Review Article

A Reappraisal of Oxandrolone in Burn Management

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Abstract

Objective: Burn injuries remain among the most severe traumatic injuries globally. With the discovery of cortisol, the use of steroids has become an essential therapy for the management of inflammatory and metabolic conditions. Several studies have shown the steroid oxandrolone improves burn injuries through stimulating anabolic and reducing catabolic processes. In this review, we examine the efficacy and applications of oxandrolone with regard to burn management and treatment. **Data Sources:** A literature search was performed using the PubMed database from January 1990 to May 2020 to identify articles on oxandrolone and burn management. A total of 18 studies were included in our review. **Study Selection and Criteria:** The keywords used in our search strategy for PubMed included "oxandrolone" and "burns." **Data Synthesis:** The main benefit of oxandrolone is the improved long-term lean body, protein, and bone mineral mass of burn patients. In addition, 3 separate meta-analyses showed oxandrolone shortened length of hospital stay, donor-site healing time, reduced weight loss, and net protein loss. However, oxandrolone therapy did not affect mortality, infection, or liver function. **Conclusion:** Oxandrolone remains an effective therapy for reducing the hypermetabolic response and comorbidities from burn injuries. Future clinical trials are needed using larger sample sizes and long-term follow-up to determine whether oxandrolone in the context of rehabilitation programs can reduce mortality, lower treatment costs, and improve function outcomes among burn patients.

Keywords

oxandrolone, adrenergic, burns, metabolism, treatment

Introduction—Oxandrolone History

With the discovery of cortisol, steroids have become an essential therapy for the management of inflammatory and metabolic conditions.[1] The synthesis of steroids was originally directed toward the treatment of rheumatoid arthritis; subsequently, it was expanded to improve metabolic function in hospitalized patients and athletes.[1] The success of cortisol also increased the use of other anabolic steroids, including oxandrolone.[1] Oxandrolone was first synthesized in the 1960s by Fox and Gherondache et al for women and children to promote lean tissue growth after surgery, trauma, and infection.[2-5] Subsequent studies later showed oxandrolone had 6 times greater anabolic activity compared with testosterone.[4,5] Given its potent anabolic activities, bodybuilders and competitive athletes abused oxandrolone to increase muscle gain without fat or water accumulation; as a result, oxandrolone was discontinued in 1989.[4,5] However, oxandrolone was reintroduced in 1995 for preserving lean mass particularly among patients with AIDS wasting, alcoholic hepatitis, and Turner syndrome.[4,5] Since then, oxandrolone has showed clinical outcomes in several catabolic conditions, such as neuromuscular disorders, alcoholic hepatitis, and chronic inflammatory illnesses. In recent years, oxandrolone has shown several beneficial effects in the treatment and management of burn injuries.

Oxandrolone Pharmacology and Guidelines

Oxandrolone is a nonreducible, nonaromatizable synthetic chemical. Oxandrolone is structurally similar to testosterone, but has a unique chemical arrangement in which an oxygen atom replaces the methylene group.[5] Oxandrolone is rapidly absorbed, with peak serum concentrations occurring in about 1 hour. With a distribution half-life of 30 minutes and an elimination half-life of approximately 9 hours, plasma oxandrolone concentrations drop in a biphasic manner. In addition, 95% of oxandrolone is bound to proteins.[5]

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Currently, oxandrolone can be given at 10 mg orally twice daily in adults and 0.1 mg/kg twice daily in children with burns greater than 20%. For elderly patients (>65 years of age), oxandrolone is given at 5 mg twice daily. Despite minimal adverse effects, oxandrolone has many of the adverse effects of steroids, such as fluid retention, high blood pressure, mood swing, and hyperglycemia.[5] Steroids, such as oxandrolone, with an alkyl group linked to the steroid nucleus are known to have hepatotoxic effects. The more serious hepatic consequences from increased liver enzymes and cholestatic jaundice include peliosis hepatis, hyperplasia, adenomas, and hepatocellular carcinoma. High doses, long-term usage (>1 year), and several concurrent anabolic drugs like oxandrolone have all been linked to these adverse effects.[5]

Administration of oxandrolone has been linked to elevated liver enzyme, most notably aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, and alkaline phosphatase. Specifically, patients who are younger and have concurrent amiodarone or vasopressor use have the highest risk of developing oxandrolone-induced transaminitis.[6] These adverse effects have been shown to develop following large doses and/or chronic use of oxandrolone. However, the elevation of transaminases returns to normal once oxandrolone is discontinued. With relatively low dosages (0.1-0.2 mg/kg/d), slight increases in liver function enzyme levels have been observed with the administration of oxandrolone.[5] However, most hepatic toxicity observed is asymptomatic and leaves no persistent liver damage.

In addition, virilizing signs in female patients taking oxandrolone is monitored on a regular basis.[5] The most common symptoms of female virilization from oxandrolone include facial hair growth, acne, alopecia, deepened voice, increased libido, and clitoromegaly. In 2 studies of oxandrolone, female patients were withdrawn due to virilizing effects of oxandrolone.[5] In 27 studies examining female virilization using oxandrolone, only 14 female patients among the total 1000 patients developed symptoms of virilization.[5] Although the rate of virilization is low, only 15% of patients in the clinical trials examining oxandrolone were female. As such, further investigation is warranted to examine the incidence of female virilization among patients taking oxandrolone.[5]

The general contraindications for using oxandrolone include suspected carcinoma of the prostate or the male breast, carcinoma of the breast in females with hypercalcemia, pregnancy, nephrosis, and hypercalcemia. Current guidelines suggest discontinuation of oxandrolone if hypercalcemia develops. In addition, the use of adrenal cortical steroids or adrenocorticotropic hormone (ACTH) with oxandrolone may also exacerbate edema. Furthermore, patients with preexisting cardiac, renal, or hepatic illness, and edema with or without congestive heart failure should be monitored closely when given oxandrolone. At relatively modest doses, oxandrolone can also cause cholestatic hepatitis and jaundice.[5] If this occurs, oxandrolone should be discontinued and the cause assessed before restarting the medication. Furthermore, androgen treatment in children may hasten bone maturation without a compensating increase in linear growth. Specifically, the younger the child, the greater the chance of the child having a lower final mature height. Therefore, current guidelines suggest oxandrolone should be examined every 6 months by measuring the bone age of the left wrist and hand.[5]

For childhood burn injuries, the National Health Services (NHS) recommends that oxandrolone be initiated at 3 to 5 days postburn injury using a dose 0.1 mg/kg once to twice daily for burns with a greater total body surface area (TBSA) of 40%.[7] Depending on the severity of the burns and the severity of the hypermetabolic reaction, oxandrolone can be continued for at least 1 to 2 years.[7] Once a collaborative decision is reached by the appointed pediatrician and burn specialist, oxandrolone can be discontinued immediately. Follow-up appointments for children prescribed oxandrolone should also occur at 1-, 3-, 6-, 9-, and 12-month postburn and then continued for at least 6 months after discontinuing oxandrolone. At each visit, the height, weight, sexual maturation and signs of virilization (acne, deep voice, clitoromegaly, pubic hair) and liver function tests should be assessed.[7] If oxandrolone is started in prepubertal children, bone aging may be accelerated. In these children, bone age analysis at 1 year and 2 years after starting oxandrolone is indicated. Similar guidelines by the American Burn Association suggest using 10 mg of oxandrolone immediately after burn injuries for adult patient populations with similar follow-up intervals to assess liver injury and virilization in female patients.[8]

Oxandrolone and Burn Management

Burn injuries remain among the most severe traumatic injuries globally.[9] As the amount of body surface burned increases, there is a corresponding increase in hypermetabolism.[10,11] The hypermetabolism results from increased stress and inflammatory mediators in response to toxic chemicals released from damaged collagen and fat.[12-14] The physiological demands to maintain this energy production require large amounts of glucose, which are maintained through gluconeogenesis through catabolism of proteins in the liver. If left untreated, the hypermetabolic response increases liver and cardiac work, impairs muscle function, increases the risk of sepsis, and alters hormone levels. These combined influences lead to a greater increase in morbidity and mortality among burn patients.[12-14] In response, several pharmacological agents have been investigated in their efficacy to reduce the hypermetabolic response and to improve outcomes in the burn patients.[15-19] Oxandrolone was one of the first anabolic steroids to be

administered for acute burn injury and rehabilitation given the drug's effect on increasing weight gain and urinary nitrogen balance without significant virilization or hepatotoxicity.[20,21]

Recent clinical trials administering oxandrolone have shown promise as an effective strategy for reducing post-burn catabolism in burn patients.[22] Oxandrolone directly binds to intracellular androgen receptors in skeletal muscle, leading to increased muscle protein synthesis, and competitively inhibits glucocorticoid receptors, which reduce cortisol muscle catabolism.[23-25] Both processes are believed to improve wound healing through an increase in insulin-like growth factor 1 (IGF-1).[23-25] Subsequent studies indicated that oxandrolone may reduce the length of hospital stay, increase weight gain, preserve lean body mass, and improve bone mineral density.[23-25] Overall, these studies suggest oxandrolone improves burn injuries through stimulating anabolic and reducing catabolic processes. In this review, we examine the efficacy and applications of oxandrolone with regard to burn management and treatment.

Method

A literature search was performed using the PubMed database from January 1990 to May 2020 to identify articles on oxandrolone and burn management. The keywords used in our search strategy for PubMed included "oxandrolone" and "burns." A total of 66 studies were identified. Evaluation of each led to 48 papers being excluded, including editorials, commentaries, basic science studies, case reports, or not being relevant to our topic of interest. Specifically, these papers investigated the use of oxandrolone in other pathologies, such as cardiovascular disease or modulating metabolism. Of the 18 articles included in this review, 4 were randomized control trials (RCTs) and 14 were original retrospective articles.

Results

One of the first studies to study the effect of oxandrolone on burn healing was conducted by Robert Demling.[21] The prospective study examined the anticatabolic activity (n = 16) 20 mg/d oxandrolone compared with 0.1 mg/kg/d human growth hormone (n = 20) in patients with burns covering over 50% TBSA or had 25% TBSA with other comorbidities (eg, elderly, malnutrition, or diabetes).[21] The study also included data from burn patients not administered oxandrolone or human growth hormone (n = 24).[21] The study found the oxandrolone reduced net weight loss compared with human growth hormone (421.8 kg) and the control group (822.1 kg).[21] The daily nitrogen loss was also lower in the oxandrolone (3 g) and human growth hormone groups (3 g) compared with the control group (1223 g).[21] Interestingly, the metabolic rate compared with baseline levels was higher in the human growth hormone (178%) than the control (155%) or oxandrolone (156%) groups.[21] Furthermore, the healing time for both human growth hormone (10 days) and oxandrolone (10 days) was reduced compared with the control (14 days).[21] Hyperglycemia (glucose over 225 mg/dL 12.5 mM) was in 100% of the human growth hormones compared with 55% of the control and 50% of the oxandrolone groups.[21] Although human growth hormone and oxandrolone decreased weight and nitrogen loss and increased healing, human growth hormone increased blood sugar levels and metabolic rate. A subsequent study by Demling and Orgill[26] confirmed that oxandrolone significantly decreased weight loss and net nitrogen loss and increased donor-site wound healing compared with the placebo controls.

The success of oxandrolone encouraged additional studies to evaluate its efficacy at reducing muscle catabolism among pediatric burn patients. A study by Hart et al[27] examined 14 burned patients who had TBSA greater than 20% over a 5-month period who received 0.1 mg/kg oxandrolone (n = 7) or standard care (n = 7). The protein kinetics were measured in the femoral arterial and venous blood samples and vastus lateralis muscle biopsies using a phenylalanine isotope infusion.[27] A kinetic modeling analysis was then performed to measure the amino acid transport among 3 primary compartments: venous, arterial, and muscle compartments. The study found that patients treated with oxandrolone had an increased net protein balance within muscles compared with baseline and time-matched control patients.[27] The increase net protein balance was due to increased protein synthesis and fraction of the available intracellular amino acids; in contrast, the rate of protein degradation remained constant. No adverse effects, such as hirsutism, acne, or behavior changes, were observed in the patients receiving oxandrolone.[27] Oxandrolone also produced minor liver damage as observed in the slight increase of alkaline phosphatase and prothrombin time.[27] The study further supported the use of oxandrolone as a safe, inexpensive, and easily administered anabolic agent for burn patients.

Given the improved protein synthesis, Hart et al conducted a second study to determine whether early administration (within the first week of admission) of oxandrolone could further increase protein synthesis among burn patients. The study included 32 patients with burns covering more than 40% TBSA who received the placebo (n = 18) or 0.1 mg/kg oxandrolone (n = 14) twice a day for 1 week.[28] As previously reported, oxandrolone increased the protein net balance compared with the control group. Furthermore, the change in total body weight (–2.3 vs –0.6 kg), lean body mass (–1.7 vs –0.6 kg), and fat free mass (–2.2 vs 0.8) was lower in the control group compared with children administered oxandrolone.[28] Biopsies collected from the patients also showed that the oxandrolone group

had increased expression of the structural and signaling proteins myosin light chain, dynein, tubulin, and calcineurin/calmodulin/Ca^{2+} signaling proteins; in contrast, protein phosphatase I inhibitor, which inhibits protein translation, was downregulated.[28] The results suggest that oxandrolone increases protein synthesis through altering structural and signaling proteins involved with muscle function and maintenance. Pham et al[29] and Sousse et al showed a similar reduction in hypermetabolism and mortality rate.

A subsequent study by Demling et al[30] studied the effect of oxandrolone with proper nutrition and exercise on the restoration of lean body mass and weight loss in older burn patients compared with younger burn patients. The study included 25 younger (25 years of age) and 15 older (60 years of age) patients who had burns covering 30% to 55% of TBSA% during the recovery phase.[30] Both the younger and older burn patients randomly received the 10 mg oxandrolone twice daily or the placebo.[30] The total weight gain increased for the younger (79%) and older (76%) burn patients compared with the control (younger: 59%; older: 51%).[30] There was a similar increase in lean body mass in the younger (73%) and older (72%) burn patients compared with the control group (younger: 69%; older: 60%).[30] Furthermore, administering oxandrolone reduced length of hospital stay by 30%. Therefore, the use of oxandrolone for maintaining weight gain and lean body mass in burn patients does not depend on age.

Current clinical studies suggest burn injuries reduce muscle protein through an increase in acute phase proteins, such as C-reactive protein, C3 complement, and fibrinogen.[31] Given that oxandrolone improved muscle protein, it was hypothesized oxandrolone reduced acute phase protein synthesis in the liver. A study by Thomas et al[31] examined 35 children with burns covering more than 40% TBSA who received either the placebo or 0.1 mg/kg oxandrolone for a period of 1 year. The study found a decrease in constitutive proteins, such as albumin, prealbumin, and retinol-binding protein, and acute phase proteins, such as α1-acid glycoprotein, C3 complement, β2-macroglobulin, and fibrinogen, in the oxandrolone group than the placebo group.[31] Furthermore, albumin supplementation during hospitalization was reduced in the oxandrolone group.[31] Therefore, administration of oxandrolone after acute burn injuries may reduce weight loss and catabolic processes in burn patients.

Although oxandrolone reduced weight loss and catabolic processes, it was unclear whether the effects would be retained 6 months after stopping oxandrolone.[32] A study by Demling and DeSanti[32] studied 45 patients who were in the recovery phase who received standard nutrition support (n = 22) or nutrition support with 20 mg/d oxandrolone (n = 23) during their rehabilitation. The study found that the patients receiving oxandrolone regained total weight and lean mass 2 to 3 times faster compared with the control.[32] After 6 months, the body weight and lean mass of the patients treated with oxandrolone were maintained; in contrast, the lean body mass in the control group was not restored.[32] A similar study was performed by Salisbury[33] examined whether oxandrolone could reverse hypermetabolism among pediatric burn patients for 1 year after sustaining burn injuries. Specifically, the study included 84 pediatric patients with burns covering 40% who received either 0.1 mg/kg oxandrolone (n = 42) or placebo (n = 42).[33] The study also found that lean body mass and bone mineral density was higher in children treated with oxandrolone compared with the control group.[33]

Therefore, oxandrolone provides long-term improvements in burn patient's weight and lean body mass even after discontinuation. This suggests oxandrolone shifts a burn patient's metabolism from catabolic to anabolic processes.[34] To investigate this shift, Barrow et al[34] examined 14 patients with burns covering 40% TBSA who received either 0.1 mg/kg oxandrolone twice a day (n = 7) or the placebo (n = 7). Using a human high-density oligonucleotide array, the expression of several genes in skeletal muscle was analyzed. The study found that patients treated with oxandrolone had an increase in several genes related to normal skeletal physiology, including ATP synthase, succinate dehydrogenase complex, *N*-acylsphingosine amidohydrolase, synaptic nuclei expressed gene b1, and phosphoserine phosphatase.[34] In contrast, oxandrolone also decreased several genes involved in growth arrest and proliferation, including growth arrest and DNA-damage-inducible α/β, Jun B proto-oncogene, and GRO2 oncogene.[34] Interestingly, there were 32 genes altered in male patients treated with oxandrolone compared with 12 genes in female patients treated with oxandrolone.[34] This gender difference in oxandrolone response may be due to increased steroid sensitivity found in males compared with females.[34] However, larger sample sizes are needed to confirm these results. Overall, the study suggests oxandrolone restores skeletal muscle function by reducing several genes associated with inflammation and stress response signal transduction pathways resulting from thermal trauma.

Similar to Salisbury, Przkora et al studied burn patients treated with oxandrolone for 1 year and followed the patients for 1 year after the drug was discontinued. The study included children with burns covering greater than 40% TBSA who received 0.1 mg/kg oxandrolone (n = 30) or placebo (n = 31) for 12 months.[35] The study found that patients treated with oxandrolone showed an increase in lean body mass, bone mineral content (BMC), and muscle strength as well as serum IGF-1, triiodothyronine, and free thyroxine index during and after oxandrolone was discontinued.

Given the improved metabolic outcomes over long periods with oxandrolone, Przorka et al[36] hypothesized that rehabilitation with oxandrolone treatments may further increase lean body mass and muscle strength in burn

patients. The study included 51 children with burns covering greater than 40% TBSA who received 0.1 mg/kg per day oxandrolone alone (n = 9), oxandrolone and exercise (n = 14), placebo and no exercise (n = 11), or placebo and exercise (n = 17) for 1 year.[36] The exercise rehabilitation included bench press, leg press, shoulder press, biceps curl, leg curl, triceps curl, and toe raises.[36] The study found an increase in weight, lean body mass, muscle strength, and peak cardiopulmonary capacity in the oxandrolone and exercise group compared with the placebo and exercise, oxandrolone alone, or placebo and no exercise groups.[36] Furthermore, IGF-1 and insulin-like binding-protein 3 in the oxandrolone and exercise group compared with the other groups included.[36] Oxandrolone and exercise are thought to impact body composition in distinct ways. Oxandrolone raises total body BMC via IGF-1. However, the failure of oxandrolone with exercise to significantly boost IGF-1 levels above those achieved by oxandrolone alone implies that the exercise effect is not mediated by IGF-1. The fact that lean body mass rises with exercise and oxandrolone suggests that BMC rises as a result of increased skeletal loading.[37]

Given the effects of oxandrolone in weight gain and muscle function, several RCT studies were performed to further investigate oxandrolone's effect in burn patients. The first RCT studying oxandrolone was performed by Mozingo.[38] Specifically, the RCT was designed to study the effects of oxandrolone on the length of hospital stay.[38] The study included 81 patients with burns covering 20% to 80% TBSA who received either 10 mg oxandrolone every 12 hours (n = 46) or the placebo (n = 35).[38] The study found that the length of stay was shorter in the oxandrolone (31.6 days) group than placebo (43.3 days) group.[38] This difference between the placebo and oxandrolone groups was strengthened when deaths were excluded and hospital stay normalized by TBSA (1.24 days/TBSA burned vs 0.87 days/TBSA burned).[38] A subsequent study by Cochran et al[39] showed a similar reduction in length of hospital stay in burn patients treated with oxandrolone. The results suggest that oxandrolone may accelerate burn recovery and reduce the risk of hospital-acquired infections with the decreased length of hospital stays. However, the authors noted the oxandrolone increased hepatic transaminases and may require intermittent monitoring to prevent further complications.

To address the risk of oxandrolone and liver injury, a study by McCullough et al[40] examined the incidence of hepatic dysfunction in 14 burn patients who received 5 mg (n = 8) or 10 mg (n = 6) oxandrolone compared with 61 control patients based on TBSA. The study showed that 2 of the 8 (25%) oxandrolone patients receiving 5 mg and 4 of the 6 (67%) oxandrolone patients receiving 10 mg showed increased hepatic dysfunction.[40] In contrast, 26 of the 61 (43%) control patients had evidence of hepatic dysfunction.[40] Despite previous concerns on liver damage and oxandrolone, the study suggests that oxandrolone does not increase the incidence of liver damage compared with the control group. However, a larger sample size for the oxandrolone group is needed to confirm the results of the study.[40] Furthermore, a recent study by Kiracofe et al[41] found that among 66 patients administered 10 mg of oxandrolone, 28 (42%) developed transaminitis, which increased in patients with other concomitant medications. Therefore, caution should still be taken when administering oxandrolone to burn patients.

Previous studies on oxandrolone demonstrated its effectiveness for improving weight gain, lean body weight, and muscle mass up to 1 year after discontinuation. However, the long-term efficacy or safety of oxandrolone had not been examined in an RCT. To investigate this, Porro et al[37] studied 222 patients with burns covering greater than 30% TBSA who received either the placebo (n = 152) or 0.1 mg/kg oxandrolone (n = 70) for 1 year; after which, the patients were regularly assessed for another 4 years. After being discharged, patients were also randomized into a 12-week exercise program (n = 35) or standard of care (n = 187). The study found that oxandrolone decreased resting energy expenditure, rate pressure product, and increased IGF-1 during the first year after burn injury; furthermore, combining exercise further improved lean body mass and muscle strength as reported previously.[37]

Interestingly, the percentage of patients below 2 standard deviations of the mean height velocity of the oxandrolone group at 1 and 2 years (first year: 8%; second year: 7%) postburn was less than the control group (first year: 48%; second year: 32%). Furthermore, it was observed that the maximal effect of oxandrolone on height and metabolism was greatest in children aged 7 to 18 years. No adverse effects were attributed to long-term administration of oxandrolone compared with the placebo.[37] The improvements in resting energy expenditure, rate pressure product, IGF-1, lean body mass, muscle strength, and height persisted 5 years postburn.[37] A subsequent study by Reeves et al[42] also confirmed that oxandrolone improved height, BMC, cardiac work, and muscle strength up to 5 years postburn.

Limitations

Oxandrolone remains an effective therapy for reducing the hypermetabolic response and comorbidities from burn injuries. However, these studies would also benefit from stratifying pediatric and adult patients based on gender to determine whether the efficacy of oxandrolone differs in male or female patients. Furthermore, additional research is required to assess whether combining other pharmaceuticals with oxandrolone may further reduce hypermetabolism and other postburn outcomes. Specifically, studies using

β-blockers, such as propranolol, have shown effectiveness in reducing hypermetabolism responses after burn injuries.[43] Only a few studies have examined the combined effect of β-blockers with oxandrolone to improve hypermetabolism responses in children and adults. Additional studies with these agents could provide greater efficacy and long-term outcomes for burn patients. Lastly, many of the studies did not assess the long-term effects of oxandrolone after burn injuries in adults and children. Longitudinal studies assessing the long-term efficacy and effects of steroids after burn injuries may provide insight into any other potential benefits or complications associated with the use of these pharmacological agents.

Conclusion

We have presented a summary of literature that provide quality data showing the benefit to the use of oxandrolone in burn patients. Oxandrolone remains one of the first-line drugs administered for the treatment and recovery of severe burns through reducing hypermetabolism.[44,45] Without treatment, hypermetabolism leads to insulin resistance, lipolysis, bone loss, and proteolysis, which can increase morbidity and mortality among burn patients.[45] The main benefit of oxandrolone is the improved long-term lean body, protein, and bone mineral mass of patients after sustaining a severe burn injury. Three meta-analyses showed oxandrolone shortened length of hospital stay, donor-site healing time, reduced weight loss, and net protein loss.[23-25] Furthermore, oxandrolone therapy did not affect mortality, infection, or liver dysfunction compared with the control groups.[23-25] Over 6 to 12 months, oxandrolone also reduces weight loss and increases lean body mass.[23-25] The improved metabolism and cardiopulmonary outcomes for years after discontinuing oxandrolone suggest the drug may attenuate inflammatory response and transcription factors increasing in catabolic process among burn patients. The recent studies showing improved outcomes with rehabilitation exercises and oxandrolone suggest combination therapies with rehabilitation programs may provide further long-term functional and physical recovery in burn patients. Therefore, future RCT may examine whether combinations of pharmaceutical agents and rehabilitation strategies may improve overall quality of life for burn patients.

Author Contributions

(I) Conception and design: JK, GS, and JG
(II) Administrative support: N/A
(III) Provision of study materials or patients: N/A
(IV) Collection and assembly of data: N/A
(V) Data analysis and interpretation: N/A
(VI) Manuscript writing: JK and GS
(VII) Final approval of manuscript: JG

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Consent for Publication

We consent for this manuscript to be published and reviewed.

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