Effect of Pseudoephedrine on 800-m-Run Times of Female Collegiate Track Athletes

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Context: Pseudoephedrine (PSE) is an over-the-counter decongestant that might have ergogenic effects. The World Anti-Doping Agency has prohibited large doses (>150 μg/mL) of PSE, while the National Collegiate Athletic Association (NCAA) does not include it on their banned-substance list. Purpose: This study examined the effect of body-weight dosing of PSE on 800-m-run times of NCAA female runners. Methods: Fifteen NCAA female track athletes volunteered to participate in the randomized, double-blind, crossover design. Participants were given 2.5 mg/kg PSE or placebo in trials separated by a week. Ninety minutes postingestion, participants completed an 800-m individual time trial on an indoor track. Finishing time was recorded with an automated video timing device. Heart rate and anxiety state scores were recorded immediately after each trial. Results: Fourteen runners completed both trials, and 1 was an outlier: N = 13. Despite the dose being well above normal therapeutic levels (144 ± 17 mg), there was no significant difference (P = .92) in 800-m times between PSE (2:39.447 ± 9.584) and placebo (2:39.372 ± 9.636) trials, in postexercise heart rate (P = .635; PSE = 177.9 ± 14.5 beats/min, placebo = 178.4 ± 18.5 beats/min), or in anxiety-state levels (P = .650; PSE = 38.4 ± 11.6, placebo = 38.1 ± 8.8). Conclusion: A 2.5-mg/kg dose of PSE had no effect on 800-m performance for female NCAA runners. More research is needed to determine if PSE should be a specified banned substance.

Keywords: drugs, doping, ergogenic aid, performance, running

Pseudoephedrine (PSE), the active ingredient in many over-the-counter decongestants, is a sympathomimetic amine that comes from the plant genus Ephedra. Although not as potent as amphetamines, sympathomimetic drugs are known stimulants. Under normal conditions, a buildup of norepinephrine in the synaptic cleft activates α2 autoreceptors on the presynaptic nerve to inhibit further release of norepinephrine; however, PSE stimulates adrenergic neurons by removing this negative-feedback inhibition and directly binding to α1 and β receptors on the postsynaptic nerve. In essence, PSE mimics the actions of catecholamines.

In theory, the stimulant properties of PSE could aid athletic performance by increasing blood pressure, heart rate, oxygen consumption, glycogenolysis, vasoconstriction in the skin, and vasodilation in muscle arterioles, as well as stimulating the central nervous system. The effect of PSE on the central nervous system could cause an amphetamine-like reaction in the athlete and suppress feelings of fatigue. Despite the theoretical advantages of PSE, the results of studies to document its effectiveness as an ergogenic aid are equivocal. Most have found PSE to be ineffective as an ergogenic aid; however, a few researchers have reported enhanced athletic performance when PSE was administered in larger-than-therapeutic doses.

In addition to equivocal findings among researchers, even the sport-governing bodies seem to have different opinions on the efficacy of PSE as a performance enhancer and whether it should be a banned substance. PSE was banned by the International Olympic Committee until 2004, when the World Anti-Doping Agency (WADA) removed it from the prohibited substance list. In 2010 WADA reinstated PSE to the prohibited list as a specified stimulant prohibited in competition at a urinary threshold of 150 μg/mL, and that is its current position as of this writing. However, the National Collegiate Athletic Association (NCAA), which governs collegiate athletes in the United States, specifically exempts PSE as a banned stimulant.

Given the conflicting standards of sport-governing bodies and the inconclusive evidence regarding the ergogenic effect of PSE, the purpose of the current study was to examine the effect of 2.5 mg/kg body weight of PSE on 800-m-run times of NCAA Division I female distance runners. Women were asked to participate for several reasons. First, most research on this topic, including the only studies in which PSE was found to have a significant ergogenic effect, studied only small samples of males. Second, the only studies that have included female participants used 60- to 120-mg therapeutic doses of PSE rather than the larger doses thought to be necessary to...
enhance performance. Third, it is suspected that women absorb sympathomimetic amines more extensively in their gastrointestinal tract than men, which may make the effect of PSE more apparent in them. Finally, according to Hopkins and Hewson, female elite runners have less variability in time-trial times than elite men, making it easier to detect performance changes as a result of the treatment. Thus, in giving larger-than-therapeutic doses of PSE to female 800-m runners, we believe that this study fills a gap in the literature and will help clarify questions surrounding the ergogenic effects of this sympathomimetic drug.

**Methods**

**Subjects**

Fifteen female student athletes from an NCAA Division I track team were recruited to participate in this study. One week before testing, a physician completed an initial screening and medical-history evaluation of each participant. The valve function and heart rhythm of the subjects were examined aurally. If it was not deemed safe for them to participate, they were excluded from the study. Runners with blood pressure ≥140/90 mm Hg were also not allowed to participate. Each subject signed an informed consent before participating in the study, which the institutional review board of the University of Utah approved. The testing was done at the end of an aerobic-training cycle and the beginning of the fall cross-country season.

**Design**

Each participant completed two 800-m time trials, 1 with PSE and 1 with a placebo in amounts relative to body weight. Treatments were administered in random order, with the trials separated by 7 days. PSE has a half-life of 5 to 8 hours, making 7 days sufficient for drug clearance. The subjects and the test administrator were blinded to the treatment.

**Methodology**

Pretesting instructions were given to the athletes at the time of the physician screening 1 week before the first trial, and they were reminded of the pretest conditions the day before each trial. Participants were asked to abstain from prescription or over-the-counter medications that contain PSE (eg, Sudafed) or could react with PSE the week before and during testing. They were also asked to abstain from alcohol and caffeinated foods and beverages within 24 hours of testing and fast for 8 hours before testing in order to minimize nutritional variability between trials. The body weight of each runner was also measured to the nearest 0.5 kg on a balance-beam scale (model 700, Seca, Ontario, Canada) at this pretesting session to determine the amount of PSE (Par Pharmaceutical, Woodcliff Lake, NJ) or placebo (maltodextrin) that would be administered. A dosage of 2.5 mg/kg body weight was measured, and the PSE and placebo were placed in identical gelatin capsules.

Each 800-m trial was performed on the same 200-m indoor track. An indoor track was used to eliminate weather variability between testing sessions. On participants’ arrival at the track, the PSE or placebo was administered with a Nutrament (Nestle S.A., Vevey, Switzerland) high-energy shake at 7 ml/kg body weight to standardize pretesting nutrition. Nutrient distribution of the shake is as follows: protein 18%, carbohydrate 58%, and fat 25%. Water was available ad libitum.

After the treatment was administered, the student athletes rested for 70 minutes, sitting and doing homework or reading. At the end of the rest period, they completed a standardized 20-minute warm-up. The 800-m trial was run individually and commenced at precisely 90 minutes after ingestion of the treatment. The subjects were unable to wear watches and were given no encouragement during the run. Split times were given every 200 m to simulate a race. Each trial was timed to the nearest 0.01 second using the Pyro-bright system (Flash Timing, Hilsboro, OR). Pyro-bright uses a scope with an internal clock that is started automatically in synchrony with the firing of the starter’s pistol. The signal from the scope was sent to a video recorder, which recorded the finish from a video camcorder, with the time overlaid on the screen.

Immediately after the trial, postexercise heart rate was recorded from a heart-rate monitor (T31, Polar Electro Inc, Lake Success, NY) to assess the effects of PSE on heart rate. Participants then completed Spielberger’s self-evaluation questionnaire to determine state anxiety. This 20-item questionnaire is a benchmark assessment for state anxiety. The testing procedure was repeated 7 days later, with each participant receiving the alternative treatment. Participants were encouraged to maintain the same training regimen for the 7 days before each trial.

**Statistical Analyses**

An a priori statistical power analysis was performed based on data from Hodges et al using GPower 3.1 for sample-size estimation. With a 1-tailed alpha of .05 and power of .80, the projected sample size was N = 6 for this comparison of dependent group means. Thus, our proposed sample size of N = 15 should have been more than adequate for the main objective of this study. According to the same power analysis, each participant would have needed to differ by 3.1 seconds between the PSE and placebo trials to achieve statistical significance.

Paired-sample t tests were used to determine if the mean difference in 800-m-run time was significant between PSE and placebo trials, as well as to compare mean differences in postexercise heart rate and anxiety state between trials. Statistical significance was set at P < .05. Statistical analysis was done using PASW, version 18.0 (IBM, Somers, NY).
Results

Fifteen student athletes began the study. Due to injury, 1 participant was unable to finish. Another participant was considered an outlier, with a difference in 800-m times between trials exceeding a standardized score of 3.29. Thus, the number of participants used for statistical analysis was 13. Both descriptive and experimental data are presented in Table 1.

Despite the participants’ being dosed well above normally prescribed levels, the mean difference in 800-m times between the placebo and PSE trials was not significantly different ($P = .92$). Individual time differences between trials are illustrated in Figure 1. These differences were less than 2% in all but 2 subjects. Likewise, there was no significant difference between trials for postexercise heart rate ($P = .635$) or state anxiety ($P = .650$).

Discussion

The current study was modeled after that of Hodges et al, who reported that a 2.5-mg/kg dose of PSE improved 1500-m-run times of elite male runners by 2.1%. However, there are several key differences between the current study and that of Hodges et al that may contribute to the discrepancy in results between the 2. The current study used female athletes running a shorter distance. Despite the same relative dosage being administered in both studies, the larger male athletes in the Hodges et al study received a larger absolute amount of PSE (180 mg). In addition, the 800-m run was done indoors while the 1500-m time trial was run outdoors, but Hodges et al reported no significant difference for environmental variables between PSE and placebo trials.

Recently, Pritchard-Peschek et al also reported an ergogenic effect of PSE. After being given 180 mg of Sudafed, male cyclists improved their performance by 5.1% during a cycling time trial that averaged about 30 minutes. Both Pritchard-Peschek et al and Hodges et al

<table>
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<th>Variable</th>
<th>Mean ± SD</th>
<th>Range</th>
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<tr>
<td>Age (y)</td>
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<td>18–23</td>
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<tr>
<td>Height (cm)</td>
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<tr>
<td>Weight (kg)</td>
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<td>Body-mass index (kg/m²)</td>
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<td>18.5–23.2</td>
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<td>Dose (mg)</td>
<td>144 ± 17</td>
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</tr>
<tr>
<td>800-m time placebo</td>
<td>2:39.37 ± 9.64</td>
<td>2:24.70–2:55.11</td>
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<tr>
<td>Heart rate placebo</td>
<td>177 ± 19</td>
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<tr>
<td>pseudoephedrine</td>
<td>177 ± 15</td>
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</tr>
<tr>
<td>Anxiety score placebo</td>
<td>38.2 ± 8.8</td>
<td>25–53</td>
</tr>
<tr>
<td>pseudoephedrine</td>
<td>38.4 ± 11.7</td>
<td>23–67</td>
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Figure 1 — Time difference between trials (pseudoephedrine and placebo) for each participant.
speculated that the sympathetic action of norepinephrine on the central nervous system might be the mechanism by which performance is enhanced with PSE. Pritchard-Peschek et al even found postexercise plasma norepinephrine to be significantly higher after the PSE trial. However, similar to the current study, neither Pritchard-Peschek et al nor others have observed an increase in heart rate with PSE, placing this theory into doubt. In addition, we found no difference in the postexercise anxiety score between the PSE and placebo trials, and both Hodges et al and Pritchard-Peschek et al reported no adverse effects with PSE despite the large doses given.

In contrast to the findings of Hodges et al and Pritchard-Peschek et al, and consistent with our results, other researchers have reported no ergogenic benefit from PSE. Despite giving runners 60 mg of PSE 4 times per day for 36 hours, Chester et al reported no improvement in the time to complete a 5000-m time trial. Similarly, PSE did not lower cyclists’ times in a 40-km time trial. Nor has PSE improved VO\(_{2}\)-max or time to exhaustion during maximal cycle ergometry or treadmill tests. A commonality among these studies is that they are primarily aerobic, but success in the 800-m run is due mostly to one’s anaerobic capacity. In reviewing anaerobic studies, PSE given in 60- to 120-mg doses does not affect peak power in Wingate tests. However, Gillies et al reported an increase in Wingate peak power from a 180-mg dose of PSE, even though total work was not increased.

The current study has several limitations. First, Gillies et al showed that a single urine sample is not a reliable indicator of the amount of PSE ingested, and we did not have the financial resources to perform multiple urinalyses to detect whether the dose given would have exceeded the WADA limits. Gillies et al reported PSE concentrations of 7 to 261 μg/mL in urine samples collected 1 hour postexercise from a 120-mg dose and noted that, due to individual variation, very high urine PSE concentrations can be achieved from therapeutic doses. Given that the dose ingested by our participants was, on average, about 2.5 times the normal 60-mg therapeutic dose, it is likely that at least a few of the athletes would have produced urine samples that exceeded the WADA limits. Second, we did not limit the 800-m trials to a specific phase of the menstrual cycle. However, the trials were randomized, and a review of the literature suggests that menstrual-cycle phase does not affect the performance of intense anaerobic-aerobic efforts such as the 800-m run. Furthermore, there is no evidence that the action of PSE is influenced by the phase of the menstrual cycle.

In summary, the research consistently shows that there does not appear to be a performance benefit, either aerobic or anaerobic, from PSE when taken in 60- to 120-mg doses. However, several researchers have found that PSE in large doses of 180 mg offers an ergogenic effect, but the mechanism of action remains a mystery. We were the first to examine the influence of PSE in aerobically trained female athletes participating in an event that has both an aerobic and anaerobic component, the 800-m run. Despite giving the athletes a large relative dose of PSE equal to that of other studies that have shown an ergogenic effect, we found no performance benefit. More research is needed to determine if a large absolute dose (eg, 180 mg) of PSE, regardless of body mass, is needed in order to see ergogenic effects.

**Conclusion and Practical Applications**

The NCAA does not currently restrict the amount of PSE that an athlete can take; however, PSE is specifically banned by WADA if the urinary excretion exceeds 150 μg/mL. Despite female track athletes’ being given doses well above normal therapeutic levels (144 mg ± 17 mg), their 800-m-run times, postexercise heart rates, and postexercise anxiety scores were not affected. Furthermore, Gillies et al noted that urinalysis for PSE concentration postexercise is unreliable due to individual variations in urinary excretion patterns of the drug. Obviously, it is important to have strict doping controls in sport to disqualify and bar athletes who willfully use banned substances to improve performance. However, when the ergogenic effect of a substance and the ability to accurately test for it are questionable, athletes are at risk for being unfairly banned from competition or disqualified. Given that even a large dose of PSE offered no ergogenic advantage in this study and that it is a common ingredient in cold medicine, it seems prudent that more research be done on this drug before restricting it.

**Acknowledgments**

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**References**

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