Effects of Inhaled Salbutamol on Sport-Specific Fitness of Non-Asthmatic Football Players

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Abstract- In this article, we investigated the effectiveness of inhaled salbutamol withtherapeutic dose on the sport-specific performance of non-asthmatic young football players. In a double-blinded, randomised placebo controlled trial with 2-treatment, 2-period crossover design, twenty participants who were non-asthmatic junior professional football players were randomly allocated to two groups. Fifteen minutes before sport-specific fitness testing, each group randomly received 2 inhalations (200 micrograms) of salbutamol or placebo, respectively. After 1 week wash-out period, each participant has tested again, this time with the alternative inhaler. The primary outcomes were the differences between salbutamol and placebo groups in six tests of 7×30-m repeated sprint, Loughborough soccer dribbling, vertical jump, agility, Loughborough soccer passing, 20-m multistage shuttle run. A total of twenty players did two test batteries completely. There was no significant difference between salbutamol and placebo users in the tests [Treatment effect (CI95%); 7×30 sprint: -2.4 (-7.6-2.9), dribbling: -3.8 (-12.2-4.5), vertical jump: -1.2 (-3.7-1.3), agility: -0.4 (-0.9-0.1), passing: 0.2 (-12-12.4), shuttle run distance: -112 (-503.2-279.2)]. Furthermore, no period or carry-over effects were detected. It seems that single therapeutic dose of inhaled salbutamol (200 micrograms) does not appear to improve football related performance.

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Introduction

Elite athletes are at increased risk of asthma and exercise-induced bronchospasm (EIB), particularly in endurance sports (1). Football is the most popular sport all around the world (2) and may be considered as an endurance sport with numerous explosive activities (3). As EIB is more prevalent in sports involving sustained high minute ventilation and football has a high ventilatory demand, football players may have a higher risk compared to other sports with lower ventilation demands (4).

Inhaled β_2-agonists especially salbutamol are the most commonly used drugs for the acute management of asthma and EIB (5). Since 1984, the frequency of athletes consuming inhaled β2-agonists at the Olympic Games has slightly increased (6). Whether this is a real increase because of EIB or a misuse by non-asthmatic athletes because of alleged ergogenic effects remains controversial (7). During the past four decades, anti-doping authorities including the International Olympic Committee (IOC) and World Anti-Doping Agency (WADA) have frequently changed the rules in the approach to the use of inhaled β_2-agonists by athletes. Contributing factors have included the developing knowledge of the effects of inhaled and oral β_2-agonists on human physical performance, possible misuse by some athletes and concerns over side effects on the health of athletes (6). The starting point of these rules can be traced back to 1972 when inhaled Salbutamol was prohibited for the first time at the Olympic Games. Since then, inhaled β_2-agonists have alternately been allowed and prohibited. Currently, inhaled salbutamol is not prohibited, but urinary salbutamol concentration is not permitted to exceed 1000 ng/ml (8-9).

Despite the low incidence of doping among football players (0.4%), (10) more than 20000 doping controls are performed annually on football players showing the great force of authorities to fight against doping in football (11). There are some unpublished reports

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indicating the frequent use of inhaled salbutamol by some non-asthmatic football players for its assumed ergogenic effects. So, the effectiveness of inhaled salbutamol on football players' performance should be addressed.

A systematic review on the effects of inhaled salbutamol on some performance variables has shown no improvement following acute inhalation of salbutamol with therapeutic dose (8). However, one main criticism of the majority of studies examining the ergogenic effects of inhaled salbutamol is that they did not evaluate changes in performance using a sport-specific test with competitive athletes (12). Therefore, the purpose of this study was to examine the effects of inhaled salbutamol on sport-specific fitness parameters of professional football players.

Materials and Methods

The study flowchart is illustrated according to the CONSORT statement (13) (Figure 1).

Participants

Twenty-five professional junior football players gave their informed consent and participated in the trial (Figure 1). Individuals were recruited when they were committed to professional football teams and had a regular and undisrupted training program during the last three months, and did not have any history or symptoms of asthma, exercise-induced bronchospasm (EIB), restrictive pulmonary disease, known cardiovascular disease, viral respiratory disease during the last month, atopy and chest skeletal abnormalities. Exclusion criteria were any musculoskeletal injury or pulmonary disease during the washout period.

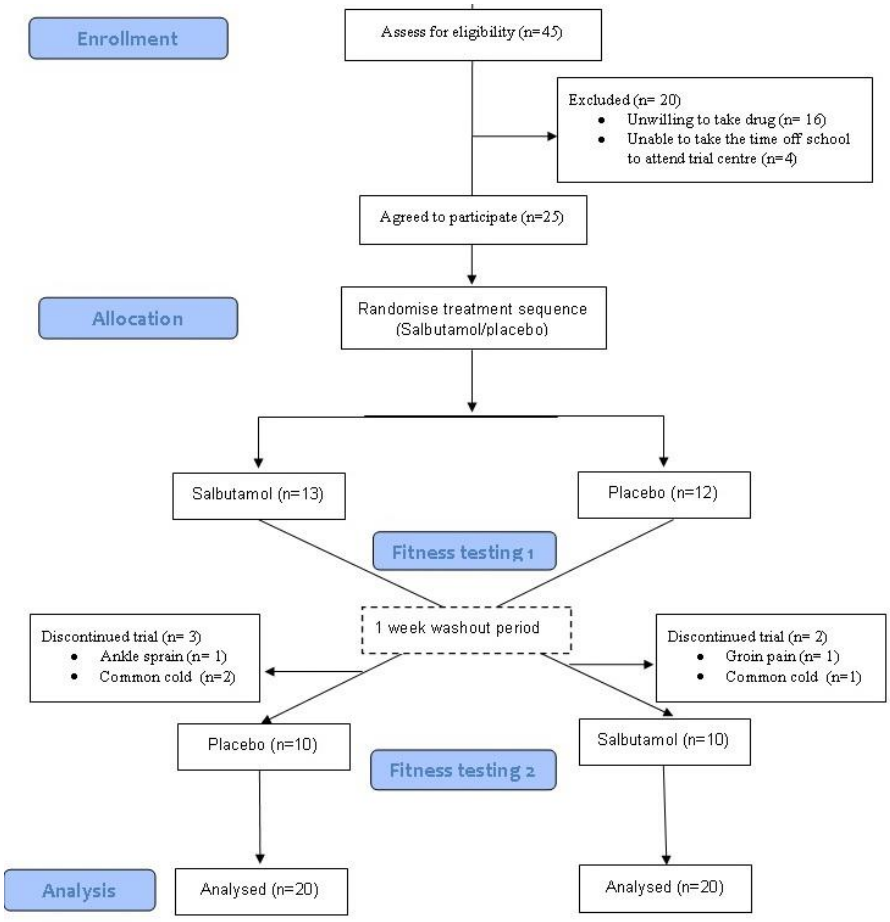

Figure 1. Study flow chart

Design

The study was double-blinded, randomized and placebo controlled with 2-treatment, 2-period (2×2) crossover design. Participants were randomized by an

automated computer-generated scheme after providing informed consent. Ethical approval for this trial has been granted by the Medical Ethics Committee of the Tehran University of Medical Sciences.

Interventions

First, all participants were randomly allocated to two groups. The sequence of using Salbutamol or placebo inhaler for each group was determined. Group 1 and 2 first used inhalers A and B, respectively and after the washout period, inhalers B and A were administered. The participants as well as the study personnel, who delivered the inhalers to the participants and performed all tests, were blinded to the condition allocation throughout the study period. A technician, responsible for preparation of the inhalers, was the only person aware of the randomization code during the trial. She was not involved in other study functions.

Salbutamol (2 nebulised inhalations, 100 micrograms per inhalation) and placebo (2 inhalations), were administered using inhalers with a similar color and appearance supplied by the salbutamol manufacturer company (JaberEbneHayyan pharmaceutical Co.).

In both groups, specific fitness testing was performed 10-30 minutes after use of 2 inhalations.

Then, all players underwent a football-specific fitness battery including 6 stations (7×30 m repeated sprint test,Loughborough soccer dribbling test, vertical jump test, 4-line agility test, Loughborough soccer passing test and 20-m multistage shuttle run test). The participants conduct the tests in order stations 1 through 6. This test battery has been used in other investigations into football performance (14).

After a wash-out period of at least 1 week, all tests were repeated, while the used inhaler changed for each participant (salbutamol instead of placebo, vice versa). Moreover, to reduce the variability of pulmonary functions during the day, both measurements were performed at the same hour in a day. Also, all tests were done in relatively similar air conditions (temperature: 28-30˚ C, humidity: 10-14%, wind speed: 2-3 m/s).

Fitness testing battery included 6 stations as the following:

Station 1

7×30-m repeated sprint test consisted of seven maximal 30-m sprints (with an intermediary split time at 10 m) followed by a 25-s active recovery between sprints, in which the players jogged back to the starting position and awaited the next start command (14-16). (Figure 2) Proper reliability of this test has been shown in field hockey and football players (15-16).

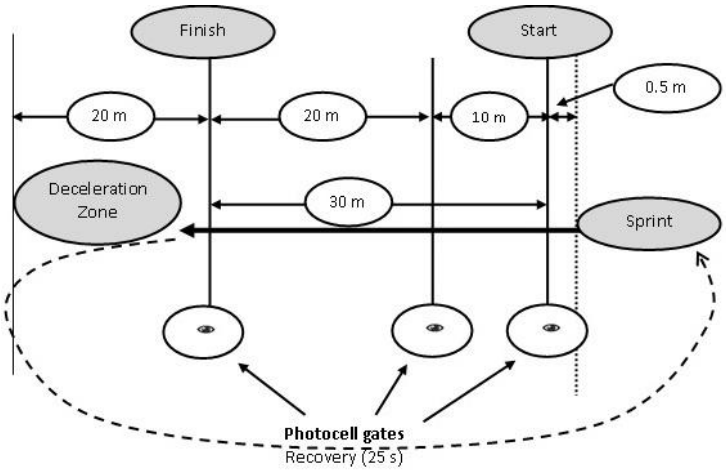

Figure 2. 7 ×30-m repeated sprint test (14)

The sprints were performed on a natural grass running track, and the players wore their favored running shoes. The test was performed with standards described in original articles (14,16). A fatigue index for each trial was computed as the percentage difference between the fastest time and the slowest time.

Station 2

Loughborough Soccer Dribbling Test (LSDT). In this test, the player should dribble as fast as possible, out and back, slaloming between lines of six cones spaced at 3-m intervals from the start point and finish gates defined by cones placed 2.5 m apart (17-18) (Figure 3).

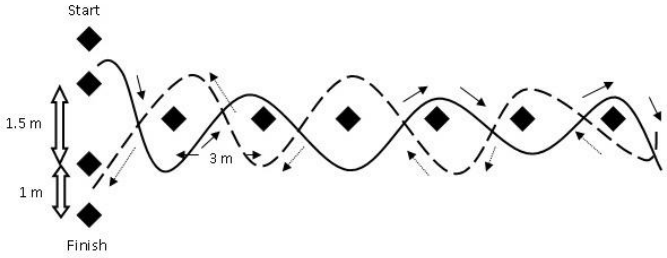

Figure 3. Loughborough soccer dribbling test (14)

Six trials were completed with 1-minute rest between trials. Each run was manually timed with a stopwatch. The sum of the six trials (excluding the rest periods) was used as the final score for this test. This has excellent reported test-retest reliability (18).

Station 3

Vertical jump test; this test involves measuring the difference between the standing reach and the height reached the peak of a vertical jump. To do this test, the player warmed up for at least 5 minutes. Then he chalked the end of his fingertips. The player stood side onto the wall, keeping both feet remaining on the ground, reached up as high as possible with one hand and marked the wall with the tips of the fingers. The player from a static position jumped as high as possible and marked the wall with the chalk on his fingers. The vertical displacement was then calculated on a tape mounted on the wall. Then each player performed three jumps with two minutes of rest in between, and the best jump was selected for analysis (19-21). This test has a very good reliability (20).

Station 4

Four-line agility test. This test was done within an area marked by four parallel lines. The player lay prone with his arms extended to touch the line a (start line). On a verbal command from the technician, the player jumped to his feet and ran 10 m to line B, which he touched with his foot. He then turned and ran 20 m to touch line C with his foot, before turning again and running 10 m back to line A. On touching this line, he turned once again and sprinted 30 m to line D (the finish line). Time was measured manually with a stopwatch. (14,17,22) (Figure 4).

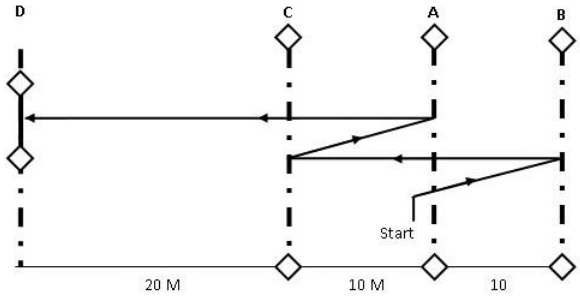

Figure 4. Four-line agility test (14)

Station 5

Loughborough Soccer Passing Test (LSPT). This test was performed in an area marked by tape (Figure 5). Participants were required to complete 16 passes (8 long and 8 short) being made from the marked passing zone to one of the four colored targets that were called out in a randomized order. Time penalties of 2-s were added if the target was missed, if the pass was made outside the passing zone, or if any cone was stuck; a 5-s penalty was added if the bench was missed. Each player completed two trials using a different list of randomizedcolor order for each trial. The total time, in seconds, to complete both trials plus time penalties was recorded for analysis. A good reliability (0.83) for this test has been reported (23) (Figure 5).

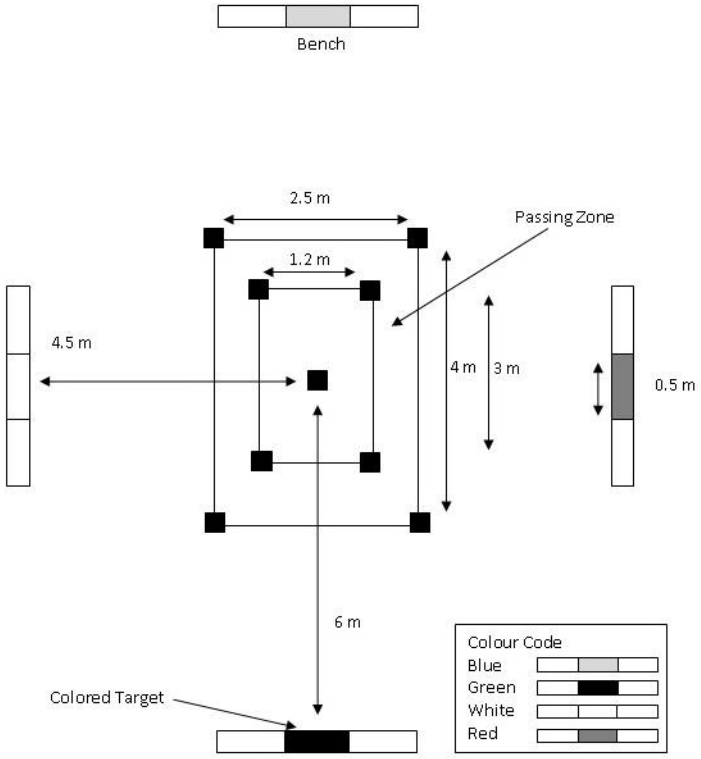

Figure 5. Loughborough soccer passing test (14)

Station 6

20-m multistage shuttle run test (MSRT). This test needed to be performed after completion of all tests for Stations 1–5. The test field had lines marked on the floor that was 20 meters apart with approximately 1.5 meter turning area behind each of the two lines. Cones were placed on the lines to mark out an approximately 1–1.5 meter running lane for each player. Ten players took the MSRT on each occasion, and all had at least a 30-min rest period after finishing the test at Station 5 and before starting the shuttle run. The audiotape with the recorded audio signals for the test was played through a sound system in the field (24-25).

The test was conducted according to the standards explained in other articles (14,24) and covered distance and estimated maximal oxygen consumption (VO2max) were recorded for each player. For each team of players, two MSRTs were run to accommodate all the players. This procedure has a reported reliability of 0.95 (25).

Statistical analysis

We used standard statistical T- tests for the analysis of 2-treatment, 2-period (2×2) crossover design with continuous outcomes (26), as follows: For each outcome variable, the 3 following effects have been estimated (with 95% confidence intervals) and tested using a sequence of two-sample t-tests: (i) the treatment effect, (ii) the period effect, and (iii) the carryover effect, i.e., the period by treatment interaction. Using SPSS Statistics for Windows, Version 21.0 (SPSS Inc., Chicago, Illinois) the level of significance was set at $P<0.05$ for treatment effect. If the carryover effect is significant at 10% level, then only period 1 data will be used to estimate treatment effect (26).

Results

Among 25 recruited junior professional football players, 20 participants [Age: 17.2 (0.8), Weight: 67.30 (6.30), Height: 176.70 (6.35)] finally fulfilled the tests.

No significant difference was shown between test results using salbutamol or placebo (Table 1).

As shown in table 2, no significant treatment effect was found in all tests.

Throughout all trials, participants reported no side effects from inhalation of salbutamol or placebo.

Table 1. Results of different performance tests in players using salbutamol or placebo

Test		Salbutamol	Placebo
Agility (S)		14.94 (0.52)	14.74 (0.66)
Loughborough soccer passing test (LSPT) (S)		62.50 (7.70)	62.60 (10.13)
Vertical Jump (Cm)		46.59 (4.02)	46.00 (4.25)
Loughborough soccer dribbling test (LSDT) (S)		83.35 (7.28)	81.45 (8.10)
7×30-m repeated sprint test	**- Fastest 0-10m (S)**	2.02 (0.13)	2.05 (0.14)
	- FI%0-10m	-15.38 (8.44)	-18.58 (8.87)
	- Fastest 0-30m (S)	4.52 (0.32)	4.50 (0.22)
	- FI% 0-30m	-12.10 (3.31)	-13.27 (5.85)
20-m multistage shuttle run test	**- Distance**	1313 (312.42)	1257 (296.74)
	- VO_2 max (ml/kg/min)	41.23 (5.04)	40.28 (4.95)

Table 2. The treatment effect, period effect and carryover effect of salbutamol against placebo in different tests

Test		Treatment effect (CI95%)	*P*	Period effect (CI95%)	*P*	Carryover effect (CI95%)	*P*
Agility (S)		- 0.40 (-0.86 – 0.07)	0.09	-0.10 (-0.57 – 0.36)	0.64	- 0.09 (-1.14 – 0.97)	0.87
Loughborough soccer passing test (LSPT) (S)		0.19 (-11.97 – 12.35)	0.97	-1.67 (-13.82 – 10.49)	0.77	-1.45 (-14.23 – 11.32)	0.81
Vertical Jump (Cm)		-1.20 (-3.73 – 1.34)	0.33	-2.13 (-4.63 – 0.37)	0.37	-1.73 (-9.20 – 5.74)	0.63
Loughborough soccer dribbling test (LSDT) (S)		-3.81 (-12.16 – 4.53)	0.35	-12.06 (-20.33-3.79)	0.007	-3.43 (-14.12 – 7.26)	0.51
7 ×30-m repeated sprint test	**Fastest 0-10m (S)**	0.06 (-0.13 – 0.25)	0.51	0.02 (-0.17 – 0.21)	0.84	0.03 (-0.16 – 0.21)	0.77
	FI%0-10m	-6.39 (-16.49 – 3.72)	0.19	-3.53 (-13.64 – 6.57)	0.46	8.44 (-4.79 – 21.67)	0.19
	Fastest 0-30m (S)	-0.03 (-0.34 – 0.28)	0.83	0.14 (-0.17 – 0.45)	0.45	0.02 (-0.42 – 0.46)	0.91
	FI% 0-30m	-2.35 (-7.62 – 2.92)	0.36	8.29 (3.02 – 13.56)	0.004	0.02 (-0.42 – 0.46)	0.91
20-m multistage shuttle run test	**Distance (m)**	-112 (-503.15 – 279.15)	0.55	-276 (-667.15 – 115.15)	0.16	120 (-294.10 – 534.10)	0.61
	VO_2 max (ml/kg/min)	-1.91 (-8.34 – 4.53)	0.54	-4.30 (-10.73 – 2.14)	0.18	2.15 (-4.64 – 8.95)	0.51

Discussion

This is the first study to investigate the acute impact of inhaled salbutamol at a single dose of 200 µg (2 inhalations) on sport-specific field tests of elite football players.

The results from the current study suggest that inhaling 200 µg of salbutamol 10-30 minutes prior to each stage of a sport-specific fitness battery did not bear any advantage for athletes in terms ofsport-specific agility, endurance, and anaerobic power, sprint, passing and dribbling parameters. Even more, salbutamol users may encounter some degrees of disadvantage for the majority of measurements, although these are not statistically significant.

Previous studies on the effects of inhaled β_2-agonists (especially salbutamol) on physical performance of non-asthmatic athletes have mostly investigated the standardized laboratory tests such as VO_2max, anaerobic threshold, running time until exhaustion and maximal lactate (12,27-45). Otherwise, they have focused on performance of athletes in other sports such as cyclists, (27,33-38) cross-country skiers, (40-41) triathletes, (28) middle and long distance runners, (42-43) power athletes (44) and athletes of mixed sports disciplines (12,32,39) and they have not addressed actual team sports and field test parameters.

A meta-analysis of the studies has demonstrated no improvement following acute inhalation of up to 800µg of salbutamol on endurance time to exhaustion, VO_2max, peak power, 20 km cycling time-trial and total work during a 30s Wingate test, although results of studies had been contradictory (8).

Only two studies have addressed the effects of inhaled salbutamol on non-asthmatic football players and have shown that high doses of inhaled salbutamol (800 and 1600 µg) may improve the FEV_1 and exert a significant bronchodilatory effect following the use prior to the football-specific treadmill run. However, this study did not observe any improvement in repeated sprint ability despite the improved FEV_1 (46-47).

The results of thecurrent study are in accordance

with the studies in which no difference was observed between inhaled salbutamol and placebo on sports performance of non-asthmatic athletes (12,28,33-44,48).

This study has some limitations. One of our limitations was that our study sample consisted of a relatively small, homogenous group of participants (junior professional football players). Whether the results of the current investigation may be generalized to other populations (such as recreational athletes, those in other age groups) remains to be elucidated.

The second limitation was that we have not objectively confirmed athletes have not asthma or EIB and merely rely on the players' medical history and their self-report. The third limitation was that we could not realize how much of the inhalant was inhaled into the lower airways and how much remained in theupper airway. To minimize this problem, we educated the players regarding the proper technique of inhalation by a medical expert and also used standard nebulizers to facilitate the delivery of inhalant into the lower airways. Furthermore, we have only examined single dose of salbutamol (200 µg). Athletes can take up to 1600 µg (16 inhalations) in one day. However, due to ethical considerations for using this supratherapeutic dose and concerns regarding the potential side effects, we just studied this minimal dose.

In this study, no significant difference was shown between salbutamol and placebo users in sport-specific tests of football players. Accordingly, it seems that single therapeutic dose of inhaled salbutamol actually may not have any beneficial effect on sports performance of elite football players. Future research should be directed to the effect of oral or supratherapeutic doses of inhaled salbutamol on the sport-specific performance of football players.

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