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Review Article

Impact of GH administration on athletic performance in healthy young adults: A systematic review and meta-analysis of placebo-controlled trials

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ABSTRACT

Objective: Illicit use of growth hormone (GH) as a performance-enhancing drug among athletes is prevalent, although the evidence of such effects in healthy, young subjects is sparse. We therefore performed a meta-analysis of published studies on the effect of GH administration on body composition, substrate metabolism, and athletic performance in healthy, young subjects.

Design: The English-language based databases PubMed, EMBASE, and Cochrane Central Register of Controlled Trials were searched, and eligible articles were reviewed in accordance with the PRISMA guidelines. Fifty-four potentially relevant articles were retrieved of which 11 were included in this analysis comprising 254 subjects.

Results: Administration of GH significantly increased lean body mass ($p < 0.01$) and decreased fat mass ($p < 0.01$). In addition, GH increased the exercising levels of glycerol ($p = 0.01$) and free fatty acids ($p < 0.01$), but did not alter the respiratory quotient during exercise ($p = 0.30$). GH significantly increased anaerobic exercise capacity ($p < 0.01$) in the only study which investigated this, but did not over weeks to months improve muscle strength ($p = 0.36$) or maximum oxygen uptake ($p = 0.89$).

Conclusion: GH administration elicits significant changes in body composition, but does not increase either muscle strength or aerobic exercise capacity in healthy, young subjects.

1. Introduction

Illicit use of GH among elite and recreational athletes is widespread and frequently combined with other performance-enhancing drugs [1]. The salutatory effects include reduction in fat mass, increased lean body mass and increased aerobic exercise capacity, which have been documented in GH-replaced adult patients with hypopituitarism [2,3]. However, it is controversial whether GH administration exerts comparable effects in healthy subjects. Nevertheless, GH is considered a doping agent by the World Anti-Doping Agency and its use is prohibited at all times (in and out-of-competition) [4].

The aim of this meta-analysis was to assess the effects of placebo-controlled GH administration on body composition, indices of lipolysis, muscle strength, and exercise capacity in healthy, young subjects.

2. Materials and methods

2.1. Identification of relevant trials

The study was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [5]. The English-language based databases including PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched to identify potentially relevant studies. All databases were comprehensively searched from their respective inception until 2th December 2016 without restrictions to language or date of publication. The search was limited to human adults (19 + years of age). Where possible, the following MeSH terms were used: “growth hormone” in combination with either “sports”, “performance”, “exercise”, or “doping” (details in Appendix A). To ensure the inclusion of studies not yet indexed with MeSH terms, a free text search was performed using the same terms. In addition, the

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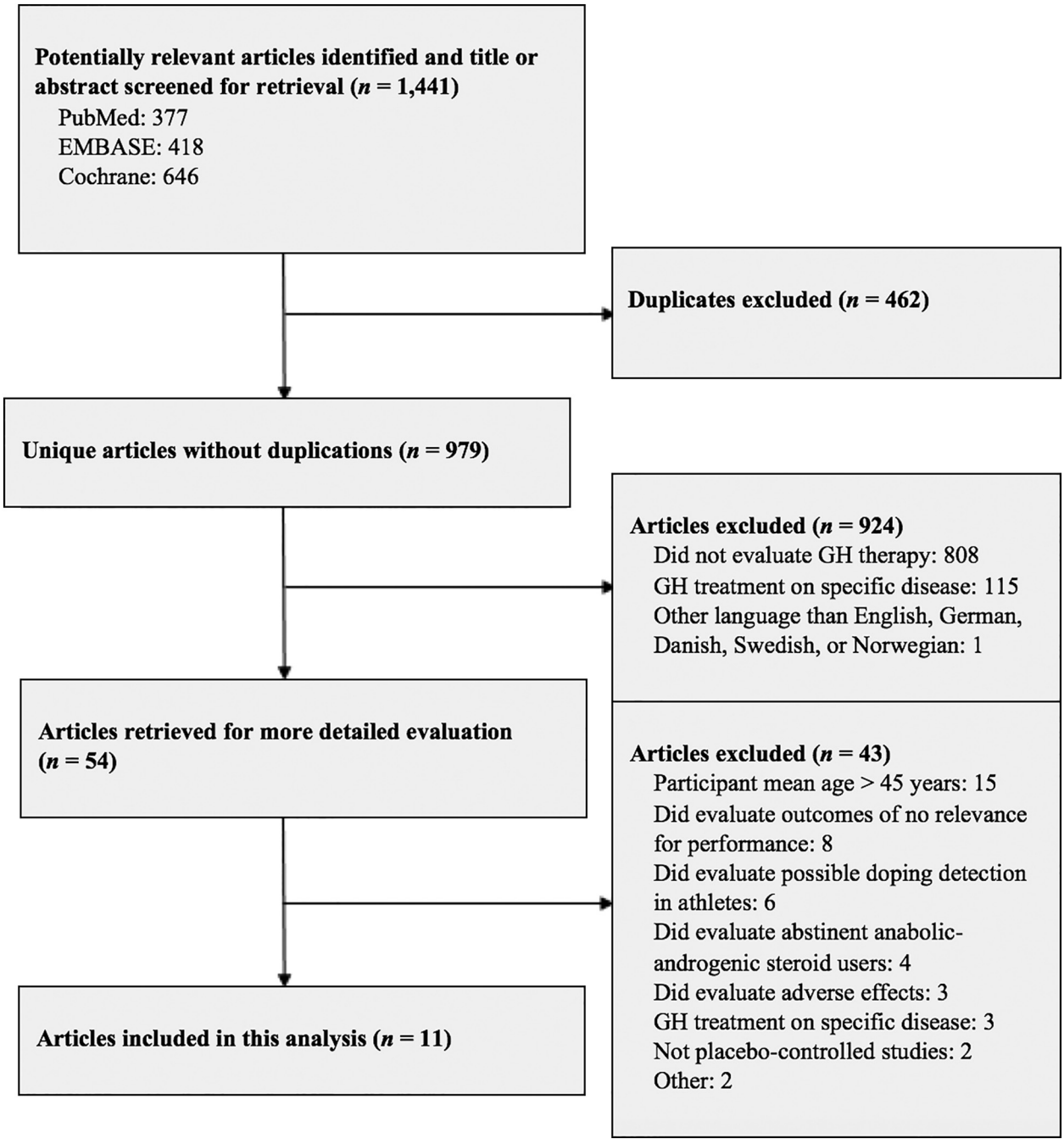

Fig. 1. Flowchart of study selection.

references of relevant articles were also reviewed to identify potentially eligible articles. The literature search and data extraction was performed by one author (K Hermansen). Two other authors (M Bengtsen and JOL Jørgensen) conducted an independent review of the extracted articles, and discrepancies were solved by discussion.

2.2. Inclusion criteria

All randomized, double-blind, placebo-controlled trials of GH administration were included if they provided at least one of the following outcome measures: body composition (e.g. weight, lean body mass, extracellular water, body cell mass, or fat mass), strength (e.g. biceps strength, quadriceps strength, or isometric deadlift strength), indices of lipolysis (e.g. circulating levels of glycerol and/or free fatty acids, or respiratory exchange ratio) or exercise capacity (e.g. lactate levels, bicycling speed, or maximum oxygen uptake). Restriction was applied on participants' age and health status. All participants should be healthy without evidence of pituitary disease. Moreover, studies specifically targeting children, adolescents (< 18 years of age), or older adults (> 45 years of age) were excluded. The terms *lean body mass* and *fat-free mass* are used interchangeably in the literature, why lean body mass and fat-free mass are reported as a single category of lean body mass.

2.3. Data extraction

The following data were extracted from each study: population characteristics (e.g. age, gender, body-mass index, maximum oxygen uptake, and initial IGF-1 levels), study interventions (e.g. dose, route, frequency, and duration of GH administration), study quality (e.g.

design, randomization, and statistical method), and clinical outcomes. Where necessary, graphical data were extracted by using the graph-digitizing program DigitizeIt, version 2.2.

2.4. Risk of bias assessment

An assessment of the methodological quality of the studies was based on the Cochrane Collaboration's tool for assessing risk of bias [6]. For RCTs, this comprised the following domains: random sequence generation (i.e. selection bias); allocation concealment (i.e. selection bias); blinding of participants, personnel, and outcome assessors (i.e. performance bias); incomplete outcome data (i.e. detection bias); selective reporting and other sources of bias that may have affected the results (e.g. baseline imbalance and source of funding). For each domain, the risk of bias was assessed as low, high, or unclear. Unclear risk of bias was assigned for a domain if insufficient details were reported, or if what happened in the study was known, but its contribution to the risk of bias was unknown or unclear.

2.5. Statistical analysis

The weighted mean differences with associated 95% confidence intervals (CIs) were calculated for continuous variables by using the fixed-effects inverse-variance model and DerSimonian-Laird random-effects model. Heterogeneity was assessed by using chi^2 and I^2 analyses [7]. The random-effects model was used in case of significant heterogeneity (i.e. $I^2 \geq 50\%$) [8]. The fixed-effects model was used in cases without significant heterogeneity (i.e. $I^2 < 50\%$). In the test for overall effect, which was given by the Z score, a two-tailed p value < 0.05 was considered significant. Forest plots showing the point estimate and confidence intervals were created for each outcome. All statistical analyses were performed using Review Manager 5.3 (RevMan, version 5.3; The Cochrane Collaboration, Oxford, UK).

3. Results

3.1. Study selection

The initial search in the databases provided a total of 1441 articles (377 in PubMed, 418 in EMBASE, and 646 in Cochrane), of which 979 were unique without duplications. After screening titles and abstract, 54 potentially relevant articles remained for more detailed evaluation. Of these studies, 43 were excluded from further analysis because the studies did not meet the inclusion criteria. Any discrepancies in the articles considered important were resolved by consensus among the authors. Finally, 11 articles [9–19] were included in this review. The study search flow is shown in Fig. 1.

3.2. Participants' characteristics

The enrolled participants were predominantly male (72%) with a mean age of 26.7 years [SD: 1.9] ranging between 18 and 40 years across trials. They were lean with a mean body-mass index of 23.4 kg/m^2 [SD: 0.8] and physically fit with a mean maximum oxygen uptake of 50.5 kg/m^2 [SD: 7.9]. The participants' mean IGF-1 level was 210 μg/l [SD: 82] at baseline. The baseline characteristics of study participants are shown in Table 1.

3.3. Study characteristics

In total, the included studies enrolled 224 participants. Of these, 117 participants (52%) received GH treatment representing a total of 11.7 person-years of treatment. Most study sizes were small with a mean number of participants at enrollment of 23.

The mode of GH intervention varied considerably among the included studies. Two studies [13,18] evaluated the acute effect of a single GH injection. The other studies [9–12,14–17,19] provided longer treatment duration ranging from 2 to 12 weeks with a mean of 5.2 weeks [SD: 3.3]. The daily dose of GH ranged from 25 to 67 μg/kg with a mean of 36.5 μg/kg [SD: 12.7] among the included studies. All the included studies provided subcutaneous GH injections.

3.4. Assessment of study quality

One study [19] fulfilled all the evaluated quality criteria and was the only one to document adequate concealment of treatment allocation at study enrollment. Six additional studies [9,12,15–18] fulfilled 6 of 7 criteria. Incomplete outcome data were addressed in three studies [10,11,13], and the generation of a randomized sequence was unclear in one study [11]. Caregivers, investigators, and assessors were all blind to the intervention in all the included studies [9–19]. The risk of bias is summarized in Appendix B.

3.5. Quantitative data synthesis

Seven studies [9–11,14–17,19] provided data on the effects on body composition, whereas only limited data were available on the effects on lipolytic markers, strength, and exercise capacity.

3.6. Body composition

Weight increased significantly after GH compared to placebo (weighted mean difference in weight, 1.62 kg [95% CI, 0.79 to 2.45 kg], $p < 0.01$). Similarly, GH increased LBM (weighted mean difference: 2.86 kg [95% CI, 2.22 to 3.50 kg], $p < 0.01$). The lean body mass consists of a compartment of extracellular water and a functional cellular compartment, the body cell mass. The increase in lean body mass was accompanied by an expansion of the extracellular water (weighted mean difference: 1.77 kg [95% CI, 1.01 to 2.53 kg], $p < 0.01$). One study [19] observed a statistically insignificant increase in body cell mass (mean difference: 0.90 kg [95% CI, − 0.09 to 1.89 kg], $p = 0.07$). In addition, fat mass decreased significantly in response to GH (weighted mean difference: − 1.22 kg [95% CI, − 1.71 to − 0.74 kg], $p < 0.01$) (Fig. 2).

3.7. Indices of lipolysis

Three studies [13,14,18] employing acute GH exposure reported a significant increase in exercising levels of glycerol (weighted mean difference: 146 μmol/l [95% CI, 34 to 258 μmol/l], $p = 0.01$), and free fatty acids (weighted mean difference: 281 μmol/l [95% CI, 134 to 428 μmol/l], $p < 0.01$) after GH as compared to placebo. However, no significant decrease was observed in exercising respiratory exchange ratio (weighted mean difference: − 0.03 [95% CI, − 0.10 to 0.03], $p = 0.30$) (Fig. 3).

3.8. Muscle strength

One study [11] reported that GH treatment did not increase biceps strength (mean difference: − 0.90 kg [95% CI, − 2.71 to 0.91 kg], $p = 0.33$) or quadriceps strength (mean difference: − 1.00 kg [95% CI, − 2.83 to 0.83 kg], $p = 0.28$) assessed by 1-repetition maximum voluntary strength. Another study [10] evaluated change in the strength of seven muscle groups and reported no significant difference between GH and placebo (mean difference: − 0.10 kg [95% CI, − 0.61 to 0.41 kg], $p = 0.70$). Similarly, one study [19] showed that neither muscle strength nor maximal explosive power were improved by GH treatment assessed by isometric deadlift (mean difference: 2.00 kg

Table 1
Baseline characteristics of participants.

Study (year)	Mean age (SD) (*year*)		Participants (*n at start//end of trial*)		Mean BMI (SD) (kg/m^2)		Mean VO_2max (SD) (*ml/kg per* min)		IGF-1 (SD) (μg/*l*)		Study intervention	
	GH	Control	GH	Control	GH	Control	GH	Control	GH	Control	Duration (*days*)	Dose (μg/*kg*/*d*)
Crist et al. [9]	27.9 (3.7)	27.9 (3.7)	8/8	8/8	NA	NA	NA	NA	NA	NA	42	38[‡]
Yarasheski et al. [10]	27.0 (4.2)[a]	27.0 (4.2)[a]	9/7	9/9	23.5 (NA)[†]	23.5 (NA)[†]	NA	NA	NA	NA	84	40
Deyssig et al. [11]	23.4 (2.8)[a]	23.4 (2.8)[a]	11/8	11/10	NA	NA	NA	NA	359 (NA)[§]	308 (NA)[§]	42	30
Wolthers et al. [12]	21–29[#]	21–29[#]	8/8	8/8	22.5–27.0[#]	22.5–27.0[#]	NA	NA	158 (20)	170 (37)	10	33
Lange et al. [13]	26.0 (2.6)	26.0 (2.6)	7/5	7/7	23.0 (1.3)	23.0 (1.3)	65.0 (2.6)	65.0 (2.6)	259 (NA)[§]	233 (NA)[§]	1	33[‡]
Healy et al. [14]	31.0 (NA)	33.0 (NA)	6/6	6/6	24.0 (NA)	25.0 (NA)	54.2 (NA)	53.4 (NA)	188 (23)	197 (21)	28	67
Ehrnborg et al. [15]	25.6 (4.2)	27.0 (4.4)	20/20	10/10	23.1 (2.6)	23.2 (3.9)	NA	NA	310 (97)	301 (69)	28	33/67
Berggren et al. [16]	25.6 (4.2)	27.0 (4.4)	20/20	10/10	22.8 (NA)[†]	23.1 (NA)[†]	44.4 (4.3)	45.3 (4.3)	310 (100)	301 (69)	28	33/67
Hansen et al. [17]	24.0 (4.0)	25.0 (4.0)	8/8	8/8	22.2 (2.0)	21.4 (1.6)	60.1 (9.6)	57.8 (7.2)	214 (NA)[§]	241 (NA)[§]	14	28[‡]
Hansen et al. [18]	25.1 (5.7)	25.1 (5.7)	8/7	8/7	22.6 (1.7)	22.6 (1.7)	62.0 (2.8)	62.0 (2.8)	NA	NA	1	33[‡]
Meinhardt et al. [19]	27.6 (5.7)	28.3 (5.0)	32/32	32/32	23.3 (2.8)	24.5 (3.1)	45.6 (9.9)	43.4 (9.9)	126 (37)	124 (37)	56	28[‡]

BMI = body mass index; VO_2 max = maximum oxygen uptake; IGF-1 = insulin-like growth factor-1.
[†] Based on average body weight and height presented in study.
[#] Reported as ranges.
[‡] Based on absolute doses and mean body weight presented in study.
[§] Data abstracted in terms of graphs by using the graph-digitizing program DigitizeIt, version 2.2.
[a] Data from growth hormone-treated and placebo groups aggregated.

[95% CI, −1.29 to 5.29 kg], $p = 0.23$) or jump height (mean difference: −1.30 cm [95% CI, −2.19 to 0.41 cm], $p < 0.01$), respectively. Taken together, GH administration did not improve muscle strength (relative change in muscle strength, −0.02 [95% CI, −0.05 to 0.02, $p = 0.36$] (Fig. 4).

3.9. Exercise capacity

Three studies [13,16,19] reported no significant difference in aerobic exercise capacity between GH and placebo assessed by maximum oxygen uptake (weighted mean difference in maximum oxygen uptake: 0.01 l/min [95% CI, −0.11 to 0.13 l/min], $p = 0.89$) (Fig. 4).

In addition, an insignificant increase in lactate levels was observed in the GH-treated groups in two studies [13,18] (mean difference: 330 μmol/l [95% CI, −341 to 1000 μmol/l], $p = 0.33$). Furthermore, one study [13] reported no effect on bicycling speed in growth hormone-treated participants (mean difference: 0.00 km/h [95% CI, −2.35 to 2.35 km/h], $p = 1.00$).

Until now, there is only one study [19] evaluating anaerobic exercise capacity. This study [19] showed a significant increase in anaerobic work capacity assessed by sprint cycle ergometry (i.e. Wingate test) (mean difference in Wingate value: 0.60 kJ [95% CI, 0.23 to 0.97 kJ], $p < 0.01$).

4. Discussion

Growth hormone is widely used as a performance-enhancing drug in sports. The present analysis of published studies suggests that GH administration in healthy young adults primarily induces moderate changes in body composition and has limited if any effects on key performance outcomes in relation to endurance and strength dominated sports.

Administration of GH in healthy young subjects increases total body weight and lean body mass and decreases fat mass. However, methods for quantifying lean body mass (i.e. dual-energy x-ray absorptiometry) do not reliably distinguish lean solid tissue from fluid mass. In this regard, it is noteworthy that GH significantly increases extracellular water volume [20], and it is likely that fluid retention accounts for a major proportion of the increase in LBM reported in GH studies in healthy subjects.

Substrate metabolism is significantly affected by acute GH exposure and a pivotal feature is stimulation of lipolysis [21]. In the present studies, the exercise-induced increase in circulating levels of glycerol and free fatty acids was significantly amplified by GH, even though an increase in lipid oxidation rates was not documented [18]. This is in accordance with data from GH-deficient adults [22] and it remains uncertain if this lipolytic effect impacts on exercise performance.

A significant GH-induced increase in plasma lactate levels to levels well above the anaerobic threshold was observed in two studies [13,18], which may be a negative determinant of exercise stamina and physical exhaustion [23]. It is believed that the increase in lactate originated from the working muscles [24], but it is unknown if this GH effect is due to increased lactate production, reduced clearance, or a combination of the two. However, Meinhardt et al. [19] reported a significant increase in anaerobic exercise capacity assessed by Wingate test and speculated that this increase in sprint capacity could translate to an improvement of 0.4 s in a 10-s sprint over 100 m. It seems unlikely that the improvement in sprint capacity is due to anabolic properties, so it is possible that GH under these conditions could regulate muscle energy metabolism and thus increase anaerobic exercise capacity which is in accordance with data from GH-deficient adults [25,26]. So far improvements in anaerobic exercise capacity has been an ignored area of exercise benefits which merits further research.

Furthermore, Meinhardt et al. reported that GH in combination with testosterone resulted in greater changes in body composition and physical performance compared to either treatment alone [19], and it is generally assumed that GH is abused in conjunction with anabolic steroids [27]. The included studies in this review show only limited evidence for efficacy of GH on athletic performance when used as a single agent. It has been hypothesized that the main performance-enhancing effect of GH is reduced recovery time via stimulation of local IGF-1 and its known musculoskeletal regenerative properties [28]. In addition, it is well-documented that GH stimulates collagen synthesis in tendon and skeletal muscle, thus strengthening the musculotendinous tissue and potentially preventing ruptures of muscle and tendons [29,30]. If this is true, GH doping may allow the athlete to train with increased frequency and higher intensities without overtraining or incurring an overuse injury, thus indirectly enhancing athletic performance.

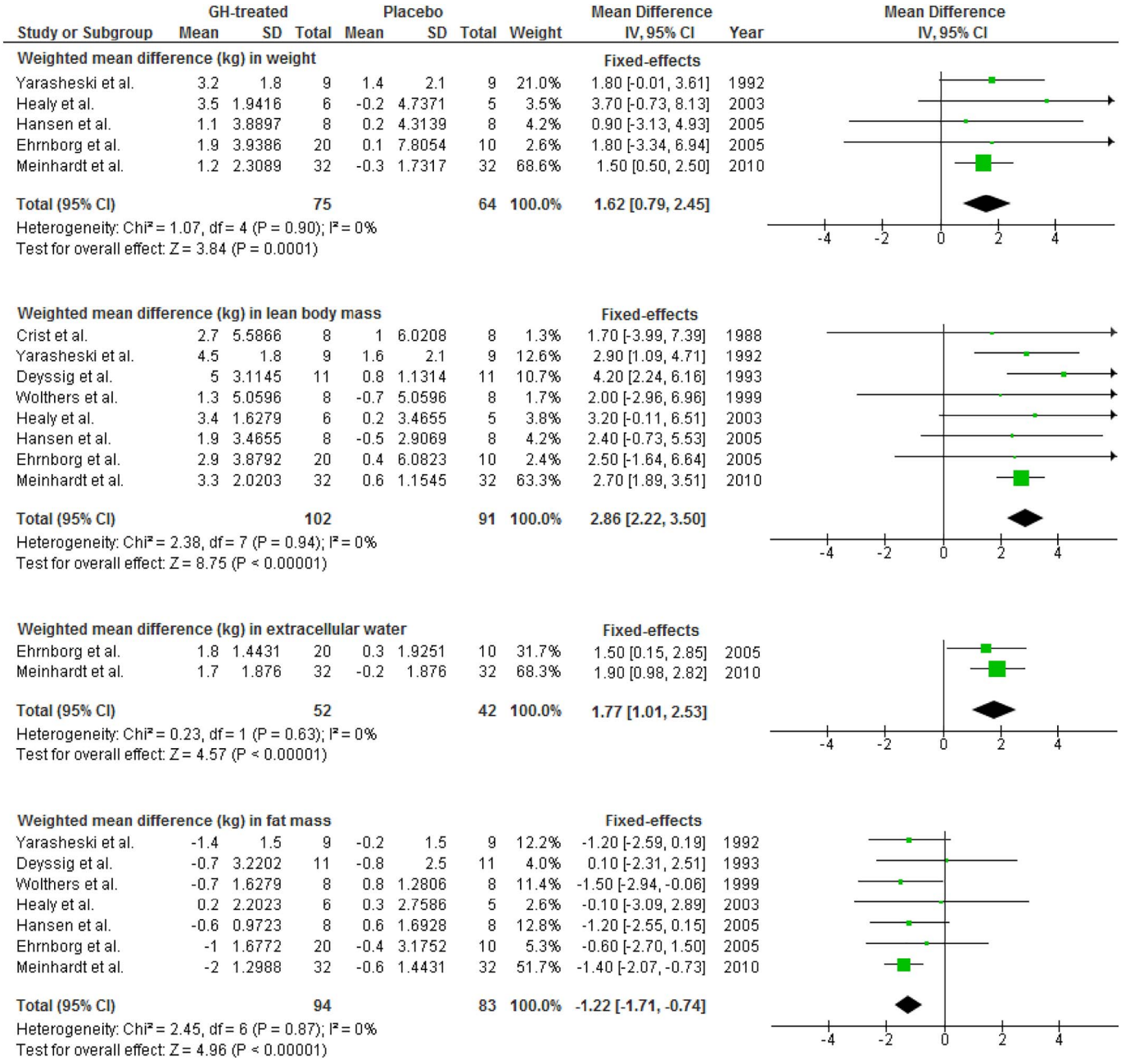

Fig. 2. Effects of GH administration on body composition.

This analysis reveals certain limitations of the published literature. First, only 11 trials with 224 participants met the inclusion criteria wherefore the sample size may be too low. We had intended to use a standard funnel plot to help identify possible publication bias. However, we did not identify enough trials to warrant this approach. Furthermore, the relatively small sample size did not permit a subgroup analysis of the potential impact of treatment dose, duration or timing.

Second, the GH dosing regimens used in the studies may differ from those used by athletes in the context of sports doping. It is suggested that athletes use GH doses ranging from 15 to 180 μg/kg per day three to four times a week in cycles of four to six weeks [1], which is higher than those used in most of the included studies in this review. However, it is unclear whether a graded dose-response exists for GH use. Furthermore, GH is typically co-administered with other performance-enhancing drugs [1,31] (e.g. insulin, androgenic anabolic steroids in power sports, or erythropoietin in endurance sports), and rarely used as a single agent [32]. Finally, measurement of clinical outcomes and methods were heterogeneous, which made comparisons between studies difficult.

Taken together, this meta-analysis suggests that GH administration in healthy young subjects is associated with distinct albeit moderate changes in body composition and lipolysis compatible with anabolic and lipolytic effects as previously documented in GH-deficient patients. By contrast, no consistent effects across studies were detected as regards to aerobic exercise capacity, whereas anaerobic exercise capacity may be improved by GH administration.

Conflicts of interest

The authors have nothing to disclose.

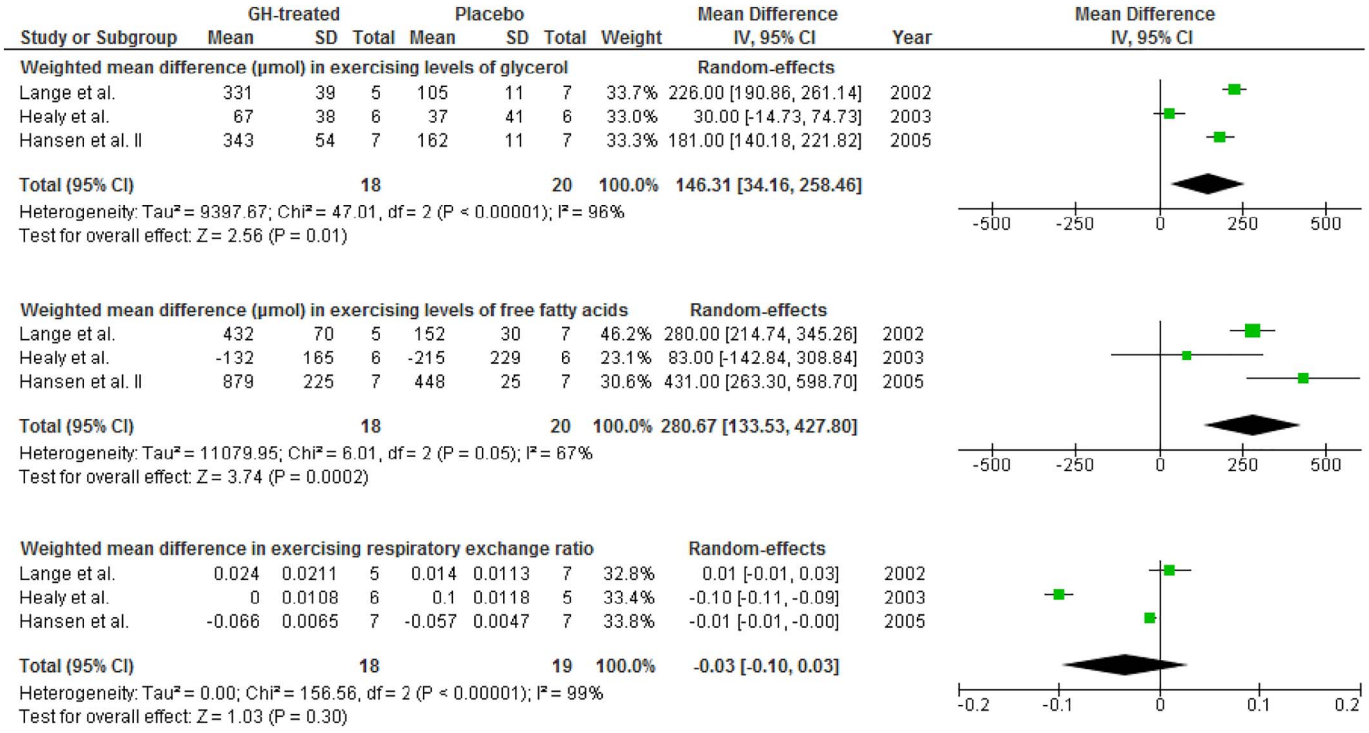

Fig. 3. Effects of GH administration on lipolytic markers.

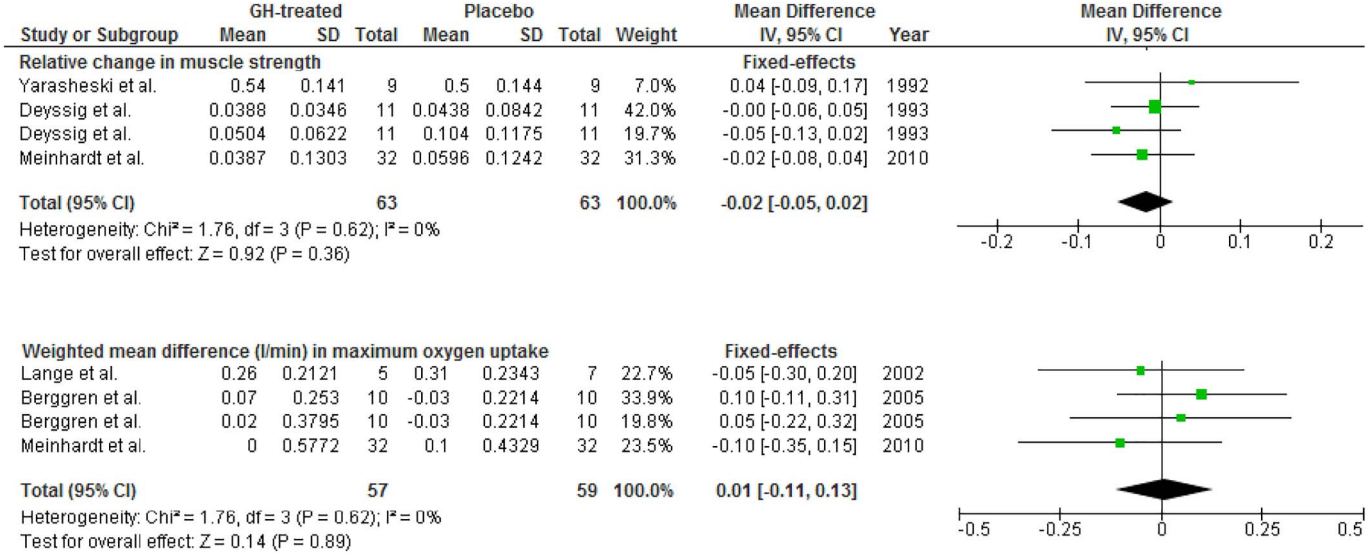

Fig. 4. Effects of GH administration on strength and exercise capacity.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ghir.2017.05.005.

References

[1] M. Saugy, N. Robinson, C. Saudan, N. Baume, L. Avois, P. Mangin, Human growth hormone doping in sport, Br. J. Sports Med. 40 (2006) 35–39.
[2] J.O. Jørgensen, S.A. Pedersen, L. Thuesen, J. Jørgensen, T. Ingemann-Hansen, N.E. Skakkebaek, J.S. Christiansen, Beneficial effects of growth hormone treatment in GH-deficient adults, Lancet 3 (1989) 1221–1225.
[3] K.Z. Rubeck, S. Bertelsen, P. Vestergaard, J.O. Jørgensen, Impact of GH substitution on exercise capacity and muscle strength in GH-deficient adults: a meta-analysis of blinded, placebo-controlled trials, Clin. Endocrinol. 71 (2009) 860–866.
[4] World Anti-Doping Agency: The 2016 Prohibited List. Accessed at http://list.wada-ama.org/prohibited-all-times/prohibited-substances/on 22th August 2016.
[5] Moher D, Liberati A, Tetzlaff J, Altman DG, and the PRISMA Group (2010): Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int. J. Surg., 8, 336–341.
[6] Higgins JP (2011): Handbook for systematic reviews of interventions version 5.1.0. The Cochrane Collaboration.
[7] J.P. Higgins, S.G. Thompson, Quantifying heterogeneity in a meta-analysis, Stat. Med. 21 (2002) 1539–1558.
[8] R. DerSimonian, N. Laird, Meta-analysis in clinical trials, Control. Clin. Trials 7 (1986) 177–188.
[9] D.M. Crist, G.T. Peake, P.A. Egan, D.L. Waters, Body composition response to exogenous growth hormone during training in highly conditioned adults, J. Appl. Physiol. 65 (1988) 579–584.
[10] K.E. Yarasheski, J.A. Campbell, K. Smith, M.J. Rennie, J.O. Holloszy, D.M. Bier, Effect of growth hormone and resistance exercise on muscle growth in young men, Am. J. Physiol. 262 (1992) 261–267.
[11] R. Deyssig, H. Frisch, W.F. Blum, T. Waldhör, Effect of growth hormone treatment on hormonal parameters, body composition and strength in athletes, Acta Endocrinol. 128 (1993) 313–318.
[12] Wolthers T, Lechuga A, Grøfte T, Nørrelund H, Møller N, Christiansen JS, and Jørgensen JOL: Serum leptin concentrations during short-term administration of

growth hormone and triiodo-thyronine in healthy adults: a randomized, double-blind placebo-controlled study. Hormone and Metabolic Research, 31, 37–40.
[13] K.H. Lange, B. Larsson, A. Flyvbjerg, R. Dall, M. Bennekou, M.H. Rasmussen, H. Ørskov, M. Kjaer, Acute growth hormone administration causes exaggerated increases in plasma lactate and glycerol during moderate to high intensity bicycling in trained young men, J. Clin. Endocrinol. Metab. 87 (2002) 4966–4975.
[14] M.L. Healy, J. Gibney, D.L. Russell-Jones, C. Pentecost, P. Croos, P.H. Sönksen, A.M. Umpleby, High dose growth hormone exerts an anabolic effect at rest and during exercise in endurance-trained athletes, J. Clin. Endocrinol. Metab. 88 (2003) 5221–5226.
[15] C. Ehrnborg, L. Ellegård, I. Bosaeus, B.A. Bengtsson, T. Rosén, Supraphysiological growth hormone: less fat, more extracellular fluid but uncertain effects on muscles in healthy, active young adults, Clin. Endocrinol. 62 (2005) 449–457.
[16] A. Berggren, C. Ehrnborg, T. Rosén, L. Ellegård, B.A. Bengtsson, K. Caidahl, Short-term administration of supraphysiological recombinant human growth hormone (GH) does not improve maximum endurance exercise capacity in healthy, young men and women with normal GH-insulin-like factor I axes, J. Clin. Endocrinol. Metab. 90 (2005) 3268–3273.
[17] M. Hansen, R. Morthorst, B. Larsson, A. Flyvbjerg, M.H. Rasmussen, H. Orskov, A. Astrup, M. Kjaer, K.H. Lange, Effects of 2 wk of GH administration on 24-h indirect calorimetry in young, healthy, lean men, Am. J. Physiol. 289 (2005) 1030–1038.
[18] M. Hansen, R. Morthorst, B. Larsson, R. Dall, A. Flyvbjerg, M.H. Rasmussen, H. Orskov, M. Kjaer, K.H. Lange, No effect of growth hormone administration on substrate oxidation during exercise in young, lean men, J. Physiol. 567 (2005) 1035–1045.
[19] U. Meinhardt, A.E. Nelson, J.L. Hansen, V. Birzniece, D. Clifford, K.C. Leung, K. Graham, K.K. Ho, The effects of growth hormone on body composition and physical performance in recreational athletes: a randomized trial, Ann. Intern. Med. 152 (2010) 568–577.
[20] J. Moller, J.O. Jorgensen, E. Frandsen, T. Laursen, J.S. Christiansen, Body fluids, circadian blood pressure and plasma renin during growth hormone administration: a placebo-controlled study with two growth hormone doses in healthy adults, Scand. J. Clin. Lab. Invest. 55 (1995) 663–669.
[21] N. Møller, J.O. Jørgensen, Effects of growth hormone on glucose, lipid, and protein metabolism in human subjects, Endocr. Rev. 30 (2009) 152–177.
[22] J.A. Kanaley, R. Dall, N. Møller, S.C. Nielsen, J.S. Christiansen, M.D. Jensen, J.O. Jørgensen, Acute exposure to GH during exercise stimulates the turnover of free fatty acids in GH-deficient men, J. Appl. Physiol. 96 (2004) 747–753.
[23] V.L. Billat, P. Sirvent, G. Py, J.P. Koralsztein, J. Mercier, The concept of maximal lactate steady state: a bridge between biochemistry, physiology and sport science, Sports Med. 33 (2003) 407–426.
[24] R.H. Fitts, Cellular mechanisms of muscle fatigue, Physiol. Rev. 74 (1994) 49–94.
[25] V. Chikani, R.C. Cuneo, I. Hickman, K.K. Ho, Impairment of anaerobic capacity in adults with growth hormone deficiency, Journal of Clinical Endocrinology 100 (2015) 1811–1818.
[26] V. Chikani, R.C. Cuneo, I. Hickman, K.K. Ho, Growth hormone (GH) enhances anaerobic capacity: impact on physical function and quality of life in adults with GH deficiency, Clin. Endocrinol. 85 (2016) 660–668.
[27] P.H. Sönksen, R.I. Holt, GH & IGF Research issue on doping with growth hormone, Growth Hormone and IGF Research 19 (2009) 283–284.
[28] A.P. Boesen, K. Dideriksen, C. Couppé, S.P. Magnusson, P. Schjerling, M. Boesen, M. Kjaer, H. Langberg, Tendon and skeletal muscle matrix gene expression and functional responses to immobilization and rehabilitation in young males: effect of growth hormone administration, J. Physiol. 591 (2013) 6039–6052.
[29] Doessing S, Heinemeier KM, Holm L, Mackey AL, Schjerling P, Rennie M, Smith K, Reitelseder S, Kappelgaard AM, Rasmussen MH, Flyvbjerg A, and Kjaer M: Growth hormone stimulates the collagen synthesis in human tendon and skeletal muscle without affecting myofibrillar protein synthesis. Journal of Physiology, 588, 341–351.
[30] S. Doessing, M. Kjaer, Growth hormone and connective tissue in exercise, Scand. J. Med. Sci. Sports 15 (2005) 202–210.
[31] A.E. Nelson, K.K. Ho, Abuse of growth hormone by athletes, Nat. Clin. Pract. Endocrinol. Metab. 3 (2007) 198–199.
[32] M. Fainaru-Wada, L. Williams, Game of Shadows, (2007).