A Systematic Review and Meta-Analysis on the Effects of Endurance Training on Growth Factor and Insulin-Like Growth Factor-1 in Children and Adolescents after Abdominal Surgeries

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Abstract:

Introduction & Objective: Endurance training has been shown to reduce growth hormone levels more effectively than resistance training in obese children and adolescents. However, the effects of endurance training on non-obese children and adolescents remain unclear. This study aims to determine the effects of endurance training on growth factor and insulin-like growth factor-1 (IGF-1) in children and adolescents after abdominal surgeries through a systematic review and meta-analysis.

Materials & Methods: This study is a systematic review and meta-analysis based on the PRISMA statement. Articles published up to early 2022 were searched in databases including PubMed, Web of Science, EBSCO, CINAHL, MEDLINE, SPORT Discus, Scopus, Mag Iran, and SID. The search strategy used Boolean operators with keywords: (youth or children or adolescents or teenagers or boys or girls or minors) and (hormone or growth hormone or insulin-like growth factor-1 or endocrine glands or cytokine) and (exercise or training) and (endurance or resistance) and (laparotomy or abdominal surgery).

Results: A total of nine studies (190 participants) were included in this review, and it was found that endurance exercises have beneficial effects. The meta-analysis results showed that endurance training did not significantly increase growth hormone levels at the end of the study compared to the beginning (mean difference: 48 ng/ml - CI 95%: 0.02-0.99, *P* = 0.06-2%). Similarly, endurance training did not result in a significant change in IGF-1 levels at the end of the study compared to the beginning (mean difference: 22 ng/ml - CI 95%: 12.2-92.47, I2=0%, *P* = 0.92).

Conclusions: In children and adolescents, hormonal systems adapt to long-term training, resulting in various effects. Endurance exercises have no impact on growth hormone and insulin-like growth factor 1 (IGF-1) in children and adolescents after abdominal surgeries.

Key Words: Endurance Training, Child, Adolescent, Growth Factor, Insulin-Like Growth Factor-1

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Background and Objective

The effects of various types of exercise on muscular strength, cardiovascular fitness, and other health outcomes in children and adolescents can differ markedly. Regular physical activity is instrumental in fostering the development of the musculoskeletal, cardiovascular, and respiratory systems, while also influencing metabolic processes.[1] However, in the context of children and adolescents, these physiological benefits interact intricately with the endocrine system, thereby impacting growth, metabolism, puberty,and neuropsychological development.[2] Research has consistently demonstrated that physical activity exerts a positive influence on the endocrine system, both acutely and over prolonged durations, in both adults and adolescents. Hormones such as growth hormone, insulin-like growth factor 1 (IGF-1), and sex steroids—predominantly testosterone—have attracted considerable attention from researchers and healthcare professionals due to their critical roles in tissue growth and muscular hypertrophy.[2]

It is pertinent to note that the hormonal responses to exercise in children and adolescents may differ significantly from those observed in adults, attributable to the various stages of puberty.[3] The onset of puberty is characterized by rapid physiological changes, including alterations in the secretion of sex steroids and hormones associated with the GH-IGF-I axis (growth hormone and insulin-like growth factor 1), which are vital in regulating growth and metabolism within the body. During this developmental phase, the effects of anabolic hormones as well as catabolic and inflammatory mediators become particularly salient.[4] In particular, research indicates that young males experience a greater increase in muscular strength during puberty compared to females, primarily due to a substantial rise in testosterone levels; conversely, prior to the onset of puberty, there is no discernible difference in muscular strength between boys and girls. Consequently, the enhancements in muscular strength observed following exercise in prepubescent children should be attributed predominantly to muscular adaptations rather than hormonal influences. However, there exists a paucity of data concerning hormonal and morphological adaptations resulting from exercise training in children and adolescents.[5] Exercise can elicit acute responses in hormones such as testosterone and cortisol, potentially leading to chronic changes in males and influencing growth and puberty. Both testosterone and cortisol levels have been observed to increase following acute endurance exercise in adults;[6] however, the responses of children and adolescents to such training remain unclear. Endurance exercise encompasses activities performed continuously over extended periods, aimed at enhancing cardiovascular and muscular capacity, including running, cycling, and swimming, which serve to improve endurance and mitigate fatigue. Some evidence indicates that the acute responses of cortisol and testosterone to exercise may vary based on the stage of puberty.[7]

Recently, there has been a growing emphasis on investigating the growth hormone-insulin-like growth factor 1 (GH-IGF-I) axis in relation to exercise physiology in children. The GH-IGF-I axis comprises a complex system of growth mediators, IGF-I binding proteins, and IGF receptors, all of which play pivotal roles in natural growth, cellular development, and differentiation.[8,9] Studies have reported a correlation between exercise training and the GH-IGF-I axis, highlighting that the secretion of growth hormone (GH) and concentrations of IGF-I tend to be more favorable in adults and adolescents compared to individuals with less training experience. Furthermore, both GH and IGF-I levels significantly increase in response to endurance training stimuli.[10] The acute response of GH to a single session of endurance exercise appears to be influenced by maturation. Although the acute response of IGF-I concentration in children and adolescents has received less attention, an increase is plausible. Nonetheless, most studies have not demonstrated a significant increase in IGF-I concentration following exercise. While IGF-I is a downstream hormone stimulated by GH, it is posited by some researchers that IGF-I may not be entirely dependent on GH, given that IGF-I often peaks earlier than GH following exercise.[11]

Resistance training programs lasting five weeks in children have been observed to activate catabolic processes rather than the anticipated anabolic effects within the growth hormone-insulin-like growth factor 1 (GH-IGF-I) axis. The inhibition of the GH-IGF-I axis is attributed to the concurrent activation of catabolic pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha (TNF-**α**). Previous research has demonstrated that acute and intensive bouts of specific exercise sessions elevate inflammatory cytokines in both male and female participants.[12] It has been proposed that levels of pro-inflammatory cytokines may return to baseline following an extended training period, subsequently enhancing physical performance and alleviating the suppression of IGF-I.[13] Successful adaptations to training may lead to a reduction in pro-inflammatory cytokines and the restoration of anabolic activation within the GH-IGF-I axis, resulting in elevated IGF-I levels above pre-training values. However, the precise role of inflammatory cytokines in growth and development remains uncertain, as does their interaction with prolonged training.[14]

The manner in which hormonal systems adapt to prolonged exercise in children and adolescents is not clearly understood. A systematic meta-analysis has indicated that resistance training is more effective than endurance training in lowering fasting insulin levels in overweight adolescents.[2] However, it has also been shown that obesity in children diminishes growth hormone and insulin responses to exercise, thereby exerting a more significant impact on hormonal responses compared to their lean counterparts.[15,16] Abdominal surgeries encompass any surgical procedures performed on the organs and tissues within the abdominal cavity, including the stomach, intestines, liver, spleen, and pancreas. To the best of our knowledge, no previous systematic review or meta-analysis has investigated whether different forms of prolonged resistance training yield varying effects on hormonal responses in a healthy population. Understanding the physiological mechanisms that influence children's responses to exercise is critical for the development of safe and effective training programs. Thus, this systematic review and meta-analysis were conducted to evaluate the impact of training on growth factors and insulin-like growth factor 1 in children and adolescents following abdominal surgeries.

Materials and Methods

Study design

The present investigation is a systematic review and meta-analysis conducted in accordance with the PRISMA guidelines.

Search Strategy

A comprehensive search for published articles up to the beginning of 2022 was executed across several databases, including PubMed, Web of Science, EBSCO, CINAHL, MEDLINE, Discus, Scopus, Iran Mag, and SID. The search strategy employed Boolean operators alongside keywords such as "youth," "young," "children," "adolescents," "teenage," "boys," "girls," "kid," "juvenile," "toddler," as well as "hormone," "growth hormone," "insulin-like growth factor 1," "endocrine glands," "cytokine," "exercise," "training," "endurance," "resistance," "laparotomy," and "abdominal surgery." Both Persian and English published studies were searched in the aforementioned databases without any temporal restrictions.

Eligibility Criteria

Eligibility criteria were established based on the PICOS framework. Participants: Children and adolescents who had undergone abdominal surgeries and were under the age of 18 were included in the analysis. Studies focusing on populations categorized as overweight or obese (defined by a BMI at or above the 85th percentile) were excluded, as their hormonal responses to exercise may differ from those of lean participants.

Overweight or obesity in children and adolescents is characterized by the World Health Organization as a BMI above the 85th percentile. Intervention: Endurance training programs of a minimum duration of four weeks were considered for inclusion. Comparator: Only studies that included a control group were taken into account. Outcome: Studies that presented data on hormone levels and insulin-like growth factor 1 before and after the training period were included. Research investigating changes in hormone concentrations from pre-training to post-training was considered relevant. Study Design: Both randomized and non-randomized controlled trials were included in this review. Furthermore, only studies published in English and Persian that were accessible in full text were considered for inclusion in this analysis.

Study Selection

Following the elimination of duplicate records, one author meticulously reviewed the titles and excluded articles that were deemed unrelated. The screening process adhered rigorously to the established eligibility criteria. Two independent authors, one of whom is acknowledged in this article, conducted a thorough examination of the abstracts, leading to the exclusion of any that did not satisfy the eligibility criteria. At this juncture, only studies failing to meet the criteria were removed, including those involving adults, individuals with chronic diseases, cross-sectional study designs, and non-peer-reviewed reports such as conference proceedings. All potentially relevant articles were then advanced to the subsequent stage of screening, where they underwent full-text evaluation by the aforementioned authors. Inclusion in this study was contingent upon fulfillment of the predefined inclusion criteria. Any disagreements that arose during this process were resolved through discussion and a re-evaluation of the original articles. To bolster the number of relevant articles, we also conducted a manual search of the reference lists of the identified studies.

Data Extraction

A standardized digital data extraction form, adapted from the Cochrane Consumers and Communications data extraction framework, was developed for this purpose. The information extracted included: 1) study design; 2) participant demographics (e.g., gender, height, weight, age); 3) study objective; 4) intervention characteristics (e.g., type of exercise, intensity, duration); and 5) hormonal levels. Data were extracted independently by two authors, and any discrepancies encountered during this process were resolved through discussion and re-evaluation of the original articles.

Risk of Bias Assessment

The evaluation of risk of bias was conducted using the Cochrane Collaboration tool designed for this purpose.[11]

Statistical Analysis

A meta-analysis was conducted utilizing Review Manager software, version 5.4.1. The analysis employed a random-effects model to calculate the weighted mean differences (MD) in hormonal outcomes from baseline to post-intervention across the study groups. An initial meta-analysis was executed encompassing all exercise studies, inclusive of any outcomes related to exercise intervention. Subsequent subgroup analyses were performed, taking into account the type of intervention and its effects on the specified variables. Statistical heterogeneity within the systematic review and meta-analysis was assessed using Q statistics and I^2. The mean difference between the exercise and control groups was calculated for the absolute changes in hormonal levels, accompanied by a 95% confidence interval.

Findings

The database search yielded a total of 3,689 potential studies following the removal of duplicates. The screening of titles and abstracts identified 41 potentially relevant studies, which underwent rigorous full-text evaluations for eligibility. Ultimately, 6 studies were included in the meta-analysis.

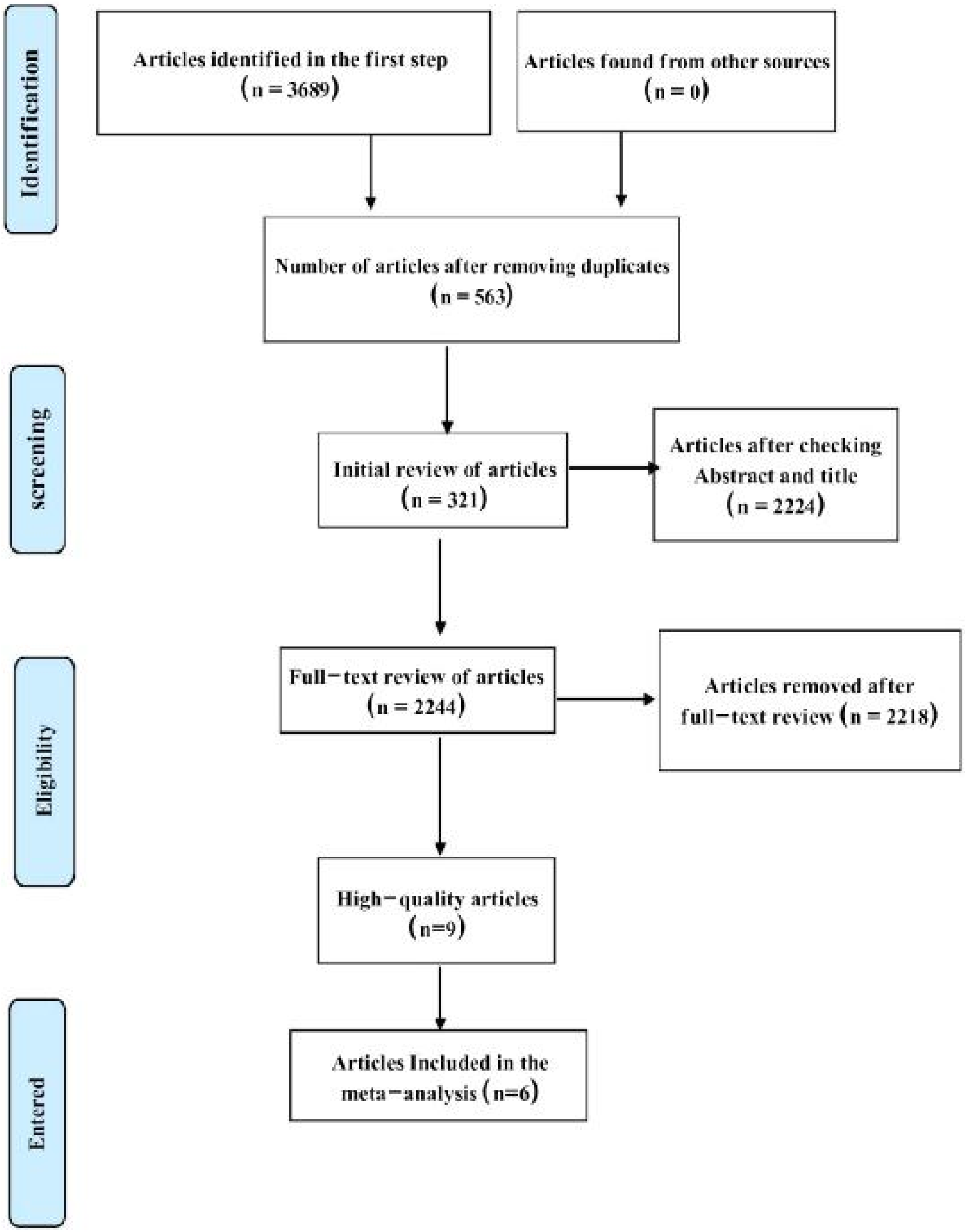

Diagram 1- The process of entering studies into the present systematic review and meta-analysis study.

Table 1- A summary of the articles included in this systematic and meta-analysis review article

Author/year	Sample size	Risk of bias	age	gender	height (cm)	weight (kg)	Intervention done
Büyükyazi / 2003(A)[17]	Intervention:12 Control:6	low risk	teenager	boy:18 girl:0	Intervention: 178.3±5.1 Control: 177.9±565	Intervention: 66.6±6.6 Control: 64.9±5.9	60 minutes of continuous running for 3 times a week and at least 4 weeks
Büyükyazi / 2003(B)[17]	Intervention:12 Control:6	low risk	teenager	boy:18 girl:0	Intervention: 175.5±4.3 Control: 174.6±5.5	Intervention: 65.5±6.9 Control: 62.3±5.11	Two courses of 60 minutes continuous running for 3 times a week and at least 4 weeks
Zakas / 1994(A)[18]	Intervention:10 Control:10	low risk	12 to 18 years old	boy:20 girl:0	Intervention: 125.2±3.4 Control: 120.4±3.6	Intervention: 35.5±1.5 Control: 39.1±3.3	30 minutes of cycling on an ergonomic bike for 3 times a week for 5 weeks
Zakas / 1994(B)[18]	Intervention:6 Control:6	Moderate risk	12 to 18 years old	boy:12 girl:0	Intervention: 154.1±6.9 Control: 160.5±8.3	Intervention: 42.5±1.5 Control: 45.1±3.3	40 minutes of continuous running for 3 times a week for 5 weeks
Zakas / 1994(C)[18]	Intervention:7 Control:6	low risk	12 to 18 years old	boy:13 girl:0	Intervention: 154.1±6.9 Control: 160.5±8.3	Intervention: 42.5±1.5 Control: 45.1±3.3	50 minutes of continuous running and 10 minutes of cycling for 3 times a week for 5 weeks
Eliakim/ 1996/[19]	Intervention:10 Control:6	low risk	high school	boy:0 girl:16	Intervention: 161.3±5.2 Control: 157.9±5.1	Intervention: 61.2±5.0 Control: 52.9±3.9	60 minutes of continuous running three times a week for 8 weeks
Eliakim / 2010/[20]	Intervention:20 Control:18	low risk	high school	boy:38 girl:0	Intervention: 169.1±9.5 Control: 170.8±9.3	Intervention: 62.2±4.2 Control: 66.1±5.1	45 minutes of aerobic exercises for 3 times a week for 6 weeks
Eliakim/ 2001/[21]	Intervention:19 Control:20	Moderate risk	Before puberty	boy:0 girl:39	Intervention: 134.4±2.3 Control: 130.1±3.0	Intervention: 35.5±2.6 Control: 33.3±2.1	Two courses of 45 minutes of slow running for 3 times a week for 5 weeks
Scheett / 2003/[22]	Intervention:12 Control:14	low risk	high school	boy:26 girl:0	Intervention: 140.2±5.9 Control: 138.9±5.5	Intervention: 33.1±3.9 Control: 32.6±3.4	90 minutes of aerobic exercises for 4 times a week for Six weeks

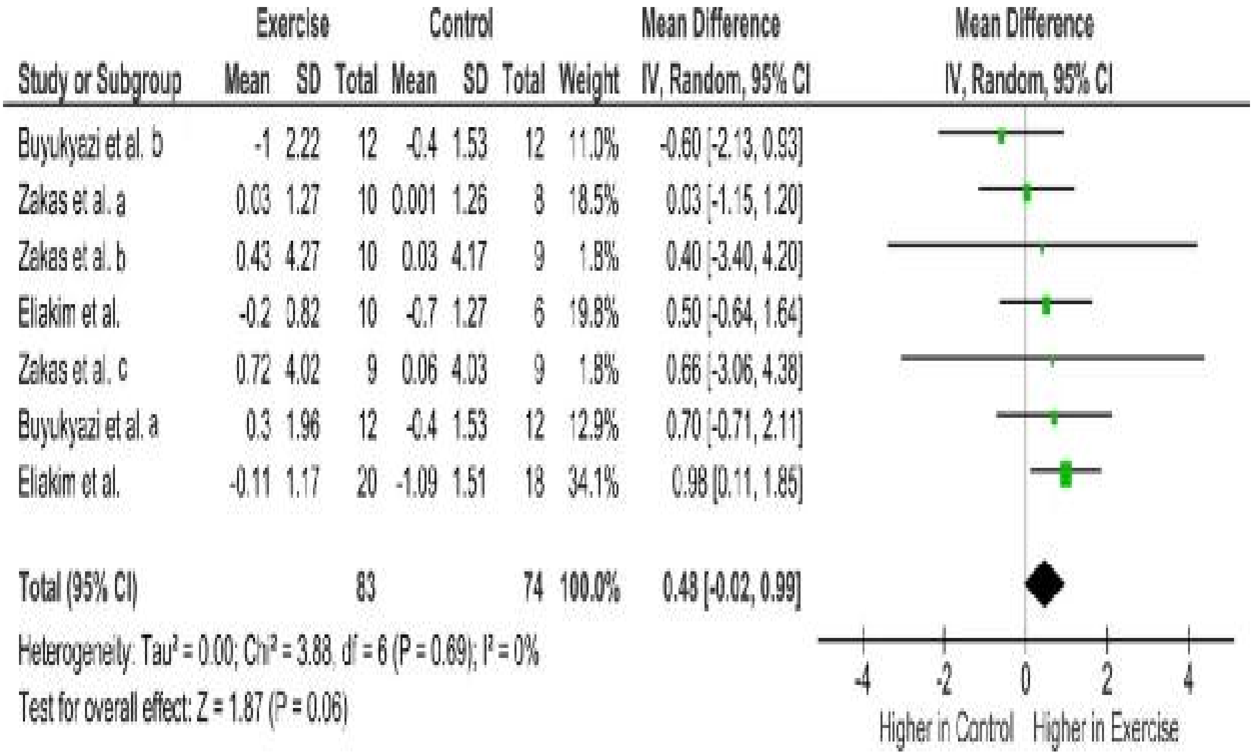

Figure 1- The results of meta-analysis of articles related to the relationship between endurance exercise and growth hormone levels

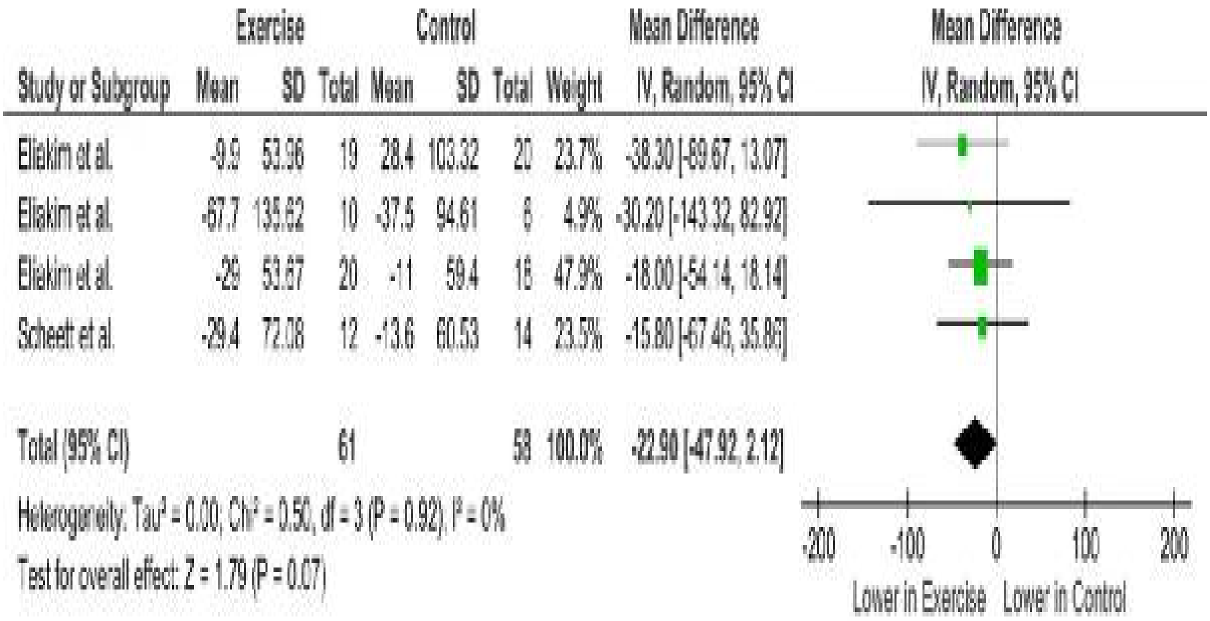

Figure 2- The results of the meta-analysis of articles related to the relationship between endurance exercise and insulin-like growth hormone levels 1

In the study conducted by Zakas et al., three distinct types of exercises were administered to the intervention group participants, with results presented separately for each modality.

Similarly, the research by Büyükyazi et al. provided findings for two different types of interventions across two separate groups, resulting in two distinct conclusions for inclusion in the meta-analysis (as illustrated in Diagram 1).

A comprehensive review of the summary of articles included in this study indicated that a total of 190 participants were assessed.

The meta-analysis results demonstrated that endurance exercise did not yield a statistically significant increase in growth hormone levels at the conclusion of the study compared to baseline (mean difference: 48 ng/ml; CI95%: (99/-02/-); I² = %; P = .06). Furthermore, the findings indicated that endurance exercise did not produce a significant change in insulin-like growth factor 1 at the end of the study relative to the beginning (mean difference: 22 ng/ml; CI95%: (12/2-92/47-); I² = %; P = .92) (see Image 2).

Assessment of Risk of Bias

All studies included in this systematic review were evaluated according to the Cochrane risk of bias assessment criteria. The overall risk of bias score for the included studies was determined to be medium, as summarized in Table 1. Notably, only one study failed to implement an appropriate randomization process. Measurement bias regarding outcomes was identified in three studies, and three studies exhibited bias related to the blinding of participants.

Discussion

This systematic review and meta-analysis aimed to evaluate whether endurance exercise results in increased levels of growth hormone and insulin-like growth factor 1 in adolescents under the age of 18. The analyses indicated that neither growth hormone nor insulin-like growth factor 1 exhibited significant responses to endurance exercise. It is posited that the growth hormone response to exercise may be contingent upon puberty; existing literature suggests that post-pubertal adolescents demonstrate more pronounced increases in growth hormone levels following endurance training compared to their pre-pubertal counterparts.[23-25] Furthermore, prior research has highlighted that exercise may yield varied effects on chronic alterations within the GH-IGF-I axis.[22,26]

The type of exercise performed appears to influence the body’s response to physical training, although this response may be specific to certain hormones. Our findings suggest that endurance training did not elicit changes in growth hormone and insulin-like growth factor 1 levels, indicating a possible adaptation of these hormones to endurance exercise routines.[15]

Impact of Exercise on Physical and Physiological Characteristics of children and adolescents, enhancing factors such as strength, muscle mass, and endurance. These effects are particularly pronounced with the onset of puberty, attributed to the elevation of anabolic hormones,notably testosterone.[27]

Evidence suggests that the extent of training adaptations resulting from endurance exercise is closely linked to the stage of puberty, with the most significant hormonal changes occurring in the post-pubertal period. Hormonal adaptations following endurance training are anticipated to be more substantial in post-pubertal compared to their pre-pubertal counterparts, owing to elevated baseline hormonal levels.[28,29] It is important to highlight that, as of now, no analogous studies have been conducted specifically on females to determine whether endurance training influences their hormonal responses.[30] The precise impact of puberty on hormonal responses induced by exercise remains inadequately defined. Factors such as the duration of training, the type of exercise, and the specific hormones under investigation warrant careful consideration when exploring this topic.[31]

The limitations of the current study include the variability in exercise programs, the diverse age range of participants, gender differences,and the small sample sizes across the studies included in this review. These factors complicate the ability to generalize the results effectively. Future research is recommended to be conducted with enhanced rigor and quality to mitigate these limitations and provide clearer insights.

Conclusion

Typically, girls enter puberty approximately two years earlier than boys and possess distinct physiological characteristics, including elevated levels of sex steroids and GH/IGF-I. This may result in differing hormonal responses to training.[32,33] However, due to the small sample sizes in the studies incorporated in this meta-analysis, the effects of puberty could not be thoroughly examined. Furthermore, the onset of sexual maturity among participants was not specified, with the exception of one study. Overall, it was concluded that endurance training does not significantly affect growth hormone and insulin-like growth factor 1 levels children and adolescents post-abdominal surgeries.

Abstract:

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Introduction & Objective: Endurance training has been shown to reduce growth hormone levels more effectively than resistance training in obese children and adolescents. However, the effects of endurance training on non-obese children and adolescents remain unclear. This study aims to determine the effects of endurance training on growth factor and insulin-like growth factor-1 (IGF-1) in children and adolescents after abdominal surgeries through a systematic review and meta-analysis.

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Results: A total of nine studies (190 participants) were included in this review, and it was found that endurance exercises have beneficial effects. The meta-analysis results showed that endurance training did not significantly increase growth hormone levels at the end of the study compared to the beginning
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Conclusions: In children and adolescents, hormonal systems adapt to long-term training, resulting in various effects. Endurance exercises have no impact on growth hormone and insulin-like growth factor 1 (IGF-1) in children and adolescents after abdominal surgeries.

Key Words:Endurance Training, Child, Adolescent, Growth Factor, Insulin-Like Growth Factor-1

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