

Pharmacodynamic Profile of Epinephrine Nasal Spray Versus Intramuscular Epinephrine Autoinjector in Healthy Adults

INTRODUCTION

- Anaphylaxis is a serious allergic reaction that can occur in response to food allergens, insect venom, medications, and other environmental exposures
- Rapid treatment for anaphylaxis is required to mitigate morbidity and possibly death¹
- Standard of care for anaphylaxis treatment is intramuscular (IM) epinephrine²
 - Epinephrine is a sympathomimetic α -adrenergic and β -adrenergic agonist; pharmacodynamic (PD) effects of epinephrine include increased heart rate and changes in blood pressure³
- Epinephrine is typically administered via an autoinjector, but patients may be reluctant to use their autoinjector because of fear of needles or injection-related injuries⁴
- An epinephrine nasal spray (ENS; NDS1C, Bryn Pharma, Lebanon, NJ) is under development as an alternative form of administration

OBJECTIVE

- To compare the PD profile of 13.2 mg ENS with that of the standard of care 0.3 mg IM epinephrine autoinjector using pooled data from 4 studies

METHODS

Study design

- Data from 4 open-label phase 1 crossover studies were pooled for PK analysis⁵⁻⁸
- Participants in all 4 studies were healthy adults
- Treatment arms:
 - Single 13.2 mg ENS dose delivered by 2 consecutive sprays of 6.6 mg each in **opposite nostrils** (n=198)
 - Single 13.2 mg ENS dose delivered by 2 consecutive sprays of 6.6 mg each in the **same nostril** (n=74)
 - Single 0.3 mg epinephrine dose delivered by IM autoinjector (n=196)
- The consecutive intranasal sprays were administered within no more than 10 seconds of each other
- In all studies, each subject served as their own control per the crossover designs, with a washout period of at least 1 day between ENS and IM autoinjector treatment periods and of at least 14 days between the 2 ENS treatment periods
- All treatments were administered by trained clinical personnel

PD analysis

- Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were measured at −30, −20, −10 minutes predose and 1, 3, 5, 7, 10, 15, 20, 25, 30, 45, 60, 90, 120, 180, and 360 minutes postdose
- An average of 3 predose measurements for BP and HR were used for baseline adjustments for each subject
- Summary statistics for PK parameters were calculated by treatment and time point



Conclusion

- The 13.2 mg ENS dose delivered in opposite nostrils or the same nostril had a pharmacodynamic effect that was similar to the 0.3 mg IM autoinjector

RESULTS

- In the pooled population, 53% were male, and the mean age was 39 years
- The pharmacological effect on SBP and DBP was similar in pattern and magnitude among all 3 treatment groups (**Figure 1**)
- The effect on HR was similar in pattern and magnitude among all 3 treatment groups over all timepoints measured (**Figure 2**)
- Postdose values for SBP, DBP, and HR were not significantly different between 13.2 mg ENS and 0.3 mg IM autoinjector (**Figure 3**)
- A plateau in BP and HR was reached in all treatment groups (**Figures 1 and 2**)
- There was no correlation between the pharmacodynamic effect and plasma epinephrine concentration
 - $R^2 \leq 0.032$ for change from baseline in SBP, DBP, and HR vs plasma epinephrine concentrations over time

Figure 1. Mean change from baseline SBP and DBP – time profiles

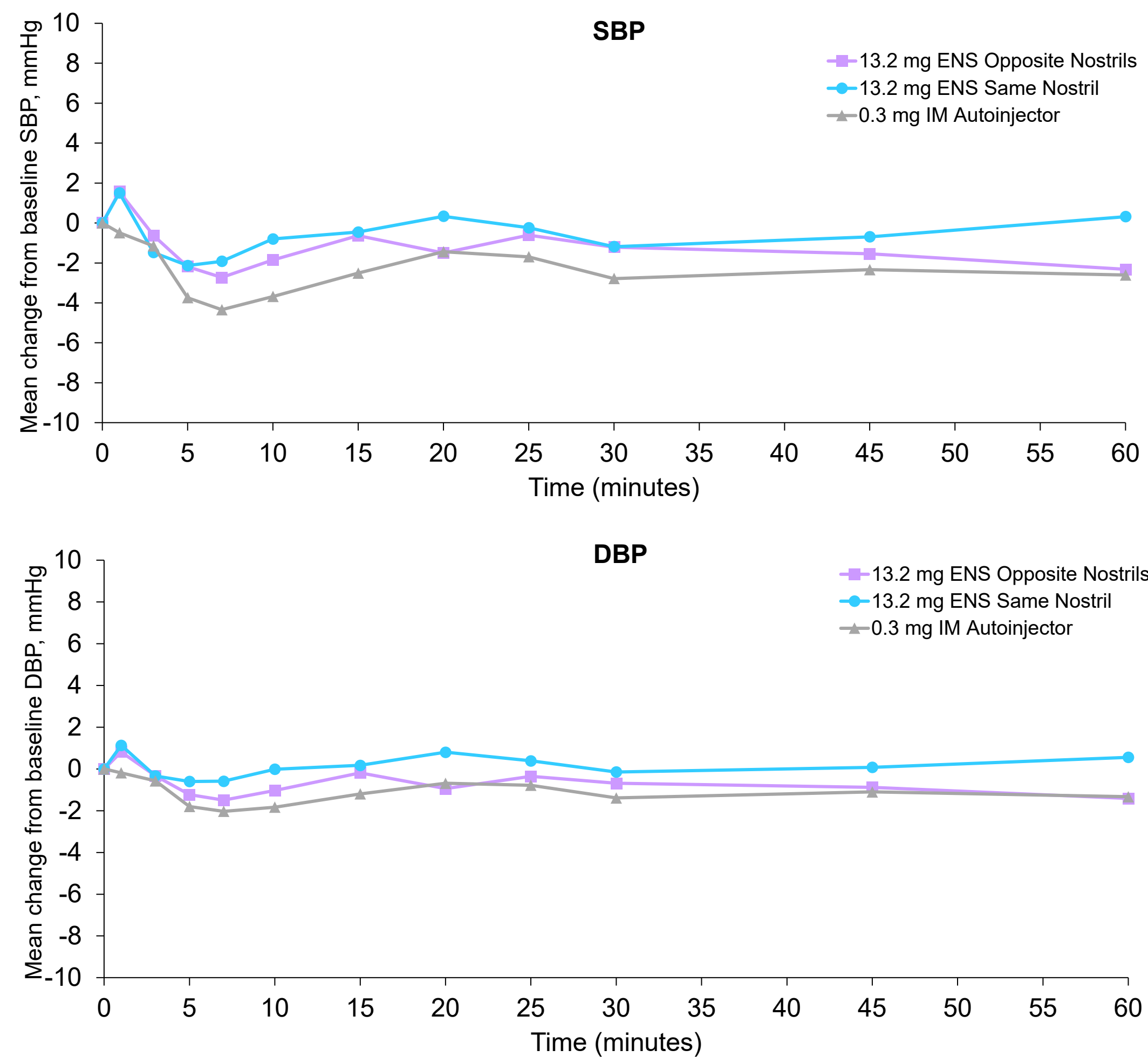


Figure 2. Mean change from baseline HR – time profiles

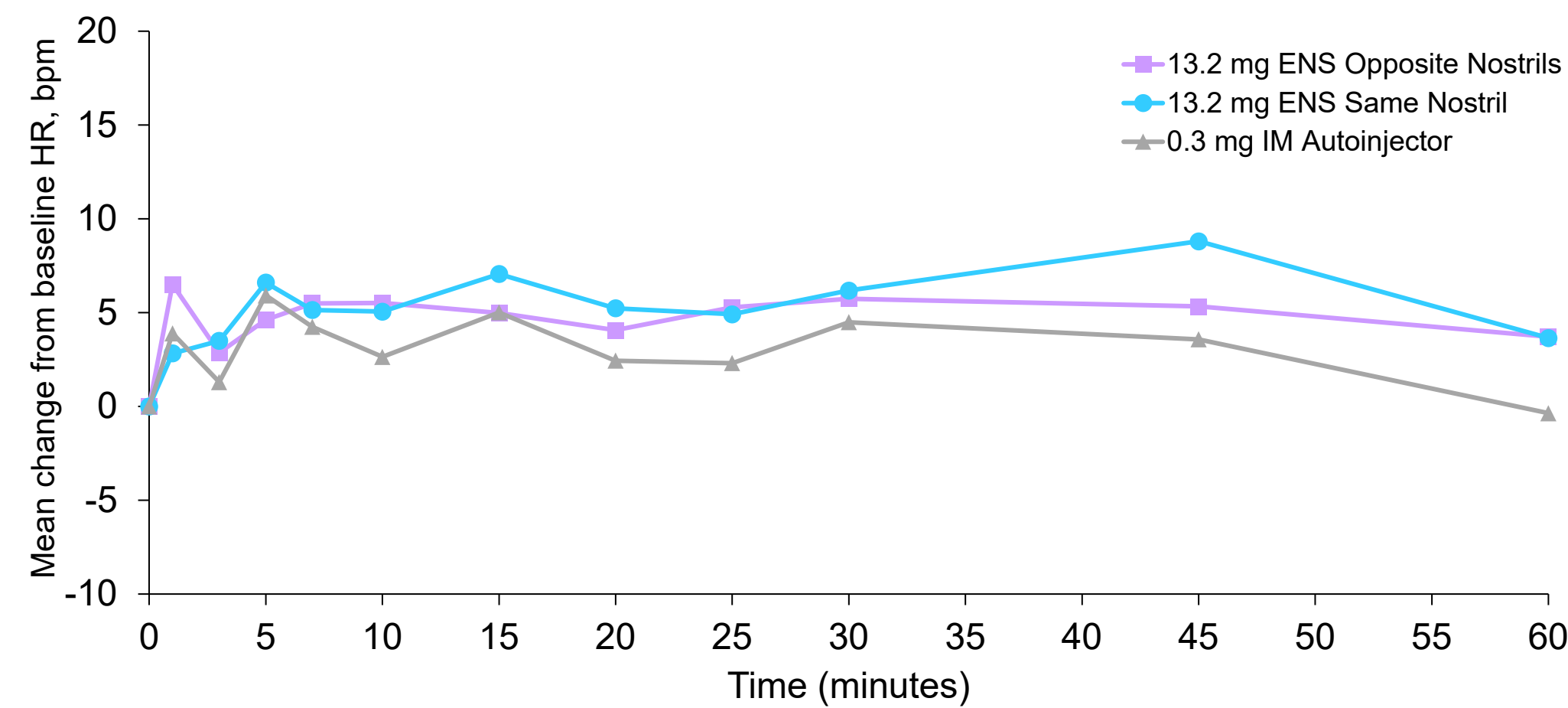
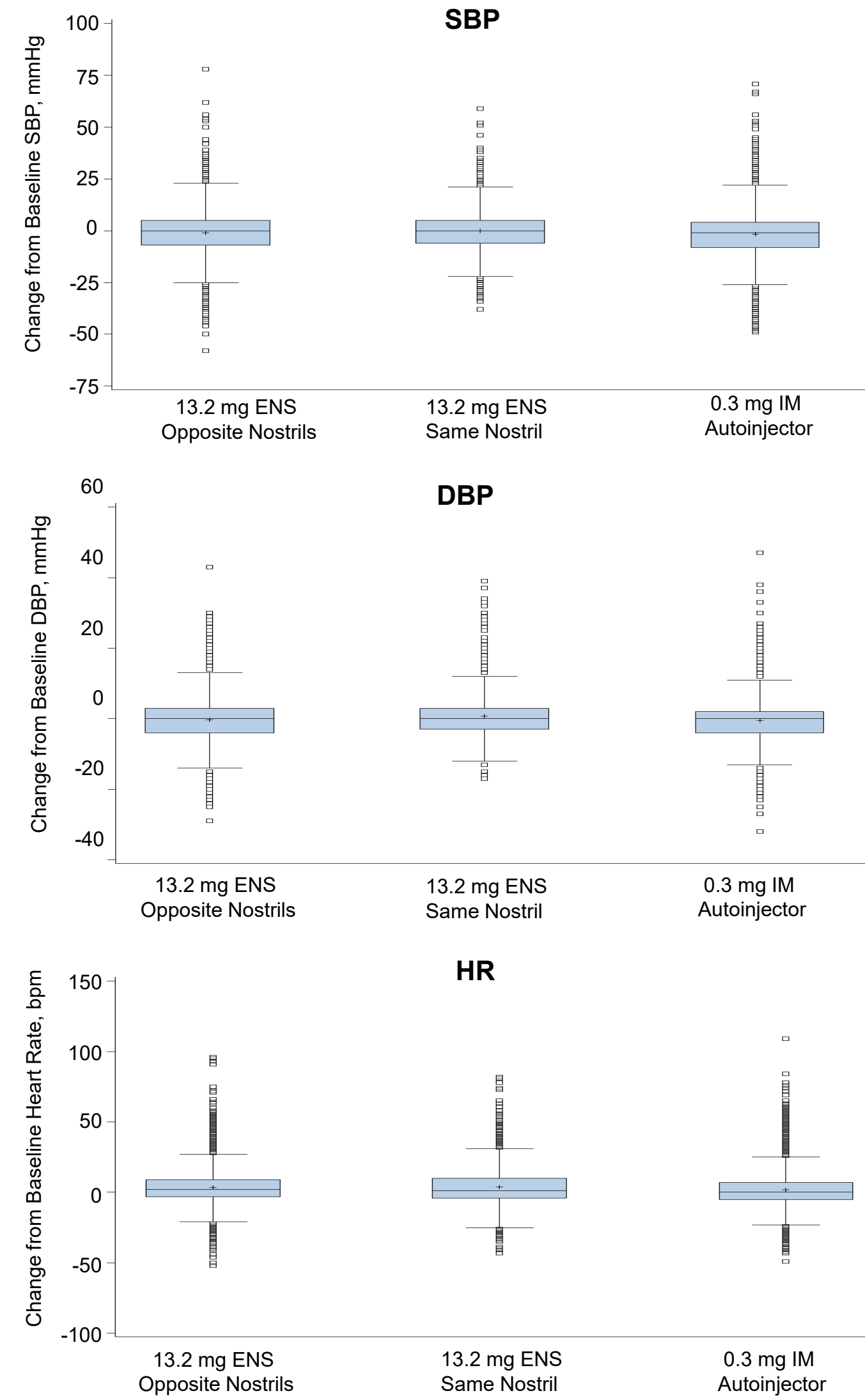


Figure 3. Overall mean and median values for all timepoints for change from baseline in SBP, DBP, and HR. Square symbols indicate any individual value outside the whisker values at any timepoint.



The solid line within the box represents the median, and the "+" represents the mean. Upper and lower whiskers represent the largest and smallest observed values within 1.5 x the interquartile range from the upper (Q3) and lower (Q1) quartiles.

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