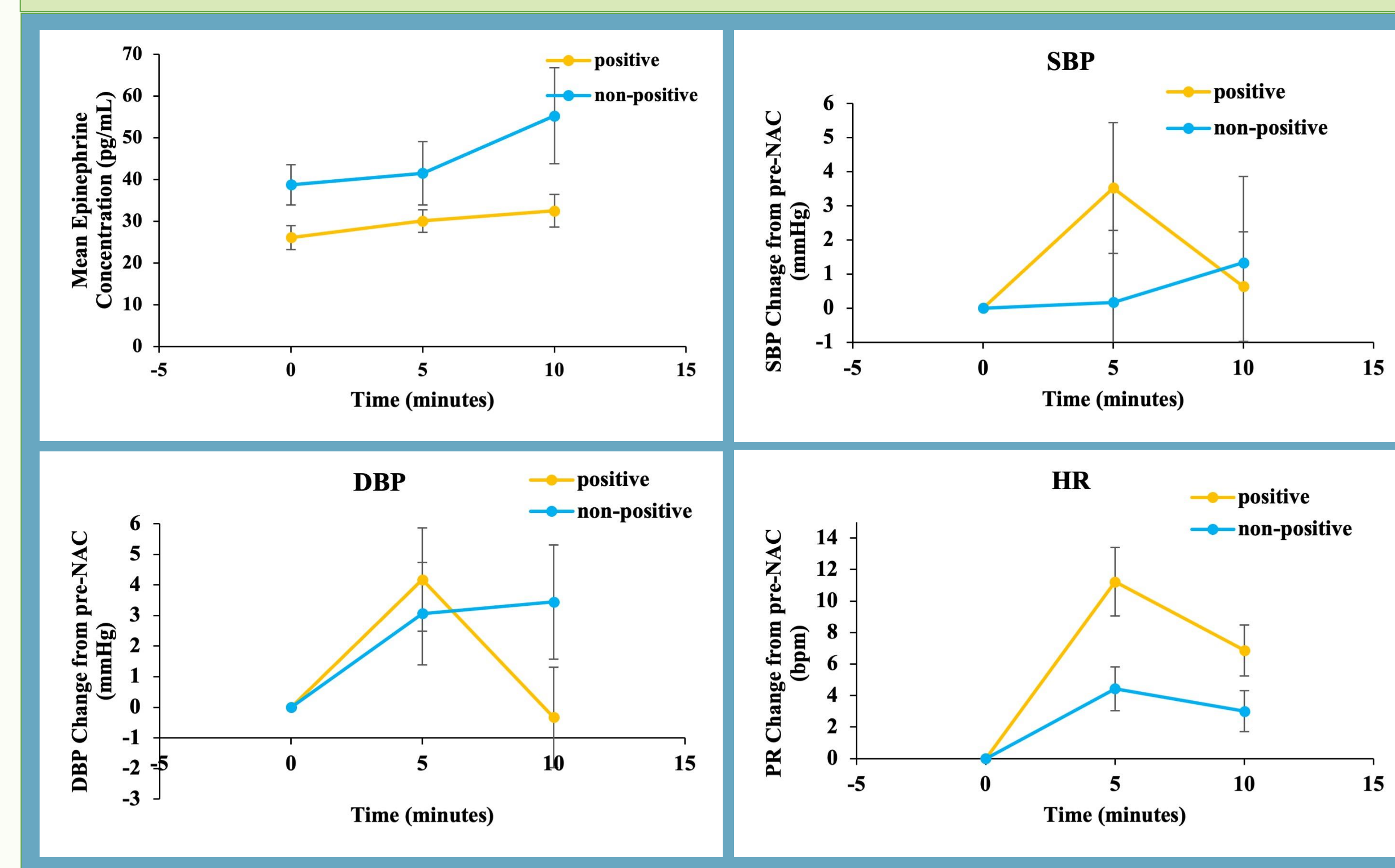
- An Oral Food Challenge (OFC) to induce anaphylaxis symptoms was conducted in 15 pediatric food allergy patients. Blood pressure and HR were measured before OFC and at the time of positive reaction (defined as Grade 2 or higher anaphylaxis symptoms [Yanagida 2017] occurring in either gastrointestinal, respiratory, or cardiovascular systems).

## RESULTS

### Study 1

- Forty-two Type I allergy patients underwent this NAC. Twenty-four patients (57.1%) exhibited positive reactions, and 18 patients exhibited non-positive reactions (42.9%).
- Endogenous epinephrine levels were higher in patients with non-positive reactions relative to patients with positive reactions (Figure 1); however, the difference was not statistically significant.
- In the positive reaction group systolic blood pressure (SBP, diastolic blood pressure (DBP) and HR increased five minutes following NAC and decreased by 10 minutes. Increases were also noted in the non-positive group; however, they were less pronounced (Figure 1). The only statistical difference between the groups was a greater increase in HR at five minutes post-NAC in the positive reaction group.

Figure 1: Endogenous Epinephrine Concentrations and SBP, DBP, and HR Changes Following NAC (Study 1)

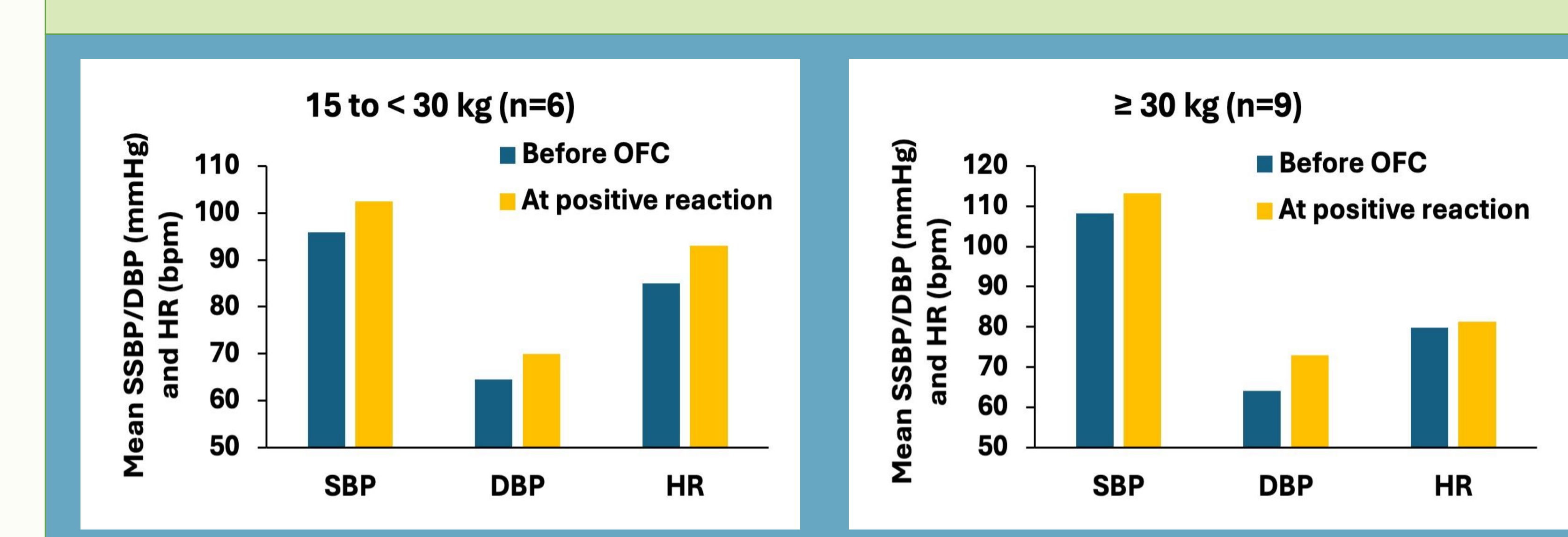


Note: Data at time 0 is an average of -30 and -15 minutes (pre-NAC); NAC conducted at 0 min

### Study 2

- Eighteen moderate anaphylactic symptoms were observed in across 15 pediatric food allergy patients (n=6 for patients 15 to < 30 kg and n=9 for patients ≥ 30 kg).
- Increases in SBP, DBP, and HR were observed in both groups (statistical analysis not conducted due to small sample size) (Figure 2).

Figure 2: SBP, DBP, And HR Before OFC and At Time of Positive Reaction (Study 2)



## CONCLUSIONS

- In both studies, increases in BP and HR were observed after positive allergic reactions at the initial time point.
- In subjects without a positive reaction (Study 1), they had higher baseline and non-significant increase in endogenous epinephrine at 5 minutes, suggesting that the increased DBP and HR was not due to epinephrine at 5 minutes.
- The rapid increase in DBP, which is not typically observed in response to epinephrine due to the early activation of the high-affinity  $\beta_2$  receptors, is also suggestive of a non-epinephrine mediated mechanism for the increased BP.

## REFERENCES

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