Professional paper

THERAPEUTIC EXEMPTION IN SPORTS AND DRUG ABUSE AIMED AT IMPROVING SPORTS PERFORMANCE^{1 2}

UDC: 796-05:615.035.3 615.2.035.3 DOI: 10.5937/snp2102099S

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Abstract: Athletes, like ordinary people, have the right to get sick and be treated, but they are not allowed to use most of the drugs that are commonly prescribed to other people, because they are on the list of prohibited doping agents. Therefore, the World Anti-Doping Agency (WADA) has introduced the "Therapeutic Use Exemptions" (TUEs), which are submitted when there is an indication for the use of substances and methods that are on the list of prohibited substances. This "exemption" serves to relieve the athlete from the danger of being declared positive during or outside a competition. In recent years, permits for the therapeutic use of illicit drugs for treatment have been increasingly sought, and the aim of this paper is to investigate the causes of seeking TUEs, as well as whether there is abuse of TUEs in order to improve athletic ability and results. Descriptive method and theoretical analysis were used for the collection, classification and analysis of the targeted research, and the data used for the research was collected with the help of Google Scholar, PubMed and KoBSON search engines. Treatment of sports injuries is the most common cause for which athletes seek TUE approval. The second on this list are stimulants, which are used for the treatment of the attention deficit hyperactivity disorder (ADHD) in athletes, while the third place is occupied by beta blockers for the chronic obstructive pulmonary disease.

Keywords: doping, therapeutic exemption, glucocorticoids, stimulants, beta blockers

INTRODUCTION

Doping in sports, in simple terms, represents any application of substances or methods that are prohibited, which leads to the improvement of the athlete's results. According to the WADA definition, some of the violations

¹ Paper received: 23 April 2021, edited: 20 May 2021, accepted for publication: 27 May 2021.

The paper was presented in the form of an oral statement on 14 May 2021 at the Fourth International Scientific Conference "Health, Sports, Recreation", which was held in Belgrade, organized by the College of Sports and Health.

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of anti-doping rules are the following: presence of prohibited substances or their metabolites, or metabolites in the body sample of athletes; use or willingness to use prohibited methods; possession of illicit substances or methods, as well as the sale and distribution of illicit substances; prescribing a prohibited substance to any athlete as well as assisting in doping, encouraging, aiding, abetting or any other type of anti-doping rule violation (WADA, 2021b).

The first synthetic testosterone was created in the 1930s. However, it is believed that a serious fight against doping began only after the tragic events that occurred on the sports fields. The first recorded tragic event occurred in 1960 at the Olympic Games in Rome, when an athlete died on the field due to the use of amphetamines. It was followed by an accident at the Tour de France cycling competition in 1967, when one of the competitors died during the race.

The above facts were just one of the reasons for the International Olympic Committee (IOC) to adopt the first anti-doping rules in 1967 and form a medical commission to implement them. These were the beginnings of the fight against doping, which was not too successful since during the 1970s, many Eastern Bloc countries systematically used doping for their athletes, with East Germany in the lead (Franke & Bedrendonk, 1997). The problem increased from decade to decade, and it was not until 1999 that the World Anti-Doping Agency was formed, which started a serious and extensive fight against doping in sports.

THEORETICAL APPROACH TO RESEARCH

Definition and application of TUE in sports

The question is what happens when athletes get sick, injured or have a chronic illness that requires certain therapy? Athletes, like other people, have the right to get sick and be treated, but what sets them apart is that they are not allowed to use drugs that are on the anti-doping list without prior permission.

Treatment with drugs that are on the list of banned substances is not justified sometimes. The request for "Exemption for Therapeutic Use in Sports" is submitted when there is an indication for the use of substances and methods that are on the list of prohibited drugs, and serves to relieve the athlete from the danger of being declared doping positive during or outside a competition (Gerrard & Pipe, 2017).

All athletes are entitled to a TUE, but there are clear indications for its approval. When an athlete becomes ill or injured and therefore has to take certain drugs that are on the list of prohibited substances, the athlete's doctor must first submit a request to the commission of the competent anti-doping agency for approval of a TUE. There is a large number of drugs that are used to treat appropriate diseases and which, if used in a healthy athlete, can serve as a means to improve athletic ability. Most often, such drugs are testosterone, insulin, diuretics, beta 2 agonists, psychostimulants, glucocorticosteroids and the growth hormone. It is obvious that the therapeutic effects of these drugs are often abused by athletes, first in the form of a faster recovery from injury or illness, and also for the purpose of improving their abilities. Therefore, there are appropriate criteria for submitting and approving TUEs in sport according to the Ordinance for Approving TUEs that was issued by the WADA:

- 1. There is no adequate substitution for a prohibited substance or method used for treatment of a particular condition;
- 2. The athlete's health condition is verified by valid documentation and is diagnosed in accordance with international standards;
- 3. Not taking prohibited doping substances or methods during treatment would significantly worsen the health condition of the athlete;
- 4. The necessity of the use of prohibited substances and/or methods is not entirely or partially a consequence of their previous non-therapeutic use;
- 5. The therapeutic use of substances or methods will not contribute to the improvement of the athlete's competitive abilities other than those expected after the end of treatment.

According to the WADA regulations, an athlete may request the approval of a TUE from a national anti-doping agency (if the athlete competes only at the national level), which forms a committee for granting therapeutic exemptions that may allow or prohibit the use of appropriate drugs for therapy or diagnosis. However, if the athlete competes in international competitions, the TUE should be approved by the international organization under whose jurisdiction the athlete competes (e.g.: in football – UEFA or FIFA, in basketball – FIBA, in athletics – IAAF, etc.) and the TUE board of major competitions such as the World and European Championships and the Olympic Games. The WADA has the right to review the decisions of both national and international TUE committees, and

establish whether they meet the WADA standards. The WADA makes the final decision regarding the justification of the use of the appropriate drug for therapeutic purposes when it is on the list of doping-positive substances.

An athlete must request a TUE before a competition, within 30 days before performing.

Of course, there is also a case of a retroactive request for a TUE, but only in the case of the use of prohibited means for therapeutic purposes in situations of emergency and sudden injuries at a competition, e. g. when the medical team is tasked with returning the athlete to the field as soon as possible. For these purposes, corticosteroids are most often used as extremely potent anti-inflammatory drugs (Fitch, 2012). According to the Anti-Doping Agency of Serbia, "an athlete's medical condition must be diagnosed in accordance with the existing international standards and good medical practice guidelines prescribed by the WADA, which are available on their official website" (WADA, 2021a).

In order to prevent the misuse of drugs that are on the list of banned doping substances, the WADA offers an example of diseases/medical conditions that can be treated with drugs and methods that are otherwise prohibited, including whether their use in such cases is justified by medical diagnosis. Of course, their implementation requires the approval of the TUE by the competent committee. Otherwise, an athlete who uses some of the drugs for treatment that is on the list of prohibited doping substances, without a TUE approval, risks getting a doping-positive result in one of the competitions during the season (Table 1).

Table 1. List of diseases/medical conditions for which there is a justified need for a TUE and drugs from the list of doping-positive substances that can be used to treat these diseases

DISEASE / MEDICAL CONDITION	Prohibited substance for which a TUE is required
musculoskeletal system injuries	glucocorticosteroids and narcotics
asthma	beta-2 agonists, glucocorticosteroids
diabetes mellitus	insulin
chronic inflammatory bowel disease	glucocorticoids
hypogonadism in men	testosterone, growth hormone
kidney transplantation	beta blockers, erythropoietin, glucocorticosteroids
arterial hypertension	diuretics, beta blockers
attention deficit disorder	amphetamines, methylfendidate
narcolepsy and catalepsy	psychostimulants
growth hormone deficiency in adults	growth hormone, gonadotropin
growth hormone deficiency in children	recombinant growth hormone

Source: Anđelković, 2016, p. 394

STUDY OBJECTIVES

To review the literature in order to define the reasons for seeking TUEs by athletes.

To review the literature in order to examine the existence of potential abuse of TUEs for the purpose of achieving better sports results.

STUDY HYPOTHESES

H1: Athletes seek TUE approval for usage of drugs that are on the list of banned substances and which are intended for the treatment of sports injuries.

H2: Athletes may abuse TUE approval in order to improve athletic ability, without a clear medical diagnosis or with diagnosis lacking sufficient medical evidence.

MATERIAL AND METHODS

The paper is based on a review of the available literature with the aim to define the reasons for seeking TUEs by athletes and to evaluate the potential abuse of the TUE method for the purpose of improving athletic ability.

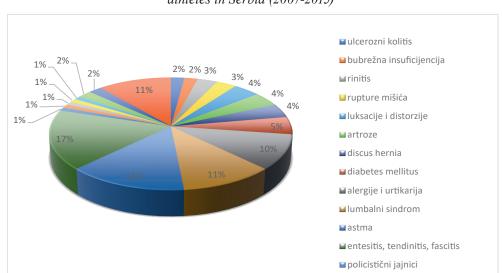
PubMed's database, KoBSON, and the Google search engine were used to search for scientific studies and papers, as well as Internet articles. Keywords used for the search were: doping, sports, substance ban, TUE, WADA.

RESULTS

According to the data from the Anti-Doping Agency of the Republic of Serbia (ADAS), Serbian athletes requested only 200 TUEs between 2007 and 2015. For example, the German Anti-Doping Agency processes 4,500 of these requests annually, which indicates the constant need to educate our athletes, their teams and their doctors about the existence and implementation of this method in order to prevent unwanted doping positive results (Anđelković, 2016).

For example, there is a number of unintentional doping-positive cases of Serbian athletes due to the use of drugs for therapeutic purposes, which are on the list of banned substances. Athletes were not aware that these drugs were banned in sports and that they could have prevented a positive doping result by seeking a TUE or by getting advice regarding a possible change in the drug, using instead a drug that is not on the list of banned substances. The most common doping-positive cases in our country were related to the use of cold medicines, which contained pseudoephedrine: Defrinol, Aspirin Complex, Rinasec, Caffetin Cold. In other athletes, for example, the usage of diuretics prescribed by doctors for the treatment of hypertension has been reported to have led to doping-positive results (Anđelković, 2016).

Of the 200 TUE applications, 66% were submitted by men, while 33% of applications came from female athletes. TUE applications were most often related to basketball, football, rowing, wrestling and water polo. Soft tissue injuries were the most dominant reason for seeking a TUE approval (17%). Diagnoses of asthma and the lumbar syndrome hold the second and the third place in terms of the number of TUE applications with a frequency of 14% and 11%, respectively (Graph 1). Glucocorticoids were the most commonly used drugs due to which athletes had to file a TUE application (over 50% of all TUE reports). Betamethasone, dexamethasone and methylprednisolone were most often prescribed within this group of drugs for the treatment of inflammatory soft tissue processes, such as enthesitis, tendinitis, fasciitis and bursitis. The second place is occupied by beta 2 agonists, such as salbutamol and formoterol, which are used to treat asthma (Anđelković, 2016; Dikić, 2006).



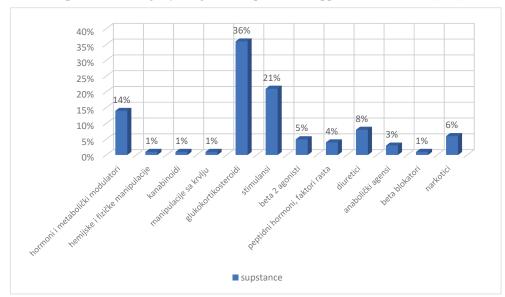
Graph 1. Representation of medical conditions (in percentages) for which TUE approval was requested by athletes in Serbia (2007-2015)

Source: Anđelković, 2016, p. 398

Analysis of TUE applications worldwide

The available statistics on the WADA reports worldwide, maintained by the WADA, indicate that glucocorticoids – just like in Serbia – are the most commonly used drugs for which athletes and their federations have sought TUE approvals (WADA, 2021a). The reason for the use of glucocorticoids are also injuries, i.e. inflammatory conditions of the musculoskeletal system. Unlike athletes in Serbia, at the global level athletes report the use of stimulants much more often and ask for TUE approvals. The diagnosis due to which stimulants are most often used is attention deficit disorder, which has not been noticed among Serbian athletes. On the other hand, the use of beta 2 agonists in world sports is much less frequent than in Serbia (Graph 2).

Of the total number of reported TUEs, only 5% relate to the use of beta 2 agonists, in contrast to 14% of cases reported in Serbia. Additionally, it was said earlier that the number of TUE applications in Serbia is significantly smaller than in other European countries and the rest of the world, and that Germany processes up to 4,500 TUE applications annually. Also, the WADA statistics point to the fact that TUE approvals are most often requested in five different sports: cycling, athletics, triathlon, swimming and skiing, and that the number of TUE applications is growing each year.



Graph 2. Percentage of drugs that require TUE approval worldwide (2017)

Source: Anđelković, 2016, p. 398

Use or abuse of drugs from list of banned substances

It was previously stated that TUEs are most often required for the use of glucocorticoids, stimulants and beta 2 agonists. There are numerous examples of abuse of these and other drugs from the list of banned substances by athletes to achieve the best possible athletic results.

Both in Serbia and globally, glucocorticoids are the most commonly used drugs for therapeutic purposes which are on the list of banned substances by the WADA. There are numerous examples of athletes who have reported a TUE for corticosteroid use. American tennis player Serena Williams has repeatedly reported TUEs due to the use of this drug for the treatment of musculoskeletal injuries (Tandon, 2018).

Also, Spanish tennis player Rafael Nadal, has repeatedly used this type of treatment to treat chronic pain in both knees (Tandon, 2016). Although the above athletes had received approval of TUEs for the use of corticosteroids, the question of medical justification for the use of this type of drugs as therapy and their abuse has often been raised in terms of returning the athlete to the training process as soon as possible without thinking about the potential harmful effects of this type of therapy (Acevedo & Beskin, 1998; Pigozzi et al., 2012).

The most famous athletes who were doping-positive for the amphetamine stimulant were cyclist Jan Ullrich, winner of the Tour de France race in 1997 (Richardson, 2004), Brazilian footballer Ricardo Lucas (FIFA, 2008) and American basketball player Jordan Riley (USADA, 2021). Several athletes tested positive for modafinil, a

stimulant used for treatment of narcolepsy, on retested samples from 2003 (this drug has been on the WADA list of doping-positive substances only since 2004), when the use of this drug was not known.

These athletes did not seek a TUE approval for the use of these drugs for therapeutic purposes and therefore the intention of the athletes to use them as doping was evident. On the other hand, there is a large number of athletes who have reported TUEs due to a diagnosis of attention deficit disorder or sleep disorder so that they can use stimulants for therapeutic purposes. One of the most famous American gymnasts, Simone Biles, has been using stimulants for the treatment of this disease since childhood due to the diagnosis of attention deficit hyperactivity disorder (ADHD). As a result of the continuous application of stimulants, the regularity of the large number of gold medals she won at world championships and the Olympic Games has been called into question.

Although the use of these drugs in every competition was justified by the approved TUEs, the gymnast repeatedly had to justify her diagnosis and the therapy she was taking for treatment (Crawford, 2016). The big question remains whether the approved TUEs were medically justified or whether there was an intention behind them to use the drugs as stimuli to win medals more easily. It is also known that the most famous American swimmer and multiple Olympic medal winner, Michael Phelps, also suffers from this disorder and that he used stimulants for therapeutic purposes. Additionally, at the Olympic Games in Brazil, two American basketball players (gold medal winners) also had a TUE approved for the use of stimulants due to the ADHD diagnosis (Crawford, 2016). After reviewing such data from the literature, there is always a suspicion of potential abuse of the TUE method and the question arises whether such a large number of top athletes really suffer from this medical diagnosis.

Regarding the use of beta-2 agonists, i.e. bronchodilators for the treatment of asthma and other obstructive pulmonary diseases, there are also numerous examples of TUE applications. Famous Danish swimmer, Rikke Moller Pedersen, winner of Olympic medals, has repeatedly reported TUEs due to the use of the drug terbutaline for treatment of asthma (LetsRun.com, 2016). The case of the Italian cyclist Alessandro Petacchi speaks volumes about the potential abuse of this type of medicine. Thanks to the diagnosis of asthma, Petacchi had an approved TUE for the use of salbutamol, however, the level of this substance in his urine was 320 mg/ml higher than the allowed 1000 mg/mL (therapeutic dose), so it is clear that the drug was not used only in therapeutic doses (Cycling weekly, 2008). Also, the use of these drugs in endurance sports, such as rowing, kayaking and canoeing, has become more frequent (Fitch, 2016).

The abuse or use of other drugs that are on the list of banned substances is also evident, but in a smaller percentage than the use of glucocorticoids, stimulants and beta 2 agonists.

These results can potentially be explained by the fact that for the use of other drugs such as anabolic steroids, the growth hormone, erythropoietin, diuretics and the like it is much more difficult to obtain a TUE approval and complex medical documentation is necessary to justify the use of these substances (Anđelković, 2016).

For example, at the Olympic Games in Athens, 80% of positive tests (there were 23 in total, which is a record to date) had androgens (anabolic steroids) in the findings, namely testosterone, nandrolone and stanozolol (Palmer, 2004). Olympic and world champion Justin Gatlin tested positive for testosterone in 2006 (Rumsby, 2017). Interestingly, hormone erythropoietin (EPO), until recently, could only be detected by blood plasma analysis and not by urine analysis, so it has been used for many years in cycling without punishment, given the fact that most doping controls in the past involved sampling an athlete's urine.

Only when the attempts to isolate EPO from urine succeeded, did the WADA start conducting retests of the so called B urine samples of former Tour de France and Giro d'Italia champions.

DISCUSSION

The results of this paper largely confirm the above hypotheses of the study. The use of glucocorticoids for the treatment of sports injuries is the most common reason why athletes seek TUE approvals. Glucocorticoids are most frequently used in the form of corticosteroid injections, which are very potent anti-inflammatory drugs and which lead to effective healing of injuries and reduction of pain.

It has already been said that many top athletes, such as Serena Williams, Rafael Nadal and others, have used this type of treatment and that journalists and the public opinion have often accused them of being "on steroids" and that their success is the result of doping (Shanet, 2010). However, public opinion very often confuses the concept of glucocorticoids and anabolic steroids, which have been proven to improve sports abilities in the form of increasing muscle mass, strength, speed and endurance. Namely, glucocorticoids do not have a clearly proven ergogenic

effect, but they are on the list of banned substances due to their potential uncritical use for therapeutic purposes, which can lead to health side effects, as well as the potential euphoric effect that they cause.

It has been proven that frequent use of corticosteroid injections with the aim of treating tendon inflammation and other soft tissue injuries can result in weakening of the tissue itself and its consequent rupture. Frequent and inadequate application of this therapy (giving injections directly into the tendon) leads to the weakening of the collagen fibers of the tendon, due to which the tissue becomes more susceptible to injury, which can be much more serious than the primary one (Pigozzi et al., 2012). Therefore, if we talk about the abuse of these substances for therapeutic purposes, by this we mean the uncritical use of these drugs by athletes and their doctors with the aim to achieve a quick recovery and return to the training process after injury. The dominant anti-inflammatory and anti-edematous effects of these drugs are the reason for the most common application of TUEs in the world of sports.

On the other hand, an insufficiently justified diagnosis of asthma represents a chance for the abuse of drugs that are used to treat this disease. It was mentioned that the WADA approved the use of these drugs for therapeutic purposes in a precisely specified dose for several beta agonists. As a result of the fact that in the past athletes exploited the diagnosis of asthma to allow them to use larger amounts of bronchodilators to dilate, i.e. expand the airways, increasing lung capacity, and thus the amount of oxygen delivered to the muscles to create more energy for work, the WADA has introduced precisely prescribed therapeutic doses of these drugs (Allen et al., 2019).

Despite the prescribed therapeutic dose, many athletes are still willing to risk a positive doping result by taking higher doses than necessary, believing that the TUE approval for the use of the drug will protect them from a potential doping control. One example is that of a cyclist Alessandro Petacchi, whose urine sample exhibited a higher concentration of the drug than allowed (Cycling weekly, 2008). Since the use of beta 2 agonists is allowed only in the form of inhalation, and the concentration of the inhaled bronchodilator in the urine can be detected shortly after use, it is clear why athletes try to abuse the use of this drug to improve their abilities (Deventer et al., 2012).

The possible potential abuse of TUEs can be seen in the example of the use of stimulants for the treatment of ADHD. If we take into account the fact that the review of world statistics regarding TUE applications clearly shows that the TUE approval for stimulants is most often sought for glucocorticoids, we should ask a question whether this disease is used by athletes as a cover for the abuse of these drugs (Anđelković, 2016). If it is known that stimulants, in addition to increasing concentration, have a positive effect on sports abilities by prolonging the duration of physical activity without decreasing the intensity of work, then there is a clear motive for athletes to use this drug to improve their abilities and not only for therapeutic purposes. There are numerous examples of American athletes who "suffer" from ADHD and therefore use stimulants in their therapy (Crawford, 2016).

The question is – does this data indicate a potential systemic abuse of this disease and stimulants, and therefore the TUE methods? Or is it just a case of a developed country that possesses appropriate diagnostic and therapeutic methods of treating this disease, which is where a large number of athletes with this diagnosis come from? It is difficult to give answers to these questions because there are no scientifically based results that can confirm or refute the stated claims. In any case, the suspicion of abuse can be justified to some extent, especially if we take into account the fact that in Serbia there have been no TUE applications for the ADHD diagnosis for years and that European countries, unlike America, are not in the lead in seeking TUE approvals for the treatment of ADHD (Anđelković, 2016).

An interesting fact also comes from the Olympic Games in Rio, where the USA dominated with 46 gold, 37 silver and 38 bronze medals, a total of 121 medals. Many predicted this dominance of American athletes, especially after the decision of the WADA to ban the participation of Russian athletes in this competition under the pretext of systemic doping. However, an insight into the documentation of the WADA system showed that more than a half of American athletes had an approved TUE for the use of certain illicit drugs (Redford, 2018).

The logical question that comes to mind is – how realistic is it that so many professional athletes are sick or injured? What is certainly most important is the fact that without new records, results and incredible sports performances, there would be no interest of the audience or sponsors and televisions that set aside billions for television rights and commercials. Very often this aspiration goes beyond the allowed methods and "fair play". One of the most famous examples is the systemic doping which was conducted in East Germany with the aim of winning as many medals as possible at major sports competitions (Franke & Bedrendonk, 1997).

There is no doubt that developed countries, great European and global powers, consider the success of their athletes, which is also a reflection of the power of a country, and for this reason they seek to provide them with a basis for better results, although all this is still in the domain of conspiracy theories for which there is no scientific basis.

CONCLUSION

According to the WADA statistics, the number of TUEs required by athletes is growing every year. One of the possible reasons for these figures may be the fact that athletes, their teams and sports professionals are becoming more aware of the existence and the manner of the application of this method.

Also, the demands of today's professional sports are increasing, causing the frequency of injuries in athletes to increase, consequently increasing the use of appropriate drugs from the list of banned substances, such as glucocorticoids. On the other hand, it is an indisputable fact that not everything in sports is always "fair play" and that TUEs can be an example of a "legal use" of doping and banned substances with the aim to improve sports results, although, predominantly, the WADA in this way allows respect for one of basic human rights, and that is the right to the health of an athlete.

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