Original Article

The effect of antipyretic medication on the relationship between heart rate, respiratory rate and temperature in acutely admitted medical patients: A retrospective study

S Sværke, AV Krusenstjerna-Hafstrøm & M Brabrand

Abstract

Research has shown an association between body temperature, heart rate and respiratory rate. We speculated that antipyretics could influence this. We performed this study with the aim of clarifying the association.

We included 1,612 acutely admitted medically ill patients and registered their use of antipyretics. We performed crude and adjusted linear regression analyses. In adjusted analysis, we found that heart rate increased with 7.3 (95% CI: 4.5, 10.1) beats/min/°C in patients who were not on antipyretics and 10.0 (95% CI: 6.2, 13.9) beats/min/°C in patients who were.

Respiratory rate increased 0.4 (95% CI: -0.2, 0.9) and 1.5 (95% CI: 0.6, 2.3), respectively. Our data shows that use of antipyretics affect the association between temperature, heart rate and respiratory rate positively.

Keywords

Antipyretics, heart rate, respiratory rate, temperature, emergency medicine

Key points

1. Antipyretic medications (e.g. NSAID, paracetamol and steroids) are commonly used drugs by many patients to decrese body temperature when febrile.
2. No prior studies have investigated the effect of antipyretic medication on heart rate and respiratory rate in febrile acutely admitted adult patients.
3. We found that use of antipyretics led to a greater increase in heart rate and respiratory rate per degree °C raise in body temperature, when adjusted for covariantes.

Sophie Sværke
MD
Department of Emergency Medicine, Holbæk Sygehus, Smedelundsgade 60, DK- 4300 Holbæk, Denmark
Department of Emergency Medicine, Odense University Hospital, J.B Winsløwsvej 4, DK-5000 Odense, Denmark

Anders Krusenstjerna-Hafstrøm
MD
Department of Emergency Medicine, Holbæk Sygehus, Smedelundsgade 60, DK- 4300 Holbæk, Denmark

Mikkel Brabrand
MD, PhD
Department of Clinical Research, University of Southern Denmark, Campusvej 55, DK - 5230 Odense M
Department of Emergency Medicine, Odense University Hospital, J.B Winsløwsvej 4, DK-5000 Odense, Denmark

Correspondence
Mikkel Brabrand
MD, PhD
Department of Emergency Medicine, Odense University Hospital, J.B Winsløwsvej 4, DK-5000 Odense, Denmark
Email: Mikkel.Brabrand@rsyd.dk

Introduction

Normal body temperature is considered to be between 36.1 to 38.0°C,[1] with an average of 37°C.[2] When the body temperature rises 1°C, the heart rate usually increases 4.4 to 18.0 beats per minute and the respiratory rate increases between 2 and 4 breaths per minute in adults.[1]

This relationship between heart rate or respiratory rate and changes in body temperature has recently been studied in acutely admitted medical patients to provide an overview of the correlation in ill elderly patients with multi co-morbid conditions and several medications.[3] The authors observed the actual response to be more modest than described in previous studies conducted in young healthy adults.[3] Antipyretic medications (e.g. Non-Steroid Anti-Inflammatory Drug (NSAID), paracetamol and steroids) are commonly used drugs in many patients and are known to influence the natural changes in body temperature in acutely ill patients with lowering the body temperature in febrile patients.[4]

No recently published studies has investigated the changes in heart rate and respiratory rate associated with body temperature changes in acutely admitted adult patients with an intake of antipyretic medication within 6 hours prior to arrival, which we aimed to do in this study. We hypothesized that patients who had a history with consumption of antipyretic medication within 6 hours of arrival to the emergency department, would experience a diminished increase of heart rate along with the rise of body temperature in febrile patients, compared to patients with no history of antipyretic medication.

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Methods

Study design

This study was a secondary analysis on data obtained from a previously prospective cohort study performed on acutely admitted medical patients who had routine recording of vital signs at arrival at the admission unit. The data was previously utilized in a study by Lyngholm et al.[5] to assess the value of normal D-dimer level (<0.5mg/l) in identifying emergency department patients at low risk of 30-day-all-cause mortality. The original study was conducted between April 24, 2017, to August 19, 2017, in the Hospital of Southwest Jutland.

Population

The original cohort included 1,700 patients of which we excluded 88 patients as one patient was included twice, two patients withdrew consent, and 85 patients had missing data on vital signs. This left us with 1,612 patients with complete vital signs for the present analysis.

Data collection

Vital signs

Vital signs (body temperature, heart rate, respiratory rate and oxygen level) were collected upon arrival to the emergency department and entered to hospital database by the regular staff.

Antipyretic medication

Patients were asked upon arrival about their intake of antipyretic medication (NSAID, paracetamol and steroids) up to 6 hours before admission to the emergency department.

Outcome measures

The primary outcome was the change in association between heart rate (in beats per minute) for every 1°C rise in body temperature. The secondary outcome was change in the respiratory rate (in breaths per minute) for every 1°C rise in body temperature.

Statistical analysis plan

Statistical analyses were performed using R version 4.4.0. We used descriptive statistics to describe baseline characteristics of the study population. Continuous variables were presented as median and interquartile range and categorical variables as numbers and percentages.

Simple linear regression analysis was used to calculate the increase in heart rate and respiratory rate per 1°C in patients with low, normal or high body temperatures and based on patients' consumption of antipyretic medication prior to arrival.

We used multivariable linear regression to adjust the increases for the covariates of age, sex, oxygen saturation and systolic blood pressure, and compared patients who had a history with consumption of antipyretics prior to arrival and those who did not.

Ethical Considerations

The original study was approved by the Danish Regional Committee on Health Research Ethics (Identifier: S-20170005) and the Danish Data Protection Agency (Identifier: Region Syddanmark 2452). The original study protocol was registered at ClinicalTrials.gov with identifier: NCT0310887). The results of the study are reported in accordance with STROBES guidelines.[6]

Results

Demographic

Of our 1,612 patients, 489 patients had a history with utilization of antipyretic medication within 6 hours prior to arrival. The average temperature was 37.0°C (35.2°C to 40.8°C). The patients' characteristics are summarized in Table 1.

Primary outcome

Overall the heart rate increased with 7.8 (95% CI: 6.4, 9.1) beats per minute for every 1°C rise in body temperature (Figure 1 and Table 2) and adjusted for covariates with 8.1 (95% CI: 5.8, 10.4) beats per minute. The increase in crude heart rate/1°C rise in body temperature was highest in patients who received antipyretic medication (Figure 2). Adjusting for covariates did not change this (Table 2).

Secondary outcomes

The crude respiratory rate (breaths per minute) increased with 1.1 (95% CI: 0.8, 1.4) when the body temperature rised 1°C (Figure 1 and Table 2). The increase in respiratory rate fell to 0.7 breaths per minute (95% CI: 0.2, 1.1) when adjusting for covariates. The crude increase in respiratory rate was highest the subgroup with no intake of antipyretic medication (Figure 2). After adjustment, the increase in respiratory rate for every 1°C rise in body temperature was greatest in the group of patients who had a history of using antipyretic medication (Table 2).

Discussion

In this study of the association between body temperature and heart rate and respiratory rate, we found after adjustments for age, sex, oxygen saturation and systolic blood pressure that patients with intake of antipyretic medications had the greatest increase in heart rate and respiratory rate per 1°C rise in body temperature.

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Table 1. Demographic data of study population.
Data presented as median (Interquartile range) or number (%)

Characteristics	No antipyretics (n=1,123)	Antipyretics* (n=489)	Total (n=1,612)
Sex			
Female	590 (52.5%)	233 (47.6%)	823 (51.1%)
Male	533 (47.5%)	256 (52.4%)	789 (48.9%)
Age (years)	62.6 (18 to 97)	67 (18 to 97)	66 (18 to 97)
Medication (antipyretics)			
Steroid		64 (13.1%)	64 (4%)
Paracetamol		300 (61.3%)	300 (18.6%)
NSAID		16 (3.3%)	16 (1%)
Combinations		109 (22.3%)	109 (6.8%)
None of the above	1,123 (100%)		1,123 (69.7%)
Heart rate (bmp)	79 (28 to 190)	80 (42 to 170)	80 (28 to 190)
Systolic blood pressure (mmHg)	138 (76 to 249)	135 (81 to 242)	137 (76 to 249)
Diastolic blood pressure (mmHg)	80 (32 to 138)	79 (36 to 130)	80 (31 to 138)
Respiratory rate	16 (8 to 48)	17 (10 to 40)	16 (8 to 48)
Temperature (°C)	36.9 (32.6 to 40.7)	37 (35.2 to 40.8)	36.90 (32.6 to 40.8)
Hypothermia	41 (3.7%)	20 (7.4%)	61 (3.8%)
Normothermia	1010 (89.9%)	433 (88.5%)	1443 (89.5%)
Hyperthermia	72 (6.3%)	36 (4.1%)	108 (6.7%)
Oxygen Saturation (%)	98 (70 to 100)	97 (60 to 100)	98 (60 to 100)
Charlson score	1 (0 to 14)	1 (0 to 12)	2 (0 to 14)
Death within 30 days (%)	25 (2.2%)	13 (2.7%)	38 (2.4%)

*NSAID, steroid, paracetamol and combinations of those

Prior studies have shown that the heart rate rises between 4.4 to 18.0 beats per minute when the body temperature rises 1°C.[1] Likewise, respiratory rate rises 2 to 4 breath per minute per 1°C rise.[1] We showed an increase in heart rate of 7.8 (95% CI: 6.4, 9.1) beats per minute and an increase of 1.1 (95% CI: 0.8, 1.4) breaths per minute per 1°C increase in body temperature within the entire cohort. This aligns with the general findings in the literature.

Antipyretic medication is known to influence the bodies normal temperature response in febrile patients.[4] We had hypothesized that patients with an intake on antipyretic medication, would experience a diminished increase of heart rate and respiratory rate with the rise of body temperature but found the opposite. Adjusted data showed the greatest increase in heart and respiratory rate in patients with an intake of antipyretic medication. This suggest antipyretic medication does not disrupt the fundamental relationship between body temperature, heart rate and respiratory rates and the relationship remains consistent. This is clinical relevant, as it indicates elevated heart rate in febrile patients likely reflects the body's natural thermoregulatory response.

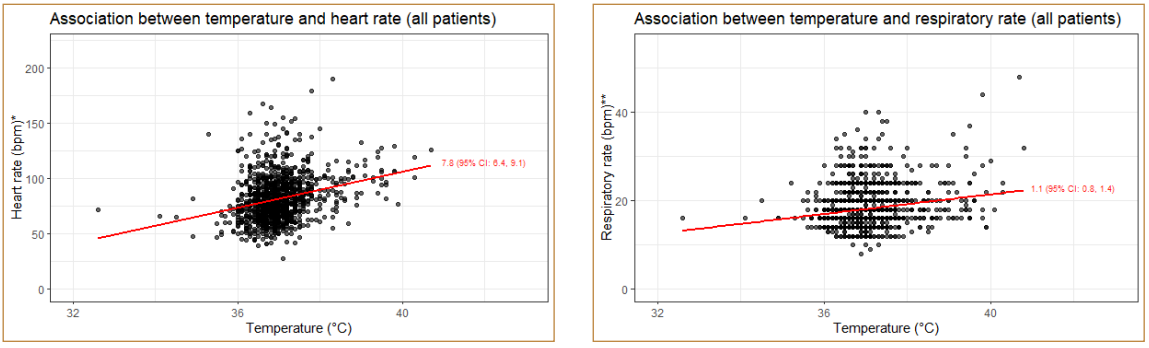


Figure 1. The association between heart rate, respiratory rate and temperature in all patients before stratification and adjustment for covariantes. *Bmp = beats per minute, **bmp= breaths per minute.

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Table 2. Coefficients of interest from regression models, stratified by research question and antipyretics

Dependent variable	Independent variable	n	Adjusted for	Coefficient (95% CI)
All patients				
Heart rate	Temperature	1,612	Age, Sex, Oxygen Saturation, Systolic blood pressure	8.1 (5.8, 10.4)
Respiratory rate	Temperature	1,612	Age, Sex, Oxygen Saturation, Systolic blood pressure	0.7 (0.2, 1.1)
No antipyretics				
Heart rate	Temperature	1,123	Age, Sex, Oxygen Saturation, Systolic blood pressure	7.3 (4.5, 10.1)
Respiratory rate	Temperature	1,123	Age, Sex, Oxygen Saturation, Systolic blood pressure	0.4 (-0.2, 0.9)
Antipyretics				
Heart rate	Temperature	489	Age, Sex, Oxygen Saturation, Systolic blood pressure	10.0 (6.2, 13.9)
Respiratory rate	Temperature	489	Age, Sex, Oxygen Saturation, Systolic blood pressure	1.5 (0.6, 2.3)

Compared to the study by Jensen et al.[3] which also examined a cohort of acutely ill adult patients, we found similar heart rate and respiratory rate associated with body temperature, when comparing the entire study group without adjusting for covariates. Adjustment for these factors revealed a heightened heart rate response to temperature in our study. When comparing our findings to the larger Swedish cohort study[7] of 9,046 acutely admitted ill patients we found a similar increase in heart rate. They reported an increase in heart rate of 8.35 beats per minute/°C.

The study's strength lies in its extensive inclusion of unselected acutely ill patients proving data very representative to daily clinical life. This ensures a robust dataset with through systematic data collection that minimizes measurement bias. The study is also the first study to investigate the relationship of changes in temperature, heart rate and respiratory rate in acutely

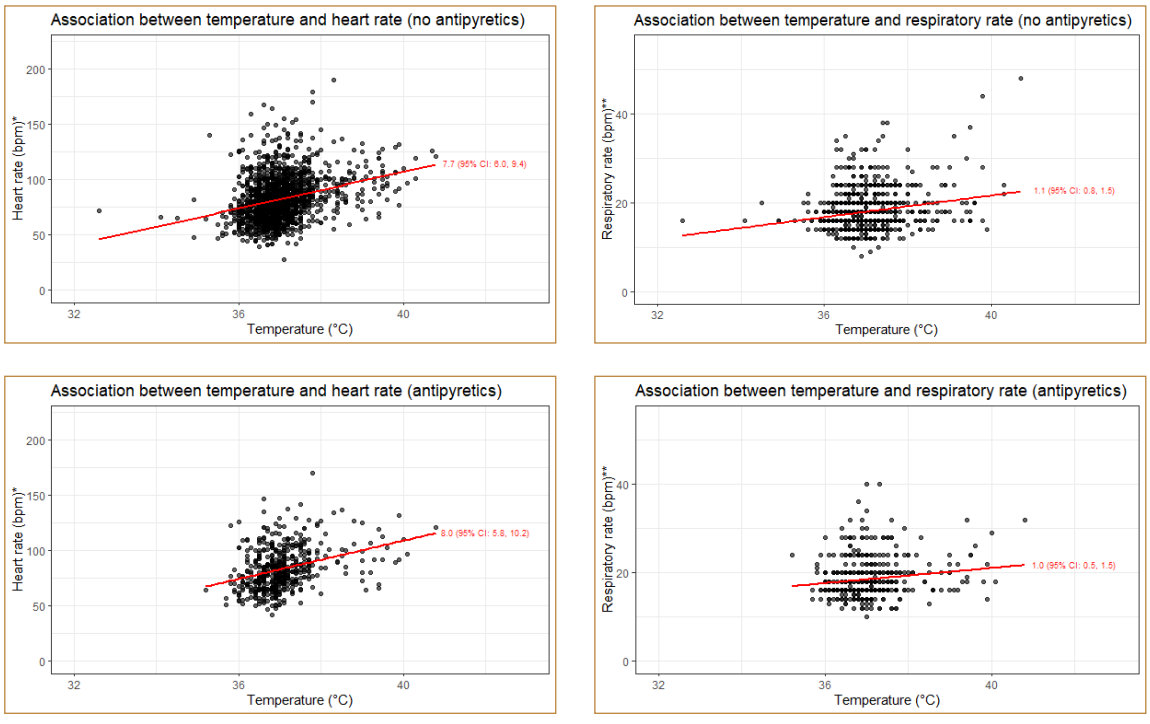


Figure 2. The association between heart rate, respiratory rate and temperature, stratified by intake of antipyretics before adjusting for covariantes.
*Bmp = beats per minute, **bmp= breaths per minute.

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admitted ill patients with known history of antipyretic medication prior to arrival.

The study has some limitations, which should be taken into account. Due to the design of the study the number of patients in each subgroup are quite diffent with a considerably larger group of patients with no intake of antipyretics. Another limitation was the lack of knowledge on patients' additional medical history, since they may have a daily intake of other medication with potential influence on the heartrate such as betablockers or calcium channel blockers. Finally, we only have a single set of vital signs.

Conclusion

The existing medical literature on changes in heart rate and respiratory rates associated with body temperature lacks detailed information regarding the use of antipyretic medications before vital sign assessments. We observed the response in heart rate and respiratory rate per 1℃ rise in body temperature to be highest in patients with a history of utilization of antipyretic medication prior to arrival. This indicates that an elevated heart rate in patients with fever likely reflects the body's natural thermoregulatory response, and antipyretics do not negatively influence this relationship.

Conflict of interest

none

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