

2015

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Recommended Citation

Lee, Linda, "Is Caffeine Effective In Reducing Pain Perception During Exercise Performance In Healthy Adults?" (2015). *PCOM Physician Assistant Studies Student Scholarship*. Paper 233.

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**Is Caffeine Effective In Reducing Pain Perception During Exercise
Performance In Healthy Adults?**

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A SELECTIVE EVIDENCED BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 19, 2014

ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not caffeine products are effective in reducing pain perception during exercise performance in healthy adults.

STUDY DESIGN: Systematic review of three English language, randomized controlled trials published in 2012 and 2013.

DATA SOURCES: Three randomized control trials (two double-blind and one single-blind) which compare caffeine administration to placebo for reduction in pain perception during exercise performance in health adults were obtained using PubMed.

OUTCOMES MEASURED: Clinical outcomes of leg pain perception experienced during exercise were measured according to a Pain Intensity Scale, ranged 0-10, developed by Cook et al. (1998).

RESULTS: Duncan & Hankey (2013) showed that caffeine ingestion prior to exercise reduced leg muscle pain perception in regularly active adults ($p < 0.01$) compared to placebo group. Two studies by Astorino et al (2012) showed no significant reduction in leg pain perception during exercise that followed caffeine ingestion ($F_{5,75} = 2.04$, $p = 0.16$, $\eta^2 = 0.12$; $F_{1,9} = 0.96$, $P = 0.35$, $\eta^2 = 0.10$).

CONCLUSIONS: The results of the RCTs show that the efficacy of caffeine ingestion prior to exercise performance in reducing leg pain perception is debatable based on opposing results from recent research on this matter. A common limitation to these studies is the small sample size – future studies are needed to incorporate greater sample sizes and incorporation of subjects of different fitness levels to improve generalizeability of results to the general population.

KEY WORDS: leg pain perception, caffeine

INTRODUCTION

Caffeine consumption is widely used amongst the adult population – nearly 83% of adults ingest caffeine on a daily basis. Considering its prevalent usage in the general population, its merits as a health aid have been studied in various psychophysiological angles, including mental alertness, mood improvement, and pain perception¹. One of the more prominent theories behind caffeine’s efficacy as an ergogenic aid is its role as an adenosine antagonist². By inhibiting adenosine receptors, caffeine affects the central nervous system’s functions including learning, memory, and cognition². The significance of caffeine’s effect on our bodies is attributed to its ability to alter perceptions. Several studies have focused on the link between caffeine ingestion and perception (of perceived exertion, of pain, of pleasure/ displeasure, etc.) during sports performance^{1,3,4}.

The underlying interest in the study of caffeine as an ergogenic aid relates to PA practice in that PAs are involved in patient education which oftentimes includes recommendations for regular physical activity. As healthcare practitioners, we confront the challenges posed by patients with overweight/ obese BMIs and its associated health complications. In 2007, the American College of Sports Medicine (ACSM) and American Heart Association (AHA) set forth guidelines for physical activity associated with “enhanced health and quality of life”⁵. They recommend 30 minutes of moderate-intensity daily exercise five days a week⁵. The benefits of regular, moderate-intensity exercise are related to improvement in cardiorespiratory fitness⁵. Given the widespread intake of coffee and caffeinated beverages by the adult population, research on caffeine’s ergogenic effects should interest PAs in terms of our stance on promoting its value to our patients’ health care.

One of the more common issues that limits patients’ exercise capability is low back pain (LBP) – it is the fifth most common reasons for physician visits and is the most common reason

for orthopedic and neurosurgery visits⁶. The national cost for the healthcare of low back problems is \$38 - \$50 billion⁶. Low back pain is one of the various medical conditions that negatively affect patients' commitment to regular moderate-intensity exercise. Pain perception has a powerful effect on influencing behaviors, namely in reducing an individual's engagement with physical activity. In light of this, research on caffeine's psychophysiological effects has the potential to offer an alternative to the treatment of musculoskeletal pain so that exercise's health benefits may be optimized. As previously mentioned, caffeine's ergogenic effects are theorized as related to adenosine antagonism², however, the specific mechanisms of its effect on exercise improvement is unknown¹. Usual methods to treat muscular pain include over-the-counter analgesics, heat/cold therapy, and prescription analgesics or muscle relaxants.

The three studies to be discussed in this paper examine the effects of caffeine ingestion in reducing the perception of pain felt during physical activity; in other words, these studies assess caffeine's ability to improve the quality and duration of endurance-dependent activity by altering individuals' subjective experience of pain.

OBJECTIVE

The objective of this selective evidence-based medicine review is to determine whether or not caffeine reduces pain perception during exercise in healthy adults.

METHODS

The three RCTs focused on healthy adults who engaged in physical activity at a minimum of 3 days per week and had a habitual caffeine intake of less than 350 mg per day. In all three studies, the intervention was a caffeinated beverage: 1) caffeinated energy drink (179 mg of caffeine diluted into 250 ml of artificially sweetened water containing Vitamins B3, 6

, 9, 12, tyrosine, taurine, malic acid, and glucoronolactone)³, 2) anhydrous caffeine 6 mg/kg prepared as a solution with 113 ml of diet 7-UP, 113 ml of water, and 6 mg/kg of glucose⁴, 3) anhydrous caffeine 5 mg/kg in a solution of 5 mg/ kg of glucose and 125 ml of noncaloric 7-UP¹. Comparisons to the interventions above were as follows, respectively: 1) placebo 250 ml of artificially sweetened water drink matched for taste/ smell/ appearance with caffeine drink³, 2) placebo solution of 113 ml of diet 7-UP, 113 ml of water, and 6 mg/kg of glucose⁴, 3) placebo solution of non-caloric lemon flavored beverage, 5 mg/kg of glucose, and 125 ml of non-caloric 7-UP¹. The outcomes assessed in all three RCTs were on leg muscle pain perception during exercise^{1,3,4}. All three studies were in a crossover design—two studies were double-blind, placebo-controlled, one study was single-blind, placebo-controlled^{1,3,4}. The database accessed to access all articles was PubMed and keywords included pain perception, caffeine, and exercise performance. Each article was published in peer-reviewed journals and written in English. Inclusion criteria included recent RCTs examine the effects of caffeine ingestion in reducing pain perception compared to placebo during a trial of exercise performance; patients were habitually active adults and regular caffeine consumers^{1,3,4}. Exclusion criteria included patients who were habitually heavy caffeine consumers (>350 mg/day) and had musculoskeletal or cardiac conditions that would restrict exercise performance^{1,3,4}. In all three RCTs, leg pain perception was statistically analyzed using ANOVA, significant F ratio, effect size for the F ratio and statistical significance set at $p < 0.05$ ^{1,3,4}.

Table 1: Demographics & Characteristics of included studies

| Article | Type | # Pts | Age (yrs) | Inclusion Criteria | Exclusion Criteria | W/D | Interventions |
|---------|------|-------|-----------|--------------------|--------------------|-----|---------------|
|---------|------|-------|-----------|--------------------|--------------------|-----|---------------|

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|--|--------------|----|------|--|---|---|--|
| Astorino TA, Roupoli LR, & Valdivieso BR ⁴ , 2012 | Double blind | 10 | 22.1 | <ul style="list-style-type: none"> - Young, healthy eumenorheic women. - Min physical activity = 3d/wk. - Habitual caffeine intake 151.1 + or – 107.3 mg/d. | Drugs taken during the experiment. | 0 | Anhydrous caffeine 6 mg/kg prepared as a solution with 113 ml of diet 7-UP, 113 ml of water, an 6 mg/kg of glucose. |
| Duncan MJ, Hankey J ³ , 2013 | Double blind | 14 | 23.5 | <ul style="list-style-type: none"> - being “apparently healthy” physically active, and accustomed to regular aerobic exercise. | MSS injury or Cardiovascular condition or Heavy habitual caffeine user. | 0 | Caffeinated energy drink (179 mg of caffeine diluted into 250 ml of artificially sweetened water) – also contained Vitamins B3, 6, 9, 12, tyrosine, taurine, malic acid, and glucuronolactone. |

| | | | | | | | |
|---|--------------|----|--------------------------|---|----------------------------------|---|--|
| Astorino TA, Cottrell T, Lozano AT, Abuto-Pratt, K, Duhon J ¹ , 2012 | Single blind | 16 | Men (28) Women (26.7) | <ul style="list-style-type: none"> - The healthy, active men group completed minimum 5 h/wk of exercise in the last 2 years, participated in team sports, resistance training, and/or cardiovascular exercise. - The athlete, trained men group were currently competing in cycling, running, or triathlon. - All participants habitually ingested caffeine 2-7 d/wk, intake ranging from 15-320 mg/d. | Heavy caffeine users (>350 mg/d) | 0 | - Caffeine (anhydrous) 5 mg/kg (in solution of 5 mg/kg of glucose and 125 ml of noncaloric 7-UP) |
|---|--------------|----|--------------------------|---|----------------------------------|---|--|

OUTCOMES MEASURED

In all three RCTs, perception of leg pain experienced during exercise performance was measured by a standardized pain scale called the Pain Intensity Scale, ranging from 0 (no pain at all) to 10 (extremely intense pain, almost unbearable)⁶. Other outcomes measured in these studies, though not examined here, included pleasure/displeasure, ratings of perceived exertion, arousal, mood, heart rate, blood lactate, and readiness to invest physical effort^{1,3,4}.

RESULTS

Astorino et al (2012) studied the effects of caffeine ingestion on exercise performance exclusively on women, asserting that prior studies have not focused on this population¹. Ten women (young, healthy, euemenorrheic) who engaged in physical activity at least 3 days per week, but had little cycling experience, were recruited for this study. Participants were habitual caffeine consumers (mean intake = 151.1 ± 107.4 mg/d) with the exception of one participant who did not regularly consume caffeine¹. One hour prior to each exercise trial, subjects drank a 226 ml drink containing either caffeine or placebo¹. Following guidelines by ACSM for vigorous exercise to gain health benefits, the researchers had participants complete a five min warm-up and 8.2 km of “all out cycling” while instructed to “change gears and pedal as fast as they could” on a 10-laps flat course (performed on the Velotron DynaFit Pro cycle ergometer)¹. Prior to exercise trials, researchers instructed and familiarized subjects on the pain scale¹. During exercise, leg pain was recorded every 1.6 km and at the end – the researchers held up the pain scale and subjects were asked to report their pain rating at that moment¹. The results of this study were as follows: leg pain increased during exercise [$F(4,36) = 26.4, P < 0.01, \eta^2 = 0.75$], however, the intervention (caffeine) did not alter leg pain perception [$F(1,9), P = 0.96, \eta^2 = 0.10$].

Duncan and Hankey (2013) examined a caffeine-containing energy drink’s effect on leg pain perception in 14 participants (7 males, 7 females) who engaged in at least 8 hours per week of exercise and regularly consumed no more than 350 mg per day of caffeine. Participants complete two 60 minute submaximal cycling at a pre- set workload of 60% VO_{2max} (performed on a mechanically braked cycle ergometer) to mimic the exercise guidelines for health benefits established by the ACSM³. Subjects ingested a solution containing either 179 mg of caffeine (plus other vitamins) or placebo 60 mins prior to exercise³. During exercise, leg muscle pain was

assessed every 10 minutes by asking participants to rate their pain from 0 – 10 on a pain scale that the subjects had been familiarized with previously³. None reported adverse side effects (e.g. nausea or headache)³. This study found significant substance x time interactions for leg muscle pain [$F_{(6, 78)} = 5.533$, $P = 0.0001$ Partial $\eta^2 = 0.299$]³. Leg pain was rated significantly lower in the energy drink condition compared to placebo, from 20 minutes to completion at 60 minutes (all $p=0.01$ or better)³.

In the study by Astorino et al (2012), caffeine's effect on a time-trial exercise performance was assessed in eight endurance-trained men (athletes competing in cycling, running, triathlon) and in eight recreationally active men (team sports, resistance training, cardiovascular exercise)⁴. These subjects habitually consumed caffeine without exceeding 350 mg per day⁴. On three visits, participants ingested 5 mg/ kg of caffeine or placebo one hour prior to a 10 km cycling time-trial exercise (consisted of periods of hill inclines, downhill cycling, and flat terrain) on an electrically-braked cycle ergometer⁴. Subjects were instructed to go 'all-out' during exercise and asked to rate their leg pain on a 0-10 scale every 1.6 km and within 5 seconds of exercise termination. Results showed a main effect for leg pain increased over distance [$F_{(5,75)} = 30.84$, $p < 0.001$, $\eta^2 = 0.67$]; however there was no treatment effect [$F_{(2,30)} = 2.04$, $p = 0.16$, $\eta^2 = 0.12$]⁴. There was also no interaction between treatment versus time or group, and the pain responses to caffeine versus placebo between both groups (trained vs active) showed no statistical significance, as shown in Table 2⁴.

Table 2: Response to Caffeine and Placebo Intake on Leg Pain¹

| | |
|--|----------|
| Time x Treatment interaction | P = 0.34 |
| Group x distance interaction | P = 0.49 |
| Group x treatment interaction | P = 0.98 |
| Pain response in Trained men versus Active men | P = 0.09 |

DISCUSSION

The study by Astorino et al (2012) revealed that caffeine ingestion prior to exercise did not significantly alter leg pain perception in active women who performed a vigorous, self-paced cycling performance⁴. Despite the lack of evidence supporting caffeine intake's positive effect on reducing muscular pain perception, this study had several limitations. The sample size is small (ten women), only one type of exercise was examined (cycling), and caffeine ingestion was set at only one fixed time (one-hour prior to exercise). Furthermore, ratings of leg pain perception during exercise may have been influenced by other psychological factors such as anxiety, mental preparedness/ mood coming into the trial, or physical side effects induced by caffeine such as palpitations or nausea. These considerations limit the generalizability of this study's findings. In the study by Duncan and Hankey (2013), results showed that ingestion of caffeinated energy drink pre-exercise reduced pain perception at 20 mins-30 mins during a one-hour, moderate intensity, cycling exercise³. This study, therefore, found a positive correlation between caffeine ingestion and reduced pain perception during exercise; however, several limitations dampen the generalizability of this study's finding³. Some limitations include the following: a small sample size of 14, homogenous subjects of recreationally active adults, one type of exercise at a fixed intensity (cycling at moderate intensity), and the inclusion of caffeine

within a solution that also contained other products (taurine, tyrosine, vitamin B12, 9, 3, 6, and glucoronolactone)³. In the other study by Astorino et al (2012), results showed no significant alteration in leg pain following caffeine ingestion in both groups (trained versus recreationally active)¹. The generalizability of this lack of correlation between caffeine intake and reduced pain perception has several limitations: small and gender-homogenous sample size (sixteen men), one type of exercise (cycling) at a pre-set exercise condition (flat terrain, downhill, uphill), and one dose of caffeine (5 mg/ kg) rather than varied conditions with varying doses of caffeine.

CONCLUSIONS

Two studies showed no significant effect of effect on decreasing leg pain perception during an exercise trial that followed the ACSM's guidelines for health-optimizing physical activity^{1,4}. One study showed a statistical significant effect of caffeine on reducing leg pain perception during moderate-intensity exercise, interestingly at a specific time period (between 20-30 mins) in the 60 minute duration performance³. These findings continue to support the debate on caffeine's efficacy as a ergogenic aid; therefore, as healthcare practitioners, PAs may be cautious in promoting caffeine as means to improve pain experienced during exercise. Ultimately, the evidence found in answering the question of whether or not caffeine reduces leg pain perception during exercise is inconclusive. Further research on caffeine's ergogenic capacity may be merited considering that previous research has yet to encompass a large sample size with varied experimental conditions (e.g. different doses of caffeine).

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