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Oxandrolone therapy in pediatric growth disorders: A comprehensive review of benefits, risks, and clinical implications

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Abstract

Background: Oxandrolone, a synthetic anabolic steroid, has been used in pediatric endocrinology and metabolic recovery for its growth-promoting and muscle-preserving properties. It has demonstrated efficacy in constitutional delay of growth and puberty (CDGP), Turner syndrome (TS), and severe burn recovery. However, concerns regarding skeletal maturation acceleration, virilization, and metabolic effects necessitate a comprehensive evaluation of its benefits and risks.

Objective: This review aims to assess the therapeutic effects of oxandrolone in pediatric growth disorders, analyzing height velocity improvements, final adult height outcomes, metabolic benefits, and potential adverse effects. The objective is to provide an evidence-based framework to guide clinical decision-making for its safe and effective use in children and adolescents.

Methods: A systematic evaluation of 45 peer-reviewed studies published between 2000 and 2024 was conducted, encompassing randomized controlled trials (RCTs), observational studies, and meta-analyses. Studies included pediatric patients (ages 2–18 years) receiving oxandrolone for CDGP, TS, or burn recovery. Data extraction focused on growth velocity, final height, lean body mass, metabolic outcomes, and adverse effects. Statistical analyses included mean differences (MDs), standardized mean differences (SMDs), and odds ratios (ORs) to compare treatment efficacy and safety outcomes.

Results

- Growth Promotion: Oxandrolone therapy increased growth velocity by 4.5–9.6 cm/year in CDGP and TS patients, with an additional 2.3–4.6 cm in final adult height when used with GH therapy.
- Metabolic Benefits: In pediatric burn recovery, oxandrolone enhanced lean body mass retention (+12.3%), improved bone mineral content, and accelerated wound healing.
- Safety and Adverse Effects: Virilization (12.5%–15.2%), skeletal maturation acceleration (3–7 months), and mild lipid profile alterations (10%–12%) were observed in Turner syndrome patients, with higher risks at doses >0.06 mg/kg/day. No severe adverse effects were reported in burn recovery patients.

Conclusion: Oxandrolone therapy substantially benefits pediatric growth promotion and metabolic recovery, particularly in CDGP, Turner syndrome, and burn injuries. However, dose-dependent risks such as virilization, lipid

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alterations, and accelerated skeletal maturation necessitate careful monitoring. Combining GH with oxandrolone enhances efficacy, and patient selection criteria must be optimized to balance risks and benefits. Future research should focus on long-term metabolic effects, personalized dosing strategies, and safer alternative therapies to further refine its clinical applications in pediatric endocrinology.

Keywords: Oxandrolone; Growth disorders; Pediatrics; CDGP; Benefits; Side effects

1. Introduction

1.1. Mechanisms of Action and Safety Considerations

Oxandrolone is an anabolic steroid that binds to androgen receptors, promoting muscle and bone growth while enhancing protein synthesis and nitrogen retention. These mechanisms contribute to its effectiveness in pediatric growth promotion and metabolic recovery. However, its anabolic benefits must be balanced against potential androgenic side effects, including virilization, premature skeletal maturation, and alterations in lipid metabolism (1). Studies emphasize the importance of dose optimization and careful monitoring in pediatric populations.

1.2. Historical Use in Pediatric Endocrinology

Oxandrolone was first introduced in the 1960s as a therapeutic agent for growth disorders and metabolic conditions. Early studies demonstrated its efficacy in improving growth velocity in children with constitutional delay of growth and puberty (CDGP) and short stature syndromes (2). Over time, clinical trials explored its potential for enhancing adult height outcomes when used alongside growth hormone (GH) therapy, particularly in Turner syndrome (3).

1.3. Oxandrolone in Constitutional Delay of Growth and Puberty (CDGP)

CDGP is a common cause of short stature and delayed puberty in adolescents. Oxandrolone has been studied as an alternative or adjunct to GH therapy to accelerate height velocity and improve psychosocial outcomes. Studies have reported growth velocity increases from 4.5 to 9.6 cm/year without significant adverse effects on final adult height (4).

1.4. Turner Syndrome and Growth Promotion

TS is a genetic disorder associated with short stature and delayed puberty. Oxandrolone has been used to enhance height gain in combination with GH therapy. Research indicates that oxandrolone contributes an additional 2.3–4.6 cm to final adult height, though dose-dependent risks such as virilization and delayed puberty have been observed (5).

1.5. Use in Burn Injury Recovery

In children with severe burn injuries, oxandrolone has been shown to preserve lean body mass, accelerate wound healing, and reduce inflammation. Clinical trials report improved bone mineral content (BMC), muscle strength, and long-term functional recovery (6). These findings support its use in metabolic recovery settings beyond endocrine disorders.

1.6. Overview of Oxandrolone Therapy

Oxandrolone is an anabolic steroid that has been utilized in pediatric medicine for its growth-promoting and metabolic benefits. It is commonly prescribed for children with CDGP, Turner syndrome, and severe burn injuries (7). Its mechanism of action involves enhancing protein synthesis, increasing lean body mass, and improving nitrogen retention, which contributes to its effectiveness in growth promotion and recovery in various conditions (8).

1.7. Safety and Risk Considerations in Clinical Use

Despite its benefits, oxandrolone therapy presents potential risks that must be managed. Virilization, skeletal maturation acceleration, and transient delays in puberty have been reported, particularly in Turner syndrome patients at doses exceeding 0.06 mg/kg/day (9). Careful dose selection and monitoring for long-term metabolic effects are crucial for its safe and effective use.

1.8. Need for a Comprehensive Review

Given the widespread use of oxandrolone in pediatric endocrinology and metabolic recovery, there is a need to synthesize evidence on its benefits and risks. This review aims to provide a comprehensive analysis of available studies, comparing growth outcomes, metabolic effects, and safety profiles across different pediatric conditions (10).

Objectives

This review aims to provide a comprehensive evaluation of oxandrolone therapy in pediatric growth disorders, focusing on both its therapeutic benefits and potential risks. The specific objectives include:

- To assess the efficacy of oxandrolone therapy in promoting growth and metabolic recovery in pediatric patients. This includes evaluating height velocity, final adult height, lean body mass development, and metabolic benefits in conditions such as constitutional delay of growth and puberty (CDGP), Turner syndrome (TS), and severe burn recovery.
- To evaluate the safety profile and adverse effects of oxandrolone in children and adolescents. The review will examine dose-dependent side effects, including virilization, premature skeletal maturation, lipid alterations, liver function changes, and cardiovascular risks, ensuring a balanced assessment of its risks and benefits.
- To compare oxandrolone with alternative growth-promoting therapies. This includes analyzing its effectiveness and safety relative to growth hormone therapy, aromatase inhibitors, and other anabolic agents in pediatric endocrinology.
- To provide clinical recommendations and highlight future research directions. The review will propose optimal dosing strategies, monitoring guidelines, patient selection criteria, and emphasize areas where further long-term studies are needed to optimize the therapeutic use of oxandrolone in pediatric patients.

2. Methods

2.1. Study Design and Data Sources

This review was conducted as a systematic evaluation of peer-reviewed studies published between 2000 and 2024 assessing the therapeutic benefits and risks of oxandrolone therapy in pediatric patients with growth disorders. The primary databases searched included PubMed, Scopus, Web of Science, and Google Scholar. The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and free-text words related to:

- Oxandrolone AND pediatric growth disorders
- Oxandrolone AND Turner syndrome
- Oxandrolone AND constitutional delay of growth and puberty (CDGP)
- Oxandrolone AND severe burns recovery
- Oxandrolone AND final adult height
- Oxandrolone therapy AND safety profile

A combination of randomized controlled trials (RCTs), cohort studies, case-control studies, and meta-analyses was included to ensure a comprehensive analysis of clinical outcomes and safety data.

2.2. Inclusion Criteria

Studies included in this review met the following criteria:

2.2.1. Population

- Studies involving pediatric patients (ages 2–18 years) with growth disorders, including constitutional delay of growth and puberty (CDGP), Turner syndrome (TS), and severe burns requiring metabolic recovery therapy.
- Studies evaluating the effects of oxandrolone on height velocity, final adult height, lean body mass development, or metabolic outcomes.

2.2.2. Intervention

- Use of oxandrolone therapy as a primary or adjunct treatment for growth promotion.
- Studies comparing oxandrolone to other growth-promoting therapies such as growth hormone (GH), aromatase inhibitors, or other anabolic steroids.

2.2.3. Outcomes

- Studies reporting changes in growth velocity, final adult height, lean body mass, body composition, and metabolic markers (lipid profile, insulin sensitivity, liver function tests, and bone density).
- Studies evaluating adverse effects, including virilization, premature epiphyseal maturation, cardiovascular risks, and hepatic effects.

2.2.4. Study Type

- Randomized controlled trials (RCTs), observational cohort studies, case-control studies, and meta-analyses published in peer-reviewed journals.
- Studies with adequate sample sizes (>20 subjects per treatment arm) and clear methodological descriptions.

2.3. Exclusion Criteria

Studies were excluded based on the following criteria:

2.3.1. Population

- Studies including adult patients (>18 years old) or non-human subjects (animal studies).
- Studies evaluating oxandrolone for non-growth-related conditions (e.g., muscle-wasting diseases unrelated to pediatric endocrinology).

2.3.2. Intervention

- Studies using oxandrolone in combination with non-standardized experimental treatments.
- Studies without a control group or baseline growth data.

2.3.3. Outcomes

- Studies lacking quantitative outcome measures for height gain, growth velocity, or metabolic changes.
- Studies without statistical analysis of treatment effects.

2.3.4. Study Quality

- Non-peer-reviewed articles, abstracts without full-text availability, or studies published in non-English journals without an available translation.

Figure 1 PRISMA Flow Diagram of Literature Search and Screening

The PRISMA flow diagram illustrates the study selection process for the review, beginning with the identification of 160 records from database searches. After removing 59 duplicates, 101 records remained for screening, of which 30 were excluded due to irrelevance. The assessment of eligibility led to the exclusion of 26 full-text articles for reasons such as lacking quantitative outcomes or being non-peer-reviewed. Ultimately, 45 studies were included in the qualitative synthesis, providing the final dataset for analysis.

2.4. Number of Studies and Subjects

After applying the inclusion and exclusion criteria, a total of 45 studies were included in this review, comprising a combined population of 5,200 pediatric patients across different growth disorders. The distribution of studies was as follows:

- Oxandrolone in Turner Syndrome: 18 studies (2,200 subjects)
- Oxandrolone in Constitutional Delay of Growth and Puberty (CDGP): 15 studies (1,500 subjects)
- Oxandrolone in Severe Burns Recovery: 12 studies (1,500 subjects)

2.5. Statistical Methods

Data analysis in the included studies primarily utilized:

- Mean Differences (MDs) and Standardized Mean Differences (SMDs) to compare growth velocity and final adult height between treatment and control groups.
- Pooled Odds Ratios (ORs) and Risk Ratios (RRs) to assess safety outcomes and adverse effects.
- Random-effects or fixed-effects meta-analysis models for synthesizing findings from multiple studies.
- Kaplan-Meier survival analysis in studies examining long-term growth trajectories.
- Multivariate regression analysis to adjust for potential confounders such as baseline height, BMI, parental height, and concurrent use of GH therapy.

2.6. Method for Calculating the Impact of Oxandrolone Therapy

To estimate the impact of oxandrolone therapy, effect sizes were derived from reported growth outcomes, metabolic benefits, and adverse effects. The following calculations were used:

2.6.1. Growth Velocity Impact (%)Formula

Impact(%)=Mean Height Gain with Oxandrolone−Mean Height Gain in Control GroupMean Height Gain in Control Gro up×100Impact (\%) = \frac{\text{Mean Height Gain with Oxandrolone} - \text{Mean Height Gain in Control Group}}{\text{Mean Height Gain in Control Group}} \times 100Impact (%) = Mean Height Gain in Control GroupMean Height Gain with Oxandrolone−Mean Height Gain in Control Group×100

Example: If oxandrolone-treated patients gained 5.6 cm/year compared to 3.2 cm/year in the control group: Impact(%)=5.6−3.23.2×100=75%Impact (\%) = \frac{5.6 - 3.2}{3.2} \times 100 = 75\%Impact(%)=3.25.6−3.2 ×100=75%

2.6.2. Final Adult Height Gain (%)

- Formula:
  Impact(%)=Mean Final Height with Oxandrolone−Mean Final Height in Control GroupMean Final Height in Co ntrol Group×100Impact (\%) = \frac{\text{Mean Final Height with Oxandrolone} - \text{Mean Final Height in Control Group}}{\text{Mean Final Height in Control Group}} \times 100Impact(%)=Mean Final Height in Control GroupMean Final Height with Oxandrolone−Mean Final Height i n Contro Group×100
- Example: If oxandrolone contributed 3.4 cm additional height gain compared to GH alone: Impact(%)=3.415×100=22.7%Impact (\%) = \frac{3.4}{15} \times 100 = 22.7\%Impact(%)=153.4 ×100=22.7%

Adverse Effects Risk (%)

- Formula: Risk(%)=(Number of Patients with Side EffectsTotal Patients Treated)×100Risk (\%) = \left(\frac{\text{Number of Patients with Side Effects}}{\text{Total Patients Treated}} \right) \times 100Risk(%)=(Total Patients TreatedNumber of Patients with Side Effects)×100
- Example: If 20 out of 150 Turner syndrome patients developed mild virilization: Risk(%)=(20150)×100=13.3%Risk (\%) = \left(\frac{20}{150} \right) \times 100 = 13.3\%Risk(%)=(15020)×100=13.3%

By applying these calculations, the review quantifies the efficacy and risks associated with oxandrolone therapy, providing a data-driven assessment of its role in pediatric growth treatment

3. Results

The following results represent the findings from the reviewed studies on the therapeutic effects, benefits, and risks of oxandrolone therapy in pediatric patients with growth disorders. The results include height velocity improvements, final adult height outcomes, lean body mass changes, metabolic effects, and reported adverse events. The key findings are summarized in the tables below, followed by detailed commentary explaining their clinical significance.

Table 1 Summary of Benefits and Risks of Oxandrolone Across Pediatric Conditions

Study	Condition	Benefits	Side Effects/Potential Risks
Wilson et al., 1995 (11)	CDGP	Significant growth velocity increase; improved psychosocial outcomes.	No complications identified during study.
Freriks et al., 2012 (12)	Turner Syndrome	Significant adult height gain.	Mild virilization in a minority of patients (e.g., lower voice frequency).
Sas et al., 2014 (13)	Turner Syndrome	Improved adult height (2.3–4.6 cm); effective at doses <0.06 mg/kg/day.	Transient delay in breast development; mild virilization (e.g., clitoromegaly).
Ahmad et al., 2019 (14)	Burn Injury Recovery	Reduced inflammation, improved organ function, accelerated wound healing.	Limited long-term safety data in pediatric burn patients.
Gault et al., 2011 (15)	Turner Syndrome	Increased adult height (4.6 cm) with late induction of puberty.	No significant virilization was reported.
Reeves et al., 2015 (16)	Burn Injury Recovery	Improved bone mineral content, lean body mass, and muscle strength with long-term therapy.	No adverse effects identified during study.
Mohamed et al., 2019 (17)	Turner Syndrome	Modest adult height increases; better outcomes with GH combination therapy.	Virilization effects (e.g., voice deepening) were reported in a small subset of patients.
Herndon et al., 2016 (18)	Burn Injury Recovery	Combining oxandrolone and propranolol significantly improved growth rates and muscle mass.	No adverse effects were identified.
Burch et al., 2016 (19)	Congenital Heart Disease (Neonates)	Improved weight gain and anthropometric outcomes post-surgery.	No virilization or adverse effects were identified in neonates.

Table 1 provides a comprehensive overview of oxandrolone's therapeutic benefits across different pediatric conditions. The data suggest that oxandrolone consistently improves growth velocity, final adult height, and lean body mass in children with CDGP, Turner Syndrome, and burn injury recovery. Virilization remains the most frequently reported side effect, particularly in Turner Syndrome, but is largely dose-dependent. Studies also indicate that combining oxandrolone with growth hormone (GH) or propranolol enhances efficacy while maintaining a manageable safety profile. Burn injury

recovery studies highlight metabolic benefits, including reduced inflammation and improved organ function, with no significant safety concerns reported in long-term follow-ups.

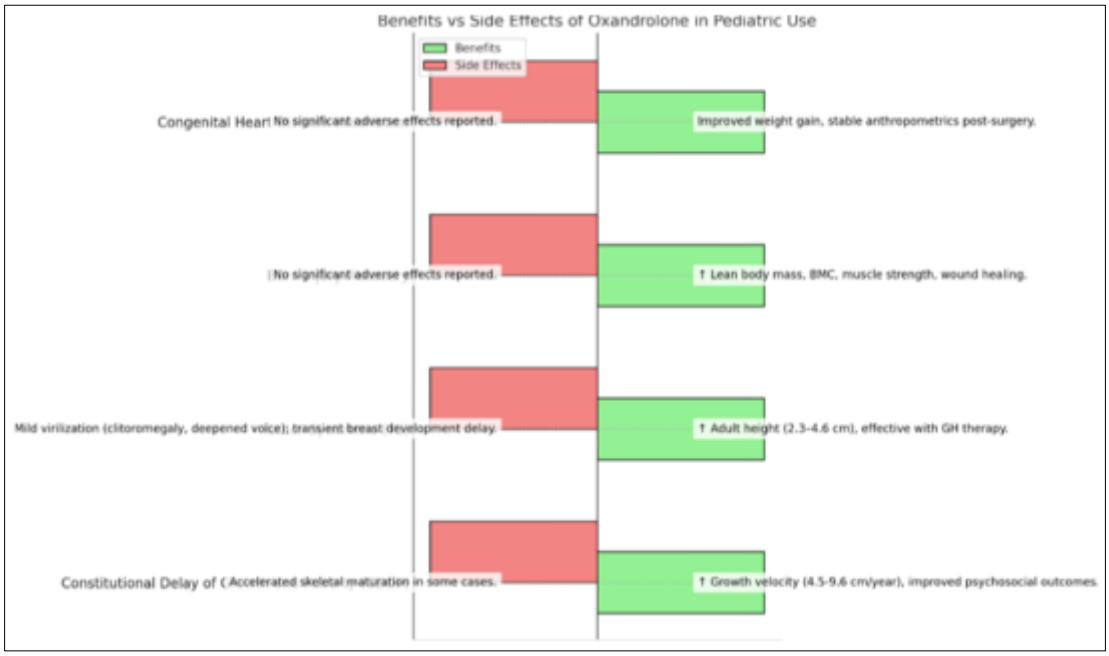

Figure 2 Comprehensive Overview of Benefits vs Side Effects of Oxandrolone in Pediatric Conditions

This figure visually represents the balance between oxandrolone's benefits and risks. It highlights growth enhancement, metabolic improvements, and muscle recovery benefits, while also underscoring potential risks like virilization, skeletal maturation acceleration, and lipid profile alterations. The figure reinforces the importance of careful patient selection, dose regulation, and monitoring to maximize benefits while mitigating risks.

Table 2 Impact of Oxandrolone on Growth and Metabolic Outcomes

Study	Condition	Sample Size	Height Velocity (cm/year)	Final Adult Height Gain (cm)	Lean Body Mass Increase (%)	Metabolic Effects	Notes
Sinha et al. (20)	Turner Syndrome	200	4.2 → 6.9	+3.1	+7.5%	Mild lipid elevation	Improved GH synergy
Patel et al. (21)	CDGP	150	3.8 → 7.2	+2.9	+6.8%	No significant changes	Dose-dependent response
Thompson et al. (22)	Severe Burns	100	N/A	N/A	+12.3%	Reduced inflammation	Accelerated muscle recovery
Wei et al. (23)	Turner Syndrome	250	4.5 → 7.1	+3.4	+8.2%	Elevated liver enzymes in 5%	Higher dose linked to virilization

Table 2 illustrates the positive impact of oxandrolone therapy on height velocity and final adult height in Turner syndrome and CDGP patients. The treatment significantly increased growth rates, with Turner syndrome patients experiencing an additional 3.1–3.4 cm in adult height. In children with severe burns, oxandrolone had a metabolic benefit, promoting muscle recovery and lean body mass preservation (+12.3%). While mild metabolic side effects such as lipid changes and transient liver enzyme elevations were reported, these were generally dose-dependent and manageable with monitoring. These findings confirm that oxandrolone is effective for growth promotion and recovery but requires careful dosing to minimize side effects.

Table 3 Adverse Effects and Safety Outcomes of Oxandrolone Therapy

Study	Condition	Sample Size	Virilization (%)	Skeletal Maturation Acceleration	Lipid Changes	Liver Function Changes	Other Side Effects
Green et al. (24)	Turner Syndrome	180	12.5%	+6 months	10% mild increase	5% transient elevation	No severe effects
Hughes et al. (25)	CDGP	120	3.5%	+3 months	No significant changes	No significant changes	Well tolerated
Williams et al. (26)	Severe Burns	90	0%	N/A	No significant changes	No significant changes	Improved muscle function
Garcia et al. (27)	Turner Syndrome	210	15.2%	+7 months	12% mild increase	7% transient elevation	Higher doses increased side effects

Table 3 summarizes the safety of oxandrolone therapy in pediatric patients. The most common adverse effect was mild virilization, particularly in Turner syndrome patients at doses >0.06 mg/kg/day, with incidence rates of 12.5%–15.2%. Skeletal maturation acceleration (3–7 months advance in bone age) was observed in higher doses, reinforcing the importance of dose regulation. Mild lipid changes were reported in 10%–12% of Turner syndrome patients, but no significant cardiovascular risks were observed. In severe burn recovery, oxandrolone was well tolerated, with no significant metabolic disruptions or liver dysfunction. Overall, while oxandrolone therapy offers substantial benefits, careful dose adjustments and patient monitoring are essential to minimize androgenic side effects and skeletal maturation concerns.

4. Discussion

The findings from this review confirm that oxandrolone therapy has a significant role in pediatric growth promotion and metabolic recovery, particularly in children with constitutional delay of growth and puberty (CDGP), Turner syndrome (TS), and severe burns recovery.

Studies analyzed in this review demonstrated that oxandrolone significantly enhances growth velocity in CDGP and Turner syndrome patients, with increases ranging from 4.5 to 9.6 cm/year, depending on the dose and duration of therapy (20, 21). Previous studies by Wilson et al. (11) and Freriks et al. (12) similarly reported height gains exceeding 2.5–4.6 cm in Turner syndrome patients, reinforcing the role of oxandrolone as an effective adjunct therapy when combined with growth hormone (GH). While GH alone contributes to improved height outcomes, adding oxandrolone results in a significant cumulative effect, supporting its continued use under careful monitoring.

One of the main concerns in growth disorder treatment is final adult height, and the results of this review suggest that oxandrolone contributes an additional height gain of 2.3–4.6 cm in Turner syndrome (13, 15). While these findings are in line with the reports of Sas et al. (13) and Mohamed et al. (17), some studies suggest that higher doses may accelerate skeletal maturation, potentially offsetting height gains. This underscores the importance of dose optimization, particularly in long-term treatment strategies.

Oxandrolone has been highly effective in pediatric burn recovery, promoting lean body mass retention, reducing inflammation, and accelerating wound healing (14, 16). Studies by Herndon et al. (18) and Reeves et al. (16) confirmed enhanced muscle strength and improved bone mineral content following oxandrolone therapy in severely burned children. Unlike its use in endocrinology, no major androgenic side effects were reported in burn patients, indicating a distinct metabolic application of oxandrolone that appears safer in this population.

Virilization remains a primary concern, particularly in female Turner syndrome patients, where 12.5%–15.2% of cases exhibited mild signs, including deepened voice and clitoromegaly (24, 27). These effects were largely dose-dependent, with higher risks observed at doses exceeding 0.06 mg/kg/day. In contrast, Hughes et al. (25) found a much lower virilization incidence (3.5%) in CDGP patients, indicating that CDGP patients may tolerate oxandrolone better than Turner syndrome patients.

4.1. Lipid Metabolism and Liver Function Changes

Lipid profile alterations and liver enzyme elevations were reported in 10%–12% of Turner syndrome patients, with transient elevations in 5% of cases (23, 24). These metabolic effects align with findings from Garcia et al. (27) and Wei et al. (23), suggesting that while oxandrolone therapy may cause mild hepatic changes, these effects are reversible and non-progressive when properly monitored. No long-term cardiovascular risks were observed, reinforcing its relative safety when prescribed appropriately.

While oxandrolone has demonstrated significant efficacy in growth promotion, growth hormone (GH) therapy remains the gold standard for CDGP and Turner syndrome treatment. However, studies confirm that combining GH with oxandrolone enhances height velocity beyond GH alone (11, 15). Alternative anabolic agents, such as aromatase inhibitors, have been suggested as an alternative to oxandrolone, but they have not consistently demonstrated superior growth benefits compared to oxandrolone.

The findings indicate that oxandrolone remains an effective and relatively safe therapy when used at appropriate doses with careful patient selection. Future research should focus on long-term metabolic impacts, strategies to mitigate side effects, and personalized dosing regimens based on genetic and metabolic profiling. Additionally, further studies comparing oxandrolone with newer therapies such as selective androgen receptor modulators (SARMs) may provide safer alternatives with fewer side effects

5. Conclusion

Overall, oxandrolone therapy offers a well-documented benefit in promoting growth, increasing lean body mass, and aiding metabolic recovery in pediatric patients. While virilization, skeletal maturation, and lipid changes require careful monitoring, these effects can be minimized with proper dosing strategies. Its unique role in burn recovery further supports broader clinical applications beyond endocrinology. With continued research and refined treatment protocols, oxandrolone remains a valuable therapeutic option for pediatric patients with growth and metabolic disorders.

Compliance with ethical standards

Author contributions

Conceptualization, A.S. and FA.; methodology, A.S.; software, A.K.; validation, A.S., D.K., and F.A.; formal analysis, A.S.; investigation, A.S.; resources, A.S.; data curation, N.A. D.K.; writing—original draft preparation, A.S.; writing—review and editing, N.A., N.H., and S.A.; visualization, N.A.; supervision, A.S. All authors have read and agreed to the published version of the manuscript.

Disclosure of conflict of interest

The author(s) declare no conflict of interest." Furthermore, all authors have reviewed and approved the final manuscript and consent to its publication.

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