

Beta 2 Agonist: Therapeutic Use Exemption, Misuse in Sports and its Adverse Effect on Health

Jaipal

PET, Jawahar Navodaya Vidyalaya-Butana, Distt-Sonepat, Haryana (India)

Abstract: ***Background:** The special approaches by the International Olympic Committee (IOC) had adapted to beta2-agonists and the implications for athlete, these are reviewed by a former Olympic team physician who later became a member of the Medical Commission of the International Olympic Committee. Steadily increasing knowledge of the effects of inhaled beta2-agonists on health is concerned with the fact that oral beta2-agonists may be anabolic, and rapid increased use of inhaled beta2-agonists by elite athletes has contributed to the changes to the IOC rules. Since 2001, the necessity for athletes to meet IOC criteria has resulted in improved management of athletes. The prevalence of beta-2 agonist use by athletes mirrors the known prevalence of asthma symptoms in each country, although athletes in endurance events have the highest prevalence. The regulations for doping control prohibit the use of beta2 agonist bronchodilators (salbutamol, salmeterol, formoterol, and terbutaline) unless the subject follows the procedure of therapeutic use exemption (TUE). **Methods:** Analytical methods was used for this article by reviewing relevant publications, primarily based on the online sports medicine journals available on Internet, Wikipedia, Elsevier, PubMed, Google Scholar, World Anti Doping Agency and National Anti Doping Agency online sources. **Objective:** This review provides an overview on therapeutic use exemption and misuse in Sports and its adverse effect on health, and to highlight that really this drug is drug should used only for asthma and bronchodilator treatment. **Conclusion:** Use of Beta -2 Agonist is in the list of prohibited substances of World Anti-Doping Agency's (WADA); the use of Beta -2 Agonist is banned both in competition and out of competition and Beta - 2 Agonist are usually tested by authorized anti-doping laboratories of WADA. Strict vigilance of fair play should be pursued, but excessive control can lead to situations of inequality for asthmatic athletes such that a third of athletes cannot be treated with beta2 agonists. Therefore under current regulations, asthmatic athletes are often denied the most effective therapeutic option. Beta 2 Agonist should be use under the medical condition otherwise it badly affects the health of user.*

Keywords: Asthma, Beta-2 agonists, Bronchial hyper responsiveness, Doping, Sports, Health

1. Introduction

The Beta-2 agonist is a family of medicines that are actually used in a variety of fields of medicine. In fact they're most frequently used as medications to treat asthma and bronchial disorder. There are two different types of beta receptors. One is the beta-1 receptor which is found in the brain but also in the heart and second is the beta-2 receptor which is found in the brain but also in the lungs and on blood vessels. So there are a variety of different types of beta receptors. The differences stem from selectivity in which beta receptor these drugs block, whether it's the beta-1 or beta-2 or both receptors. And there are clinical situations where one might want to have that selectivity. In psychiatry the most commonly used beta blocker is propranolol, or inderol, which is a non-selective beta blocker, so it blocks both beta-1 and beta-2 receptors. And beta blockers tend to be used most frequently in situations where there is performance anxiety or public speaking anxiety situation and they work primarily by actually blocking the physical manifestations of anxiety, so they have very little effect on the emotional sense of anxiety. But what they do is help with things like tremors and palpitations and shortness of breath, and sweating and the physical symptoms people experience when they're in anxiety inducing situations. So in that way they can actually make people much more functional, much more able to tolerate these types of situations that cause a lot of anxiety for them.

Food and Drug Administration (FDA) (2005) alerted healthcare professionals and patients that several long-acting bronchodilator medicines have been associated with possible increased risk of worsening wheezing in some people, and requested that manufacturers update warnings in their existing product labeling. Cornell University & Stanford

University (2006) researchers reported that a meta-analysis they conducted found that "regularly inhaled beta-agonists increased the risk of respiratory death more than twofold, compared with a placebo," while used to treat chronic obstructive pulmonary disease (COPD). In 2008, a panel of experts convened by the Food and Drug Administration (FDA) voted to ban the drugs Serevent and Foradil from use in the treatment of asthma. It was shown that, when these two drugs are used without steroids, they increase the risks of more severe attacks. The experts said that two other much more popular asthma drugs containing long-acting beta-agonists.

All beta-2 agonists are prohibited except the following:

Salbutamol (maximum 1600 micrograms over 24 hours),
Formoterol (maximum 36 micrograms over 24 hours)
Salmeterol when taken by inhalation in accordance with the legal medically advice recommended therapeutic regime. The presence in urine of salbutamol in excess of 1000 ng/mL or formoterol in excess of 30 ng/mL is presumed not to be an intended therapeutic use of the substance and will be considered as an adverse analytical finding unless the Athlete proves, through a controlled pharmacokinetic study, that the abnormal result was the consequence of the use of the therapeutic inhaled dose up to the Beta-2-Agonists are dilators which cause dilation of vessels by relaxing the smooth muscle surrounding them.

1.1 Methodology

This survey is an analysis of literature on of up to now research conducted on Beta-2 Agonist in sports medicine. The analysis involves a dozen scientific databases, examined in order to find out the health hazard approach in sports. The

gathered data are supplemented and verified from the online web source of World Anti Doping Agency, National Anti Doping Agency and National Dope Test Laboratory.

1.2 Medical Uses of Beta-2-Agonists:

Inhaled forms of Beta-2-agonists (including salmeterol, salbutamol, formoterol and terbutaline) are used for the treatment of Asthma and exercise-induced bronchospasm (EIB). Injected forms are most commonly used in the prevention of premature labour, as they act to relax the smooth muscle of the uterus and so inhibit contractions. Beta-2-adrenoreceptor agonists are drugs that act as bronchodilators. The drugs stimulate the airways in the lungs to open wider the bronchi, permitting more air to pass.

Certain beta-2 agonists were used illegally in intensive livestock farming before coming to be misused in sports as well. When administered in high doses, these substances promote protein synthesis, which in the case of animals resulted in an increase in the proportion of muscle mass to fat mass. Athletes using these substances for doping anticipate similar effects, as well as a short-term enhancement of performance due to the dilation of bronchial passages. Scientific research has not substantiated these expectations, however. Many beta-2 agonists are prohibited in sports. In some cases therapy for medical reasons must be approved by applying for a therapeutic use exemption (TUE). The drugs are especially helpful to asthmatics, who can suffer from insufficient air supply to the lungs due to narrowing of the bronchi. Athletes who take beta-2 agonists can also improve their athletic performance, because of the increased infusion of air. However, this type of athletic enhancement is illegal.

Beta-2 agonists such as salbutamol, salmeterol, terbutaline, and Eformoterol mimic the effects of adrenaline and noradrenaline that are naturally produced in the body. The latter drugs stimulate changes in the body such as bronchial dilation, which help prepare the body to react for action (the "fight or flight" reaction). When beta-2 agonists enter the lung bronchi, they interact with a particular receptor on the surface of the lung tissue. It is this agonist interaction with beta-2 receptors that stimulates the expansion of the bronchi. The drugs are typically delivered to the lungs via an inhaler, although they can be delivered via an injection, as a vapor produced by a nebulizer, as a tablet, or in syrup form.

Bronchodilation is maintained for various lengths of time, depending on the beta-2 agonist used. For example, salbutamol stimulates dilation within 30 minutes, with maximum dilation reached three or four hours later. Eformoterol acts more quickly, with dilation occurring within three minutes after application, and maximum dilation reached after one to two hours. Both agonists are long lasting, with dilation persisting for approximately 12 hours. Other beta-2 agonists produce effects for shorter time periods.

2. Misuse in Sports

Many athletes use the Beta-2 agonists to increase the oxygen intake. Beta-2 agonists such as salbutamol have become a

concern in sports because the high doses of this drug can act as an anabolic agent to promote gain in weight, mainly in the form of muscle in the body. However, this increased strength and the increased oxygen intake comes with a risk of health damage. Beta-2-adrenoreceptor (beta-2) agonists are drugs that act as bronchodilators. The drugs stimulate the airways in the lungs to open wider, permitting maximum air to pass.

Before coming to be misused in sports as well as certain beta-2 agonists were used illegally in intensive livestock farming. When administered in high doses, these substances promote protein synthesis, which in the case of animals resulted in an increase in the proportion of muscle mass to fat mass. Athletes using these substances for doping anticipate similar effects, as well as a short-term enhancement of performance due to the dilation of bronchial passages. Scientific research has not substantiated these expectations, however. Some beta-2 agonists are prohibited in sports. In some cases therapy for medical reasons must be approved by applying for a therapeutic use exemption (TUE).

The drugs are especially helpful to asthmatics athletes, who can suffer from insufficient air supply to the lungs due to narrowing of the bronchi. Athletes who take beta-2 agonists can also improve their athletic performance, because of the increased infusion of air. However, this type of athletic enhancement is illegal.

3. Adverse Effect of use of Beta-2 Agonist

Along with its desired effects, these drugs may cause some unwanted effects which may be health hazards. Although not at all of side effects may occur, if they do occur they may need medical attention.

3.1 Fatigue and Dizziness

The athletes may experience fatigue and dizziness while taking beta blockers. You may just seem more tired and sleepy than usual. Be careful if you drive or do anything that requires you to be awake and alert, states. Avoid drinking alcohol while taking this drug; it may increase drowsiness and dizziness. Fatigue and dizziness may subside over time after your body has some time to adjust to your medication.

3.2 Shortness of Breath

The athletes may experience shortness of breath while taking this drug. You may notice that you are out of breath while doing daily activities. Beta 2 agonist generally isn't used in people with asthma because of concerns that the medication may trigger severe asthma attacks. Due to use of these drugs shortness of breath becomes bothersome and impacts your daily lifestyle.

3.3 Effect on Reproductive System

Adverse effects of beta 2 agonist include a decreased sex drive (low libido), impotence. If these adverse effects become intolerable, contact your healthcare provider. They may be able to switch you to a different medication or prescribe something to alleviate your symptoms.

3.4 Major cardiac Effects

Beta-2 agonist blockade include the precipitation or worsening of congestive heart failure, and significant negative chronotropy. Increased peripheral vascular resistance, induced by nonselective beta blockers, also may contribute to the decline in myocardial function in this setting. On the other hand, drugs with intrinsic sympathetic activity (ISA), such as pindolol, may be less likely to impair myocardial function.

3.5 Other Adverse Effects

In rare cases, a serious allergic reaction may occur while using beta-2 agonist medications. Symptoms include hives, difficulty breathing and swelling of your face, lips, tongue or throat, reports. Other serious effects include depression; fainting, rapid heartbeat and jaundices. If any athletes experience any of these symptoms, seek immediate medical attention.

4. Some other adverse effect of Beta 2 Agonist

<i>Adverse effect of use of Beta-2 Agonist</i>
<ul style="list-style-type: none"> • Palpitations • Muscle cramps • Headaches • Dizziness and Nausea • Mood disorders • Sweating • Anxiety • Arrhythmias • Tremor (usually of the hands) • Weakening of the heart muscle, • Cardiac arrhythmia and angina pectoris • Uncontrollable muscle spasms • Increased glucose levels in the blood • Low level of blood Potassium • Nervousness • Insomnia • Tachycardia

5. Conclusion

In the sport use of Beta-2 Agonist is in the list of prohibited substances of World Anti-Doping Agency's (WADA); the use of Beta-2 Agonist is banned both in competition and out of competition and Beta - 2 Agonist are usually tested by authorized anti-doping laboratories of WADA. Strict vigilance of fair play should be pursued, but excessive control can lead to situations of inequality for asthmatic athletes such that a third of athletes cannot be treated with beta-2 agonists. Therefore under current regulations, asthmatic athletes are often denied the most effective therapeutic option. Beta 2 Agonist should be use under the medical condition otherwise it badly affects the health of user.

Reference

- [1] Abrahams, A. (1958), The Use and Abuse of Drugs by Athletes, British Journal of Addiction, 55 (1): 23–7.
- [2] Anderson S D, Fitch K, Perry C P. et al (2003) Responses to bronchial challenge submitted for approval to use inhaled beta-2 agonists before an event at the 2002 Winter Olympics. J Allergy Clin Immunol 2003. 11145–50.50. [PubMed]
- [3] Anderson S D, Brannan J D.(2003) Methods for indirect challenge tests including exercise, eucapnic voluntary hyperpnea and hypertonic aerosols. Clin Rev Allergy Immunol, 2003. 2463–90.90. [PubMed]
- [4] Beta-2 adrenoceptors agonists and the Olympic Games in Turin. www.olympic.org (accessed 15 Nov 2013)
- [5] Brukner, P. and K. Khan. (1993) Clinical sports medicine. Sydney: McGraw Hill, 1993.
- [6] Bagatell, C.J. and Bremner, W.J. (1996) Androgens in men – uses and abuses. New England Journal of Medicine 334, 707-714.
- [7] Brown, W. M. (1980). Ethics, Drugs and Sport. Journal of the Philosophy of Sport VII: 15-23.
- [8] Bowler, Clayton (2008). Michael Phelps Doping with Dope: Pictures Surface of Phelps Doing Bong Hits. Retrieved from Bungalow Bill Web site on 12/11/2013: <http://bungalowbillscw.blogspot.com/2009/02/michael-phelps-doping-with-dope.html>
- [9] Caruso J F, Hamill J L, De Garmo N. (2005) Oral albuterol dosing during the later stages of a resistance exercise program. J Strength Cond Res 2005. 19102–107.107.[PubMed]
- [10] Celli BR, et al. (2008). Effect of pharmacotherapy on rate of decline of lung function in chronic obstructive pulmonary disease: Results from the TORCH study. American Journal of Respiratory and Critical Care Medicine, 178(4): 332-338.
- [11] Dickinson J W, Whyte G P, McConnell A K. et al (2005) Impact of changes in the IOC-MC asthma criteria: a British perspective. Thorax 2005. 60629–632.632.[PMC free article] [PubMed]
- [12] Farland MZ, Peters CJ, Williams JD, Bielak KM, Heidel RE, Ray SM. (2013) Beta-blocker use and incidence of chronic obstructive pulmonary disease exacerbations. Ann Pharmacother. 2013;47:651-656
- [13] Fleck S J, Lucia A, Storms W W. et al (1993) Effects of acute inhalation of albuterol on sub maximal and maximal VO₂ and blood lactate. Journal of Sports Med 1993. 14239–243.243.[PubMed]
- [14] G Dunnavan and G A Mitchell and (2008) Role of {beta}-Adrenoceptors Signaling in Skeletal Muscle: Implications for Muscle Wasting and Disease, Physiol. Rev. April 1, 2008 88:729-767
- [15] Goubault C, Perault M C, Leleu E. et al (2001), Effects of inhaled salbutamol in exercising non-asthmatic athletes. Thorax 2001. 56675–679.679. [PubMed]
- [16] Rasmussen F, Taylor D R, Flannery E M. et al (2002) Risk factors for airway remodeling in asthma manifested by a low post bronchodilator FEV1/vital capacity ratio: a longitudinal population study from childhood to adulthood. American Journal of Respir Critical Care Med 2002. 1651480–1488.1488. [PubMed]

- [17] Ramanujan K. (2006) Common beta-agonist inhalers more than double death rate in COPD patients, Cornell and Stanford scientists assert. Chronicle Online. June 29, 2006. Available at: <http://www.news.cornell.edu/stories/June06/Salpeter.COPD.kr.html>. Accessed Nov 30, 2013.
- [18] Lemmer JT, Fleck SJ, Wallach JM, et al. (1995), The effects of albuterol on power output in non-asthmatic athletes. *International J Sports Med* 1995; 16:243–9.
- [19] Norris SR, Petersen SR, Jones RL. (1996), The effect of salbutamol on performance in endurance cyclists. *Eur J Appl Physiol Occup Physiol* 1996; 73: 364–8.
- [20] Morton AR, Joyce K, Papalia SM, et al. (1996), Is salmeterol ergogenic? *Clinical Journal of Sport Med* 1996; 6:220–5.
- [21] McDowell SL, Fleck SJ, Storms WW. (1997) The effects of salmeterol on power output in non asthmatic athletes. *J Allergy Clin Immunol* 1997; 99:443–9.
- [22] Carlsen KH, Hem E, Stensrud T, et al. (2001) Can asthma treatment in sports be doping? The effect of the rapid onset, long-acting inhaled beta2-agonist formoterol upon endurance performance in healthy well-trained athletes. *Respir Med* 2001; 95:571–6.
- [23] Stewart IB, Labreche JM, McKenzie DC. (2002) Acute formoterol administration has no ergogenic effect in non asthmatic athletes. *Med Sci Sports Exercise* 2002; 34:213–7.
- [24] Sporer BC, Sheel AW, McKenzie DC. (2008) Dose response of inhaled salbutamol on exercise performance and urine concentrations. *Med Sci Sports Exercise* 2008; 40:149–57.

World Wide Web Source

- [1] <http://www.nada.at/en>
- [2] <http://www.teachpe.com/drugs/doping.php>
- [3] <http://www.ncbi.nlm.nih.gov>
- [4] <http://www.doping-prevention.sp.tum.de>
- [5] <http://www.wada-ama.org>
- [6] <http://www.ndtindia.com>
- [7] <http://www.bjsportmed.com>
- [8] <http://www.olympic.org/medical.html>
- [9] <http://www.physsportsmed.com/journal.html>
- [10] <http://www.fims.org>
- [11] <http://www.nsmi.org.uk/limks.html>
- [12] <http://www.ajsm.org>
- [13] <http://www.mspweb.com/orgs.html>
- [14] <http://www.healthcenter.org.uk/hc/library/sports.htm>

Author Profile



Jaipal received the Master Degree in Physical Education (**Gold Medal**) from MDU-Rohtak and M.Phil degrees in Physical Education from KUK, PG Diploma in Sports management from Algappa University, D.Y.Ed (Diploma in Yoga Education) from Amravati University and Qualified UGC-NET in Dec 2004. He is now working on the Post of Phy Edu Teacher in Jawahar Navodaya Vidyalaya-Butana, Distt-Sonepat (Haryana) under the Ministry of Human Resource Development, Government of India.