Mini Review
Volume 13:03, 2023

Journal of Sports Medicine & Doping Studies

ISSN: 2161-0673 Open Access

Unravelling the Effects of Indomethacin on Steroid Metabolism: Implications for Endocrine Disruption and Urinary Steroid Profiling in Anti-Doping Analyses

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Abstract

Indomethacin, a commonly used non-steroidal anti-inflammatory drug, has been shown to potentially impact steroid metabolism, leading to implications for endocrine disruption and urinary steroid profiling in anti-doping analyses. This abstract presents a summary of the effects of indomethacin on steroid metabolism and its broader implications. Studies investigating the influence of indomethacin on steroid-metabolizing enzymes have demonstrated alterations in enzymatic activity, which can disrupt the normal balance of steroid hormones in the body. Consequently, these disruptions can have implications for urinary steroid profiling, potentially leading to false-positive or false-negative results in anti-doping testing. Understanding the effects of indomethacin on steroid metabolism is crucial for accurate interpretation of urinary steroid profiles in anti-doping analyses and for identifying potential endocrine disruption in individuals using the medication. Further research is needed to investigate the underlying mechanisms and long-term consequences of indomethacin-induced effects on steroid metabolism and to develop strategies to mitigate the confounding effects of indomethacin in anti-doping analyses.

Keywords: Indomethacin • Steroid metabolism • Endocrine disruption • Urinary steroid profiling • Anti-doping analyses

Introduction

In sports, Anabolic Androgenic Steroids (AAS) are frequently used. The World Anti-Doping Agency (WADA) prohibits their use as doping agents in and out of competition. The analytical detection is challenging, especially if so-called pseudo endogenous AAS (e.g., exogenous testosterone) are used as performance enhancing substances, due to their high similarity to the naturally occurring endogenous AAS (EAAS). According to the WADA technical document TD2018EAAS, anti-doping laboratories first monitor the concentrations and concentration ratios of selected EAAS in athletes' urine samples in order to detect the misuse of these pseudo-endogenous and some synthetic AAS. In the event of abuse of pseudo endogenous AAS or a few manufactured AAS, those steroid profile markers are modified and a confirmative technique utilizing Gas Chromatography Ignition Isotope-Proportion Mass-Spectrometry (GC-c-IRMS) is applied [1].

Since it has been shown that proportions of urinary steroids are steady over months and even a very long time in grown-up people yet show inter individual varieties, the steroidal module of the Athlete Biological Passport (ABP) was presented by WADA in 2014. Steroid metabolism plays a crucial role in maintaining the body's hormonal balance and is closely monitored in anti-doping analyses to detect the misuse of performance-enhancing substances. However, the influence of certain medications, such as indomethacin, on steroid metabolism and its impact on urinary steroid profiling in anti-doping analyses remains poorly understood. This study aims to unravel the effects of indomethacin on steroid metabolism, explore its potential for endocrine disruption, and discuss the implications for urinary steroid profiling in anti-doping analyses [2].

Literature Review

Indomethacin, a Non-Steroidal Anti-Inflammatory Drug (NSAID), is widely used for its analgesic and anti-inflammatory properties. However, recent studies have highlighted its potential to interfere with steroid metabolism and raise concerns about its impact on endocrine disruption. This literature review aims to provide a comprehensive overview of the existing research on the effects of indomethacin on steroid metabolism and its implications for urinary steroid profiling in anti-doping analyses.

Steroid metabolism and regulation: Steroids, including endogenous and exogenous compounds, play essential roles in various physiological processes, such as metabolism, reproduction, and immune function. Their metabolism involves complex enzymatic pathways and regulatory mechanisms within the endocrine system. Disruption of this delicate balance can lead to adverse effects on health and performance.

Indomethacin and steroid metabolism: Several studies have investigated the impact of indomethacin on steroid metabolism. It has been demonstrated that indomethacin can inhibit key enzymes involved in steroid biosynthesis, such as cytochrome P450 enzymes and 5-alpha reductase. These inhibitory effects can lead to alterations in the production of steroid hormones, including cortisol, aldosterone, and testosterone, among others. Moreover, indomethacin has been shown to affect the binding of steroid hormones to their respective receptors, further influencing their downstream effects [3].

Endocrine disruption and health implications: The disruption of steroid metabolism by indomethacin raises concerns about its potential endocrine-disrupting effects. Endocrine disruption refers to the interference with the normal functioning of the endocrine system, which can have profound consequences on development, reproduction, and overall health. Animal studies have shown that indomethacin administration can lead to altered reproductive function, hormonal imbalances, and impaired fertility. Furthermore, long-term use of indomethacin may contribute to the development of hormonal disorders and metabolic dysregulation.

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Received: 02 May, 2023, Manuscript No. jsmds-23-106162; **Editor Assigned:** 04 May, 2023, PreQC No. P-106162; **Reviewed:** 16 May, 2023, QC No. Q-106162; **Revised:** 22 May, 2023, Manuscript No. R-106162; **Published:** 29 May, 2023, DOI: 10.37421/2161-0673.2023.13.309

Urinary steroid profiling in anti-doping analyses: Urinary steroid profiling is a vital tool in anti-doping efforts to detect the misuse of anabolic steroids and other performance-enhancing substances. By analyzing the ratio of specific steroid metabolites, patterns can be established to identify potential doping practices. However, the presence of indomethacin in an athlete's system can confound the interpretation of urinary steroid profiles. It may lead to abnormal metabolite ratios or mask the detection of illicit substances, thereby compromising the accuracy and effectiveness of anti-doping analyses [4].

Discussion

Indomethacin, a non-steroidal anti-inflammatory drug commonly used to alleviate pain and inflammation, has been shown to interfere with steroid metabolism. Studies have demonstrated that indomethacin can affect the enzymatic activity of key steroid-metabolizing enzymes, such as cytochrome P450 enzymes and glucuronosyltransferases. These alterations in enzyme activity can lead to significant disruptions in steroid metabolism, potentially resulting in deviations from the normal urinary steroid profile. Urinary steroid profiling, a valuable tool in anti-doping analyses, relies on the detection of specific steroid metabolites and their ratios to identify potential doping practices [5]. However, the administration of indomethacin can confound this analysis by altering the levels of specific steroid metabolites or disrupting their normal ratios. These alterations may lead to false-positive or false-negative results, compromising the accuracy and reliability of anti-doping testing. Furthermore, indomethacin-induced endocrine disruption may have broader implications beyond anti-doping analyses. Steroid hormones play essential roles in various physiological processes, including reproductive function, immune response, and metabolism. Disruptions in steroid metabolism caused by indomethacin can potentially lead to hormonal imbalances and associated health issues. Therefore, it is crucial to consider the potential endocrine-disrupting effects of indomethacin when prescribing the medication and interpreting urinary steroid profiles [6].

Conclusion

The study highlights the potential effects of indomethacin on steroid metabolism and its implications for endocrine disruption and urinary steroid profiling in anti-doping analyses. Indomethacin has been shown to interfere with key enzymes involved in steroid biosynthesis, leading to altered hormone levels and disrupted endocrine function. These effects have significant implications for athlete health, performance, and the accuracy of anti-doping efforts. Further research is necessary to elucidate the precise mechanisms by which indomethacin influences steroid metabolism and the long-term consequences of these alterations. Improved understanding of the effects of indomethacin on steroid metabolism will facilitate the development of strategies to mitigate the confounding effects in anti-doping analyses and minimize the risk of endocrine disruption in individuals taking the medication.

Acknowledgement

None.

Conflict of Interest

There are no conflicts of interest by author.

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How to cite this article: Baglio, Sara. "Unravelling the Effects of Indomethacin on Steroid Metabolism: Implications for Endocrine Disruption and Urinary Steroid Profiling in Anti-Doping Analyses." *J Sports Med Doping Stud* 13 (2023): 309.