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Firefighting Induces Acute Inflammatory Responses that are not Relieved by Aspirin in Older Firefighters

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ABSTRACT

Objective: Sudden cardiac events account for 40% to 50% of firefighter line-of-duty deaths. Inflammatory proteins are strong biomarkers of cardiovascular inflammation. The present study investigated the effects of aspirin supplementation on inflammatory biomarkers following firefighting. **Methods**: Using a randomized, placebo-controlled, double-blind crossover design, 24 male firefighters (48.2 ± 5.9 years) were allocated into four conditions: acute (81 mg; single-dose) aspirin and placebo supplementation, and chronic (81 mg; 14 days) aspirin and placebo supplementation. Inflammatory proteins [interleukin (IL)-6, C-reactive protein (CRP), intracellular adhesion molecule (ICAM)-1, P-selectin, matrix metalloproteinase-9 (MMP-9)] and antioxidant potential [total antioxidant capacity (TAC)] were measured pre- and post-structural firefighting drills. **Results**: Firefighting activities significantly increased IL-6, MMP-9, and P-Selectin; however, no changes in TAC and ICAM-1 were detected. Neither acute nor chronic aspirin supplementation attenuated this inflammatory response. **Conclusion**: Firefighting significantly increases inflammatory biomarkers and neither acute nor chronic low-dose aspirin mitigates this response.

Among firefighters, 40% to 50% of line-of-duty deaths are attributed to sudden cardiac events (SCEs).[1] A disproportionate number of SCE deaths occur during or shortly following fire suppression activities, presumably triggered by a combined physiological, psychological, and environmental burden (eg, strenuous physical work, hyperthermia, stress, and particulate matter and toxic smoke exposure).[2,3] Impaired cardiovascular (CV), hemodynamic, thermoregulatory, and coagulatory function following arduous firefighting activities have been documented.[2,4–7] Importantly, increasing age, underlying diseases, and traditional CV risk factors elevate risk of firefighting-induced SCE.[2,3]

Although the effects of firefighting on CV and hematological markers have been reported,[2,4–6,8] there is a paucity of data on inflammatory responses to firefighting. The individual stressors common to firefighting, namely, particulate matter, heat stress, and strenuous physical activity, are also responsible for inducing inflammatory responses. For example, fly ash exposure is known to induce interleukin-6 (IL-6) and interluekin-8 (IL-8) production,[9] and heat stress, in combination with exercise, augments cytokine [IL-6 and tumor necrosis factor-alpha (TNF-α)] producing cell concentrations.[10] Proinflammatory proteins [eg, IL-6, IL-8, TNF-α, and C-reactive protein (CRP)] and intracellular adhesion molecules (ICAMs)

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have been considered critical in the pathogenesis of atherosclerosis and strong biomarkers of acute SCE.[8]

Research has also documented increased oxidative stress when exercise is performed in the heat.[11,12] A recent study investigated antioxidant ingestion on antioxidant capacity and oxidative stress in highly trained, heat acclimated individuals following a training exercise that lasted 17 to 20 minutes. In one trial, the individuals performed the drill with no heat, and in another trial, they performed the same exercise in the heat. The authors reported that, in this population, the addition of heat did not increase oxidative stress and that antioxidant ingestion did not impact markers of antioxidant status or oxidative stress.[12] The authors suggested a need for additional research on the effect of live fire training on oxidative stress.

Low-dose (<81 mg) acetylsalicylic acid (aspirin) is a common over-the-counter anti-inflammatory drug prescribed to reduce myocardial infarction risk.[13,14] By inhibiting cyclooxygenase-1 (COX-1) dependent platelet activation,[15] aspirin has been shown to attenuate thrombosis, reducing the risk of serious CV events.[16] Aspirin also preserves bioavailable nitric oxide (NO), a potent endogenous anticoagulant and vasodilator. Importantly, aspirin effectively diminishes serum levels of inflammatory markers via inhibition of the COX-2 isoform.[17] Despite its robust effects, aspirin use as both primary and secondary preventative interventions in adults over 40 is low.[18] Thus, aspirin supplementation might be a potential option to mitigate firefighting-induced vascular inflammation in older firefighters.

The purpose of this study was twofold: (1) to determine the effects of acute live firefighting drills on the inflammatory response of older-aged firefighters (40 to 60 years old) and (2) to determine if low-dose (81 mg) acute (60 minutes before firefighting) and chronic (14 consecutive days before firefighting) aspirin supplementation could alter this response. It was hypothesized that firefighting would induce an increase in inflammation and oxidative stress, which acute aspirin supplementation would attenuate, and that this effect would be greater with chronic aspirin supplementation.

METHODS

General Procedures and Subject Characteristics

Twenty-four male firefighters between the ages of 40 and 60 years (average: 48.2 ± 5.9 years old) were recruited by word of mouth through professional networks from fire departments across the state of Illinois. Exclusion criteria included diagnosis of hypertension or known coronary artery disease (CAD); contraindications to aspirin therapy; current or recent use of nonsteroidal anti-inflammatory drugs (NSAIDS), clopidogrel, or warfarin; or physician prescribed aspirin supplementation. Before participation, firefighters received a medical evaluation based on the National Fire Protection Agency 1582 Standard on Comprehensive Occupational Medical Program for Fire Departments (NFPA 1582). The NFPA 1582 based medical evaluation consisted of a CV risk factor evaluation (including lipid profile) and an exercise stress test to predict maximal oxygen consumption (estimated via a treadmill protocol to 85% of age-predicted maximal heart rate). Approval for this study was granted by the Human Institutional Review Board of the University of Illinois and was in agreement with the Declaration of Helsinki. All participants signed an informed consent before participation indicating that they understood the risks associated with the study and that their participation was voluntary.

To characterize participants, height and weight were measured using standard techniques. Height was measured (to the nearest 0.01 m) using a stadiometer and body mass (to the nearest 0.5 kg) using a digital platform (Detecto Model 6129 with Model 750 Indicator; Cardinal Scale Mfg Co, Webb City, MO). Body mass index (BMI) was calculated as body mass (expressed in kg) divided by the height squared (expressed in m; m^2). During all testing sessions, core body temperature was measured using a silicone-coated gastrointestinal capsule (Mini Mitter, VitalSense; Philips Respironics, Bend, OR) ingested 6 to 12 hours before each testing session and transmitted to a monitor. HR was measured using portable heart rate monitors (Vantage XL; Polar Electro, Inc, Lake Success, NY).

Study Design

Using a randomized, placebo-controlled, double-blind crossover experimental design, the effects of aspirin supplementation on inflammatory responses to live firefighting activities were interrogated. Low-dose aspirin was used, as this is a common recommendation for middle-aged men and is

associated with a lower risk than higher dose aspirin for long-term supplementation. Participants completed four total trials: (1) acute aspirin supplementation (81 mg aspirin 60 minutes before firefighting), (2) acute placebo supplementation (gelatin capsule containing cellulose filler 60 minutes before firefighting), (3) chronic aspirin supplementation (81 mg/day; 14 days), and (4) chronic placebo supplementation (14 days). The order of trials 1 and 2 was randomized, followed by trials 3 and 4, which were also introduced in a random order, with a 14 to 60-day washout period between each trial. Trials were separated on average by 17.7 ± 7.7 days for the acute and 27.5 ± 3.3 days for the chronic protocol. To control for diurnal variations, participants completed each of their four trials at approximately the same time of day (some participants completed testing in morning hours, other in afternoon hours).

Participants reported to testing having been instructed to drink a minimum of four bottles (500 mL) of water during the 24 hours leading up to testing and having consumed a standardized meal 60 minutes before each trial consisting of Clif Bar [240 cal; 5 g (8%) fat, 43 g (14%) carbohydrates, 9 g (18%) protein] and an Ensure Original Shake [220 cal; 6 g (9%) fat, 33 g (11%) carbohydrates, 10 g (20%) protein].

Firefighting Drills

For all experimental sessions, participants performed a standardized set of simulated firefighting activities in a live fire training structure while wearing full personal protective equipment (PPE) and a self-contained breathing apparatus (SCBA; weight ~20 kg). On the second floor of a simulated two-story mixed occupancy live-fire training structure constructed of concrete and steel, the firefighters completed 18 minutes of simulated firefighting activity as 9 two-minute periods of alternating work rest cycles. The overall structure measured approximately 12 x 18 m, but work was conducted within a ~4.5 x ~9 m room. The work cycles included stair climbing, simulated forcible entry using a Keiser sled (Keiser Sports Health Equipment, Inc, Fresno, CA), a simulated secondary search, and simulated hose advance. Initially, each participant proceeded up an exterior staircase from the first floor and all subjects worked independently. The participant then walked to a corner of the room and knelt down for a 2-minute acclimatization period. During each 2-minute "rest" cycle, a safety instructor demonstrated the next task to the participant. In addition, during each task, the instructor obtained the participant's heart rate using a Polar Heart Rate Watch (Polar Electro Inc, Bethpage, NY). After the initial 2-minute acclimatization period, the participant proceeded to walk up and down three stairs for a 2-minute duration. These stairs were 18 cm x 28 cm. After the first rest period, the participant then straddled a Keiser Force Machine, and used a 4 kg sledgehammer to drive a sled down a 2 m metal track for 2 minutes. For the next task, the participant performed a secondary (slow and thorough) search up and down a 5.5 m wall (this station only involved crawling and no interaction with simulated victims). In the final work station, the participant "advanced" a 1.2 m hose segment attached to a 4 m cable with a 4.5 kg weight on the end. Upon completion of the final scenario, participants proceeded downstairs and returned to the laboratory via a golf cart. Structure temperatures were maintained by adding small fuel packages to the fire sets and controlling the ventilation conditions in the room. Temperatures at floor-level and 1.2 m above the floor were monitored using Type K thermocouples and portable data acquisition system (OM-DAQPRO-5300; Omega Engineering, Norwalk, CT) and were maintained at approximately 35°C to 41°C and 70°C to 82°C, respectively.

Blood Analysis

Within approximately 60 minutes (range: 45 to 75 minutes) of beginning simulated firefighting activities and within 2 to 3 minutes of removing turnout gear and SCBA after activities, blood samples were collected in either sodium EDTA (plasma) or serum separator tubes (serum) by venipuncture using a 21-gauge needle from the antecubital vein using standard procedures. Blood samples were processed in a laboratory adjacent to the fireground. Blood samples were centrifuged at 1500*g* for 15 minutes at 4°C, and separated plasma and serum samples were aliquoted into microcentrifuge tubes and stored at -80°C until batch analysis. ELISA assays (Research & Diagnostic Systems, Inc, Minneapolis, MN, Quantikine Human IL-6 HS ELISA, HS600B) were run to determine IL-6 concentrations, with serum samples undiluted and run in duplicate (7.8%). High-sensitivity ELISA assays (Alpco, Inc, Salem, NH, CRP

ELISA Kit, K 9710s) were run to determine C-reactive protein (CRP) concentrations, with serum samples diluted 1 : 100 and run in duplicate (6.0%). ELISA assays (Research & Diagnostic Systems, Inc, Quantikine Human sICAM-1/CD54 ELISA, DCD540) were run to determine ICAM-1 concentrations, with plasma samples diluted 1 : 20 and run in duplicate (5.2%). ELISA assays (Research & Diagnostic Systems, Inc, Quantikine Human sP-Selectin/CD62P ELISA Kit, BBE6) were run to determine P-Selectin concentrations, with serum samples diluted 1 : 20 and run in duplicate (CV = 7.7%). ELISA assays (Research & Diagnostic Systems, Inc, Quantikine Human MMP-9 ELISA Kit, DMP900) were run to determine MMP-9 concentrations, with serum samples diluted 1 : 100 and run in duplicate (CV = 5.6%). Colorimetric assays (Cayman Chemical Company, Ann Arbor, MI, Antioxidant Assay Kit, 709001) were run to determine total antioxidant capacity (TAC), with plasma samples diluted 1 : 20 and run in duplicate (3.4%). For all ELISA assays, endpoint absorbance was read on a spectrophometric plate reader (Synergy HT; BioTek Instruments, Winooski, VT) at wavelength(s) established by the manufacturer.

Data Analysis

Statistical comparisons were performed with the use of commercially available software (SPSS v. 22.0; IBM Inc, Armonk, NY). A repeated 2 (regimen; acute or chronic) x 2 (treatment; placebo or aspirin) x 2 (time; pre or post firefighting) measures analysis of variance (ANOVA) was performed to interrogate changes in inflammatory markers and the effects of chronic and acute aspirin supplementation at two time points (pre and post-firefighting). A total of seven subjects (five from placebo and two from aspirin treatment) were removed as outliers following visual analysis of box-plots and histograms. Specifically, CRP and IL-6 values were notably higher at one experimental time point. This would be indicative of an acute illness or an inflammatory episode, which would confound data interpretation. However, when data was analyzed using the full data set, there were no appreciable changes in the interpretation of data; means, variance, and significance remained consistent. Alpha was set, a priori, at 0.05 for all comparisons. All data were presented as mean ± standard deviation (SD).

RESULTS

Table 1. Descriptive Characteristics of Participants (n = 23)

Variable	Mean ± SD	Range
Age, years	48.2 ± 5.9	40 – 59
Height, m	1.83 ± 5.8	1.73 – 1.96
Weight, kg	94.3 ± 13.8	72.7 – 118.2
Body mass index, kg/m^2	28.2 ± 3.5	21.4 – 36.6
Waist circumference, cm	100 ± 11	83 – 123
Systolic blood pressure, mm Hg (n = 20)	127 ± 12	106 – 154
Diastolic blood pressure, mm Hg (n = 20)	81 ± 9	62 – 94
Resting heart rate, bpm (n = 20)	70 ± 10	57 – 96
Maximal oxygen uptake (METs) (n = 22)	11.8 ± 2.7	7 – 17.7
Total cholesterol, mg/dL (n = 22)	201 ± 36	109 – 287
Low-density lipoprotein cholesterol, mg/dL (n =21)	129 ± 34	52 – 206
High-density lipoprotein cholesterol, mg/dL (n =21)	47 ± 12	30 – 77

METS, metabolic equivalent

Subject Characteristics

Subject descriptive characteristics can be found in Table 1 and CVD risk factor distribution in Table 2. Participants were experienced firefighters between the ages of 40 to 60 years (average: 48.2 ± 5.9 years). Mean total cholesterol, high-density lipoproteins, and low-density lipoproteins were in the high, average, and high ranges, respectively. Nine firefighters were obese based on standard BMI standards.

Table 2. Classification by Risk Factors

Risk Factor	Frequency [n (%)]
Body mass index* (kg/m^2)	
18.5 – 24.9	5 (22%)
25.0 – 29.9	9 (39%)
≥ 30	9 (39%)
Total cholesterol† (mg/dL) (n = 22)	
< 200	11 (50%)
200 – 239	9 (41%)
≥ 240	2 (9%)
Low-density lipoprotein† (mg/dL) (n = 21)	
< 100	4 (19%)
100 – 129	6 (29%)
130 – 159	7 (33%)
160 – 189	3 (14%)
≥ 190	1 (5%)
High-density lipoprotein† (mg/dL) (n = 21)	
< 40	8 (38%)
40 – 59	10 (48%)
≥ 60	3 (14%)
Physical activity‡	
Does not meet physical activity guidelines	18 (78%)
Meets/Exceeds physical activity guidelines	5 (22%)
Smoker	3 (13%)
Family history of cardiovascular disease§ (n = 22)	1 (5%)

*Classification based on established categories.[47]

†Classification based on established criteria.[48]

‡Physical activity guidelines: 30 – 60 min/day[1] (150 min/week) of purposeful moderate exercise, or 20 – 60 min/day (75 min/week) of vigorous exercise, or a combination of moderate and vigorous exercise.

§Immediate family member died of cardiovascular incident before 45 (men)/55 (women).

Blood Markers of Inflammation

Serum IL-6, CRP, ICAM-1, P-selectin, and matrix metalloproteinase-9 (MMP-9) were analyzed as inflammatory biomarkers (Table 3). No treatment x

Table 3. Markers of inflammation and Oxidative Stress Following Aspirin Supplementation

		Acute		Chronic		Significance		
	Time	Aspirin	Placebo	Aspirin	Placebo	Time	Treatment	Regimen
Inflammatory								
Interleukin-6, pg/mL	Pre	1.11 ± 0.22	1.00 ± 0.20	0.96 ± 0.16	0.88 ± 0.16	*F*=51.0;	*F*=0.19;	*F*=0.05;
	Post	2.37 ± 0.35	1.98 ± 0.28	2.26 ± 0.29	2.52 ± 0.28	*P*<0.01	*P*=0.67	*P*=0.82
C-reactive protein, mg/mL	Pre	1.91 ± 0.43	1.04 ± 0.26	1.74 ± 0.39	2.16 ± 0.52	*F*=0.46;	*F*=1.60;	*F*=2.90;
	Post	2.12 ± 0.48	1.17 ± 0.25	2.22 ± 0.43	2.13 ± 0.40	*P*=0.50	*P*=0.20	*P*=0.09
ICAM1, pg/mL	Pre	211.9 ± 15.4	191.6 ± 10.2	208.5 ± 17.4	197.3 ± 11.9	*F*=1.50;	*F*=1.60;	*F*=0.00;
	Post	221.5 ± 15.5	210.3 ± 11.7	221.6 ± 21.7	208.8 ± 12.1	*P*=0.22	*P*=0.20;	*P*=0.98
P-selectin, pg/mL	Pre	55.5 ± 4.8	49.5 ± 5.1	45.4 ± 2.6	43.6 ± 3.7	*F*=10.5;	*F*=0.90;	*F*=9.40;
	Post	63.0 ± 5.1	67.1 ± 7.2	52.1 ± 3.9	54.0 ± 3.9	*P*<0.01	*P*=0.90	*P*<0.01
MMP9, ng/ml	Pre	336.7 ± 29.4	351.9 ± 29.7	259.5 ± 24.8	282.3 ± 32.2	*F*=28.0;	*F*=0.42;	*F*=9.9;
	Post	490.4 ± 49.8	493.8 ± 41.4	387.0 ± 38.9	413.5 ± 42.3	*P*<0.01	*P*=0.52	*P*<0.01
AO								
TAC, mM	Pre	3.64 ± 0.23	3.83 ± 0.21	3.75 ± 0.19	3.83 ± 0.21	*F*=3.10;	*F*=0.51;	*F*=0.47;
	Post	3.29 ± 0.22	3.85 ± 0.23	3.54 ± 0.13	3.26 ± 0.14	*P*=0.08	*P*=0.47	*P*=0.49

Mean ± SD.

AO, antioxidant; ICAM1, intracellular adhesion molecule 1; MMP9, matrix metallopeptidase 9; TAC, total antioxidant capacity

time, regimen x time, regimen x treatment, or regimen x treatment x time interaction effects were detected for markers of inflammation. However, a significant main effect for time was detected for IL-6 (F = 51; P = 0.000), P-selectin (F = 10.5; P = 0.001), and MMP-9 (F = 28; P = 0.000), with values significantly elevated following firefighting activity. A main effect of aspirin regimen (acute vs chronic) was detected for P-selectin (F = 9.4; P = 0.003) and MMP-9 (F = 9.9; P = 0.002), and a trend was noted for CRP (F = 2.9; P = 0.09).

Blood Markers of Oxidative Stress

Antioxidant capacity was assessed through a TAC test (Table 3). A significant regimen x treatment interaction for TAC (F = 4.1; P = 0.004) was found, with lower TAC for placebo under chronic administration, but no other significant findings were detected for this marker of oxidative stress.

DISCUSSION

The present study documented the inflammatory responses to live firefighting and the effects of aspirin supplementation on that response. We found that IL-6, MMP-9, and P-selectin increased following live firefighting, and that aspirin supplementation at doses of 81 mg, administered either acutely (60 minutes pre-firefighting) or chronically (14 days), were ineffective in altering this firefighting-induced increase in inflammatory markers. Levels of P-selectin and MMP9 were significantly lower, and CRP trended toward a lower value, in the chronic aspirin group relative to the acute aspirin group.

The finding of increased IL-6 is consistent with previous reports that investigated work that simulates firefighting and exercise. Walker et al[19] recruited 42 healthy, career urban firefighters to complete a protocol that included two 20-minute bouts of simulated search and rescue in ambient temperatures of 100 ± 5°C wearing full PPE and SCBA. Significant increases in IL-6, TNF- α, leukocyte, and platelet count were detected immediately post-exercise, with the latter persisting for 24 hours. Significant IL-6 elevations were also observed in college-aged males who performed a 45-minute intermittent work-rest walking protocol in a heat chamber (49.5 ± 1.4°C; 16.9 ± 4.3%) simulating fire service instructor (FSI) workloads.[20] However, the increase in magnitude observed in the present study was smaller than in previous reports. Discrepancies in the magnitude of the IL-6 response among studies are likely due to differences in modalities, intensity of work, duration, age of participants, and varying levels of heat stress. However, the evidence suggests that firefighting leads to increases in IL-6, which has important implications, as IL-6 is responsible for regulating leukocyte adherence (capturing), MMP concentrations, and upregulation of CAMs.[21] This cytokine is also responsible for mediating atherosclerotic processes and indirectly moderating cardiac events.[8] Stressors that induce IL-6 are common to, and exacerbated by, firefighting activities, including heavy exercise, high ambient temperatures,[10] and particulate matter exposure.[9] IL-

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6 is also correlated with accelerated coagulatory processes.[22] Several studies have clearly demonstrated that firefighting increases coagulatory potential.[23,24]

In the current study, MMP-9 significantly increased following 18 minutes of intermittent fire suppression activities. Increased MMP activity, including MMP-9, is strongly correlated with plaque destabilization and vascular aneurisms. It is responsible for accelerating plaque ruptures, contributing to lethal chronic and acute CV syndromes and events.[25] Increases in MMP-9 levels have previously been documented following a single bout of maximal cycling.[26] Likewise, particulate matter induced MMP-9 generation has been observed in airway epithelial cells lasting for 48 hours.[27] This increase is consistent with the increase in risk of acute cardiac events experienced by firefighters during and immediately after firefighting.[28]

Vascular CAMs (VCAMs) are critical inflammatory biomarkers expressed on the surface of endothelial cells. Functioning as transmembrane proteins, VCAMs play an important role in extracellular binding and leukocyte transmigration into the endothelial lining, a crucial phase in the progression of atherosclerosis.[8,29] In the present study, two subtypes of CAMs were investigated: P-selectin and ICAM-1. P-selectin proteins facilitate leukocyte adhesion and rolling along the inner lining of the endothelium.[8,30] Elevated P-selectin is associated with a pro-thrombotic state, atherosclerosis, and pulmonary hypertension,[31] as well as carotid plaque formation in firefighters.[32] The current study found that live firefighting significantly increased P-selection. Our research group has also demonstrated that firefighting elevates platelet aggregation and coagulatory potential in previous studies.[2,23] Collectively, these findings suggest that increased P-selectin plays a role in mediating the procoagulatory state that exists after firefighting.

Upregulated ICAM-1 is responsible for leukocyte recruitment,[30] macrophage proliferation within the vascular intima, accelerating inflammation, and atherosclerotic progression.[8] Blood levels of ICAM-1 were reported to increase in 67% of wildland firefighters following strenuous activity.[33] In contrast, the present study detected no significant differences in blood levels of ICAM-1 following simulated live structural firefighting activities lasting 18 minutes. The differences between the present study and the earlier wildland study may be due to the intensity and duration of work, underlying health characteristics, or the magnitude and chemical composition of particulate matter. In our testing environment, firefighters wore respiratory protective equipment. Commonly—including during wildland firefighting and during overhaul in structural firefighting—firefighters may not consistently wear respiratory protection, heightening their risk for ICAM-1 generation and vascular inflammation.

TAC is an assessment of the ability to neutralize reactive oxygen species (ROS) and minimize cellular damage. Our findings suggest that antioxidant capacity is unchanged following a single bout of structural firefighting for 18 minutes. These findings suggest that a single bout of live firefighting does not alter endogenous antioxidant potential and oxidative stress. This is in contrast to Gaughan et al,[34] who reported that a 2-day bout of wildland firefighting elevated oxidative stress levels which persisted for 4 days.[34] This discrepancy may be accounted for by the differences in work duration and exposures, which affects endogenous capability to mitigate oxidative stress. It is speculated that long-term exposure to oxidative stressors lead to a more pronounced effect on mediators of ROS.

Low-dose aspirin is commonly prescribed for acute CV complications and long-term prevention of CVD.[35] Firefighting is known to cause acute hematological changes that increase coagulability[2,23,24] and firefighters are at a heightened risk of suffering a cardiac event following fire suppression activities as compared to station duties.[28,36] Accordingly, it was of interest to see whether low-dose aspirin had the ability to mitigate expected inflammatory changes associated with firefighting. Taken acutely or chronically, low-dose aspirin ingestion had no significant effects on firefighting-induced increases in IL-6, MMP-9, and P-selectin. Morris et al[37] found that low-dose aspirin (75 mg) dampens innate immune-mediated responses in response to local injury (induced blistering). However, other researchers have reported that 16 weeks of aspirin therapy (8 weeks on, 8 weeks washout period) at 325 mg/day had no effect on CRP, IL-6, and ICAM in middle-aged (41 ± 9 years old) males and females with CVD risk factors.[38] Likewise, dosages of 81 and 325 mg for 7 to 31 days

did not impact serum CRP levels.[39,40] Collectively, our results suggest that low-dose aspirin at 81 mg does not inhibit inflammatory responses to firefighting in healthy firefighters.

The pharmacological effect of aspirin may explain its inefficacy in mediating immune function. Aspirin is 170-fold more selective in its inhibition of COX-1 relative to COX-2.[41] Whereas COX-1 regulates platelet activation and aggregation, the COX-2 isoform coordinates the production and release of proinflammatory prostaglandins.[17] Therefore, a high aspirin dosage (>1000 mg) may be necessary to achieve any anti-inflammatory response.[37] However, higher dosage increases risk of gastrointestinal bleeding[42] and may exacerbate heat-stress susceptibility.[43]

CONCLUSION

The present study demonstrated that an acute bout of live firefighting increases pro-inflammatory markers (IL-6, MMP, P-selectin) in older-aged firefighters. Given that CAMs and inflammatory cytokines are strong biomarkers of inflammation, the observed changes may be important mediators of vascular and myocardial function, providing a potential mechanistic link between the stress of firefighting and SCEs in this important occupational group. Low-dose aspirin supplementation did not attenuate the rise in proinflammatory cytokines. Although this study was limited to the acute effects of firefighting, chronic long-term inflammation could play a role in atherogenesis[44] and left ventricular hypertrophy.[45,46] Therefore, further work is needed to better characterize the health effects associated with inflammatory responses in this occupational population.

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