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Effect of vitamin D supplementation and isokinetic training on muscle strength, explosive strength, lean body mass and gait in severely burned children: A randomized controlled trial

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ABSTRACT

Objective: To determine the effects of vitamin D (VD) supplementation and isokinetic training on muscle strength, explosive strength (counter movement jump) (ES), lean body mass (LBM) and gait parameters in severe pediatric burn.

Methods: Forty-eight burned children with circumferential lower extremity burns covering 40–55% of the total body surface area (TBSA), aged 10–16 years (Mean ± SD 13.01 ± 1.75), were randomized into the standard of care (n = 16), isokinetic (n = 17) and VD (n = 15) groups. Unburned children (n = 20) served as matched controls. All burned children received 12 weeks of routine physical therapy program (RPTP). In addition, the isokinetic group received isokinetic training for the quadriceps dominant limb 3 times per week at angular velocity 150°/s, and the VD group received the isokinetic training plus an oral daily dose of vitamin D_3 1000 IU (Cholecalciferol). The primary measures, assessed at baseline and 12 weeks, included quadriceps strength by isokinetic dynamometer, ES, LBM by dual-energy X-ray absorptiometry (DEXA) and gait parameters by GAITRite system.

Results: The VD and isokinetic groups showed significant improvement in quadriceps strength, ES, LBM and gait parameters compared with the standard of care, and VD group show significant improvement in the VD level as compared with the other groups. The outcome measures (and percent of improvement where applicable) for the VD, isokinetic and standard of care are as follows: quadriceps strength, 85.25 ± 0.93 Nm (85%), 64.25 ± 0.93 (36%) and 51.88 ± 1.31 Nm (12%); stride length, 94.00 ± 2.69 (7%), 110.60 ± 2.87 (25%) and 139.56 ± 2.57 (60%); step length, 67.26 ± 2.45 (72%), 55.25 ± 2.49 (43%) and 43.76 ± 1.34 (18%); velocity, 133.94 ± 1.65 (82%), 99.94 ± 1.65 (35%) and 80.11 ± 1.91 (9%); and cadence, 140.63 ± 1.36 (68%), 132.63 ± 1.36 (58%) and 90.35 ± 1.32 (9%), VD level 43.33 ± 7.48 (75%), 24.77 ± 7.38 (5%) and 25.63 ± 8.39 (4%) respectively.

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Conclusions: VD supplementation combined with exercise training significantly increased muscle strength, ES, LBM, gait and VD level in severely burned children.

1. Introduction

Childhood is a very serious time for development of motor, cognitive and social functioning [1]. Burn in children continues to be a major epidemiologic problem around the globe. Nearly a fourth of all burns occur in children under the age of 16 [2]. Burns may cause severe impairments with serious complications that can continue from childhood through adolescence into adulthood [3].

Severe pediatric burns are physically and psychologically catastrophic. Which result in a hypermetabolic and a catabolic state characterized by elevated resting energy expenditure, cardiac insufficiency, muscle weakness, loss of bone mass, and delay in growth, which are worsened by prolonged bed rest and physical inactivity [4–6].

Children with a large burn surface area are subject to a decrease in lean body mass (LBM) for at least 9 months after trauma [5]. They are vulnerable to vitamin D (VD) deficiency, this deficiency may occur during the acute phase, which caused by long hospital stay and VD renal wasting secondary to reduction in transport proteins [7]. The risk of hypovitaminosis D also continues during the chronic phase following burns. Burns restrict the impact of sun rays on the skin. So, the biosynthetic function of the skin is impaired post-burn as a scar [8].

Burned patients are especially at risk of developing VD deficiency because of low sunshine exposure, less skin capacity to synthesize VD, poorer absorption of VD with less activation in the kidneys and peripheral tissues, and fewer or lower expression of VD receptors in peripheral tissues [9,10].

VD metabolism may be inhibited by the defect in the calcium-parathyroid hormone (PTH) axis following burns. This impairment is due to systemic inflammation, which inhibitsthe calcium-sensing receptor of parathyroid gland [11,12]. A decrease in PTH levels by blood calcium leads, in turn, to a decrease in levels of circulating PTH and reduced activity of 1-alpha hydroxylase in the kidney [13]. Deficiency of VD has been related to many adverse health problems, including muscle weakness, growth retardation, skeletal deformities and mortality in the critically ill [14].

VD receptors have been identified in many other tissues including skeletal muscle [15], and VD deficiency causes rickets in children and osteomalacia in adults resulting in proximal muscle weakness. Muscle atrophy particularly VD deficiency via type 2 fibers has been described histopathologically [16].

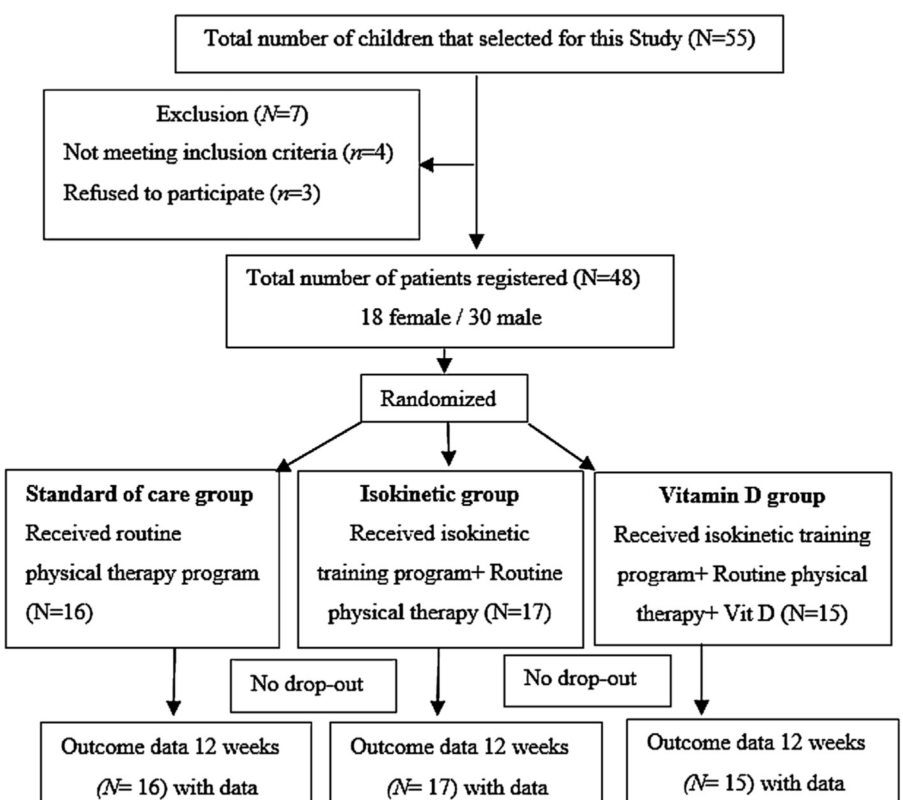

Fig. 1 – Flow diagram of the study.

Recently, there is growing evidence that dietary intakes of VD were insufficient to increase 25-hydroxy VD (25 [OH] D) levels in burned patients [17]. However, there are no formal protocols for the treatment of VD deficiency in healthy or even in burned subjects. Therefore, the use of VD supplementation is needed to fulfill the body's VD requirement.

Low physical work and muscular strength are major obstacles in allowing burned children to return to school and to perform activities of daily living. Because these activities demand muscle strength and endurance, an effective training program may needed to rehabilitate pediatric burn patient by enhancing muscular strength and ability to do work [18,19].

Suman et al. [20] confirmed the improved muscle strength and LBM after 12-weeks of exercise in severe pediatric burns. However, improvements in LBM were moderate, which seemed to be clinically effective and relevant to examine further therapeutic interventions. Therefore, this randomized controlled study was done to evaluate the effects of VD supplementation and exercise on muscle strength, mass, explosive strength, gait and VD levels in severe pediatric burn.

2. Material and methods

2.1. Subjects

This randomized controlled study included outpatient children in the Department of Burns and Plastic Surgery of Al-Noor Hospital. The measurements were taken at baseline and 12 weeks after intervention as shown in Fig. 1. This study was ethically approved by the Departmental Council of the College of Applied Medical Science, Umm Al-Qura University, Makkah, Saudi Arabia, and all participants' guardians/parents provided informed consent. Forty-eight healed pediatric burn patients (30 males and 18 females), aged 10–16 years, were enrolled from the burn unit with a circumferential lower limb deep 2nd–3rd degree injury that includes the entire lower limb. All participants received the same medical treatment and care as well as occupational and physical therapy protocol. A normal activity of daily living (ADL), diet and patient's lifestyle were maintained for all participants as much as possible.

The inclusion criteria were total body surface area (TBSA) of 40–55%, being a non-athlete and being ambulatory without an assistant. The exclusion criteria included metabolic disorders, neuropathy, visual or vestibular disorders, amputation, participation in another study [20], any adverse medication reactions, history of epilepsy, loss of balance, and lower limb deformity.

2.2. Unburned controls

Twenty unburned volunteers from the community were recruited and were pair-matched with the burned participants and served as matched healthy control. These subjects were matched as closely as possible for age and sex. Assessment of variables to the healthy controls was done similarly as the burned subjects.

2.3. Power analysis

A power analysis using $\alpha=0.05$, a power of 0.90, and an expected effect size of 0.65 was showed that a sample size of 51 was needed to avoid type II error. We used the high effect size to obtain a realistic sample size that would detect all major differences.

2.4. Randomization

The burned children were randomly allocated to one of three groups: the standard of care group (n=16), isokinetic group (n=17) or VD group (n=15). Randomization used opaque envelopes with a random number. The participants then opened the envelopes to determine their group placement. The standard of care group participated in a routine physical therapy program (RPTP) including joint range of motion exercises (ROM), muscle stretching technique for the lower limb, splinting, daily walking, and ADL training but no isokinetic training. Both the isokinetic and the VD groups participated in isokinetic training protocol using the Biodex system (Biodex Medical System, Shirley, NY, USA) for 12 weeks as well as RPTP. In addition, the VD group received VD_3 1000 IU (Cholecalciferol) oral daily dose with the food for 12 weeks [21], while the other two groups received placebo pills. The CONSORT diagram in Fig. 1 shows the number of the study participants at each stage of the study. To control for any variation between groups, all participants followed the guidelines prescribed for home exercises program (ROM exercise, stretching and daily walking) to be performed at home for 3days/week only. The participants and therapists were blinded to group assignment.

2.5. Evaluation of muscle strength

The isokinetic Biodex-4 dynamometer was linked to IBM PC-computer software (Biodex Medical System, Shirley, NY) and evaluated muscle strength at baseline and after the 12-week intervention for all of the study participants. Demographic data were collected for all participants. Questions were allowed about any part of the study; thus, the subjects were aware of the study goals and the testing procedures. Dominant quadriceps strength was evaluated. Prior to each recording session, the instrument was calibrated and the participants performed a 5min warm-up on treadmill. The participants performed bilateral quadriceps stretches, and the participants stretched each muscle group for 30s, 5 times each and alternated sides every 5min [22,23]. After warm-up, the position and stabilization of body parts was performed according to the Manual Guidelines of the Biodex system. The participants were allowed to perform three sub-maximal repetitions with no load as a warm-up. To prevent muscle fatigue, more repetitions were not allowed. The axis of rotation of the knee joint was aligned with the anatomical axis of rotation before the test, and the evaluation was executed at an angular velocity of 150°/s because this condition is well tolerated by burn patients [24]. After 3 (no load) warm-up repetitions, the participants executed 10 maximal voluntary muscle contractions without rest. To decrease the effects of fatigue, the subjects then rested for 3min and repeated the

10 repetitions again. Visual feedback from the equipment as well as verbal encouragement was given to gain the maximal level of voluntary muscle contraction [23]. The software system calculates the peak torque values.

2.6. Explosive strength

A counter movement jump (CMJ) [25] on a contact mat was performed to measure the explosive capacity of lower limb muscles after a stretch-shortening cycle. Data on average jump height from 3 separate jumps was determined in centimeters.

2.7. Lean body mass measurements

Dual-energy X-ray absorptiometry (DEXA) using QDR 4500A software (Hologic, Waltham, MA) was used to measure the total lean body mass (TLBM) and lean leg mass (LLM). The evaluation procedures were done with the children lying supine according to device guidelines. DEXA software can measure high and low energy X-ray beams and the data were compared with standard bone and soft tissue models of thickness. The calculated soft tissue values are separated into TLBM and fat mass, and the LLM or TLBM is reported in kilograms.

2.8. Evaluation of gait parameters

Gait parameters were evaluated by the GAITRite system (GAITRite Gold software, PA, USA). It is a valid and reliable walkway connected to a computer system for measuring gait in healthy adult [26]. It is an excellent tool for evaluation of gait in both normal and disabled children [27]. The children were instructed to walk barefooted on the machine mat and any unusual gait patterns were recorded. The investigator or a parent encouraged the children to complete the gait task. Each child performed at least 4 barefooted walks, each totaling a 7.66m, which included 2m off either end of the mat to avoid including periods of acceleration and deceleration. Any mistrial should be repeated, and data regarding the gait parameters were calculated via computer software.

2.9. Isokinetic protocol

Isokinetic training was performed three times per week for 12 consecutive weeks. In each session, the participants performed warm-up exercises for five-minutes on a treadmill at 4km/h, followed by five sets of stretching for the knee extensors [23,24]. The initial dose of isokinetic exercise was set at 50% of average peak torque. In the 1st–5th sessions, the increasing dose program was 1–5 sets, 6 sets were used from the 6th to 24th session and 10 from the 25th to 36th sessions; each set consisted of 10 repetitions of the concentric contraction at an angular velocity of 150°/s with 3min of rest between each set [23]. The visual feedback from the machine and verbal encouragement was provided to encourage a maximal level of effort during all contractions [22].

2.10. Outcome measures

The outcome measures included quadriceps muscle strength as measured using an isokinetic dynamometer, VD level, ES, and LBM as measured by DEXA and selected gait parameters as measured by a GAITRite system. All outcome measures were evaluated immediately after discharge as baseline and after 12 weeks.

2.11. Data analysis

Statistical data analysis used SPSS for Windows (IBM, Inc.) version 22. The G-Power 3.1 (Microsoft, USA) for Windows was used for the sample size and power calculations. The demographic characteristics of the groups were compared by descriptive statistics, and the normal distribution of data was determined by the Shapiro–Wilk test. Repeated measures ANOVA was used to analyze the data to detect overall differences between the means of the outcome measures for the 3 treatment groups, when there was differences between

Table 1 – Demographic characteristics of burned patients and unburned control.

	Burned			Unburned group (N=20)
	Standard of care group (N=16)	Isokinetic group (N=17)	VD group (N=15)	
Gender	9 male/5 female	11 male/6 female	10 male/7 female	12 male/8 female
Age (years)	12.93±1.34	13.11±1.45	13.80±1.47	12.80±1.57
Height (cm)	140.06±2.93	141.2±3.30	142.53±3.1	142.10±2.19
Weight (kg)	48.0±2.67	47.56±2.89	47.34±3.34	48.25±2.45
TBSA	49.40±3.23	50.06±2.08	48.20±2.32	NA
Average % TBSA of LE	25±2.6	26±2.8	24±3.1	NA
Average length of hospitalization	32.29±2.71	31.87±2.75	33.3±3.32	NA
VD level (ng/ml)	24.44±8.55	23.56±7.29	24.68±6.54	66.32±7.39

There were no significant differences between burned groups and unburned for age, height, weight, TBSA, average % TBSA of LE and length of hospitalization. There were no significant differences between burned groups according to VD level, but there were significant differences between all burned and unburned control.

groups post-hoc comparison was used. Means and standard deviations were reported, and the alpha level of significance was 0.05.

3. Results

In this study, 55 pediatric burned children were selected for participation (Fig. 1). Seven were excluded (four did not meet the study criteria and three refused to participate). Finally, 48 children participated in the study and were randomized into three groups. The demographic data of all participants in each group are shown in Table 1. At the beginning of the training period, there were no differences between all burned and unburned subjects regarding age, sex, weight and height (p>0.05). There was a significant difference in VD level between burned and unburned as shown in Table 1. For the standard of care, isokinetic and VD groups, the average length of hospitalization was 32.29±2.71, 31.87±2.75 and 33.87±3.32 days, and the average burned area of lower extremity was 25 ±2.6, 26±2.8 and 24±3.1%, respectively; no significant differences were found among the three groups in relation to these variables (p>0.05).

3.1. *Muscle strength*

Quadriceps muscle strength increased significantly versus baseline for all 3 groups (p<0.0001) after 12 weeks of intervention. The VD group increased the most. The percent improvement in the standard of care, isokinetic and VD groups were 12%, 36% and 85%, respectively. The quadriceps muscle torque data are shown in Table 2 and Fig. 2.

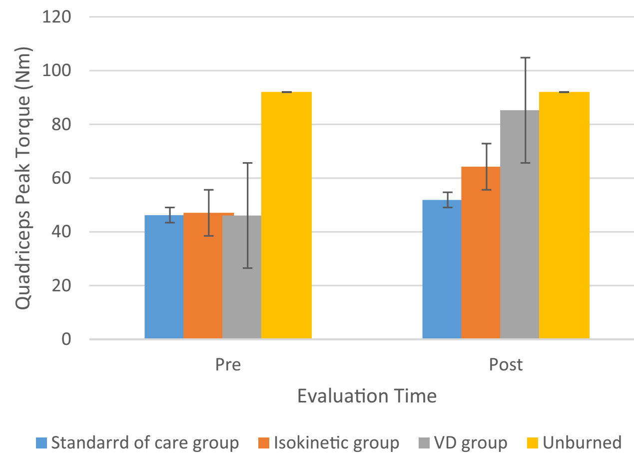

Fig. 2 – Mean values of quadriceps torque for burned and unburned control.

3.2. *VD level*

VD levels increased significantly after 12 weeks in the VD group, but its value is still below the unburned level. The other two groups showed no significant increase in VD levels after 12 weeks. Data concerning VD levels are shown in Table 2.

Table 2 – Mean values of quadriceps torque, TLBM, LLM and VD level for burned and unburned control.

Mean values of quadriceps peak torque, TLBM, LLM and VD level

	Burned						Unburned (N=20)
	Standard of care group (N=16)		Isokinetic group (N=17)		VD group (N=15)		
	Baseline	12 weeks	Baseline	12 weeks	Baseline	12 weeks	
Quadriceps peak torque (Nm)	46.23±0.97	51.88±1.31	47.06±0.99	64.25±0.93	46.08±0.55	85.25±0.93	92.10±1.37
p Value (within group)	p<0.0001*		p<0.0001*		p<0.0001*		
% of improvement	12%		36%		85%		
p Value (between group after 12 weeks)			p<0.0001*				
TLBM (kg)	30.8±1.21	31.4±1.32	30.9±1.13	33.6±1.21	31.7±1.24	36.5±1.31	39.4±1.55
p Value (within group)	0.1902**		p<0.0001*		p<0.0001*		
% of improvement	1.94%		8.73%		15.45%		
p Value (between group after 12 weeks)			p<0.0001*				
LLM (kg)	4.2±1.44	4.5±1.32	4.00±1.33	5.3±1.54	4.1±1.34	5.9±1.72	6.2±1.80
p Value (within group)	0.5437**		0.0129*		0.0018*		
% of improvement	7.14%		21.42%		43.90%		
p Value (between group after 12 weeks)			p=0.306**				
VD level (ng/ml)	24.44±8.55	25.63±8.39	23.56±7.29	24.77±7.38	24.68±6.54	43.33±7.48	66.32±7.39
p Value (within group)	0.694**		0.634**		p<0.0001*		
% of improvement	4.86%		5.13%		75.56%		
p Value (between groups after 12 weeks)			p<0.0001*				

Values are mean±SD.
* Significant.
** Non significant.

3.3. Explosive strength

The jump performance of the children increased significantly after 12 weeks of intervention versus baseline for the isokinetic and VD groups ($p<0.0001$); there was no significant change in the standard of care ($p=0.2248$). The percentages of improvement in the standard of care, isokinetic and VD groups were 5.49%, 23.20% and 39.55%, respectively. The explosive strength data are shown in Table 3 and Fig. 3.

3.4. Lean body mass

The TLBM significantly increased after 12 weeks versus baseline for the isokinetic and VD groups ($p<0.0001$) with the largest increased observed in the VD group; no significant change was seen in the standard of care group ($p=0.1902$). The percentages of improvement in the standard of care, isokinetic and VD groups were 1.94%, 8.73% and 15.45%, respectively. Similarly, the LLM increased significantly after treatment versus baseline for the isokinetic and VD groups ($p=0.0129$ and $p=0.0018$, respectively), but there was no significant change in the standard of care group ($p=0.5437$). The percent increase in the LLM for the standard of care, isokinetic and VD groups were 7.14%, 21.42% and 43.90%, respectively. The TLBM and LLM data are shown in Table 2 and Fig. 4.

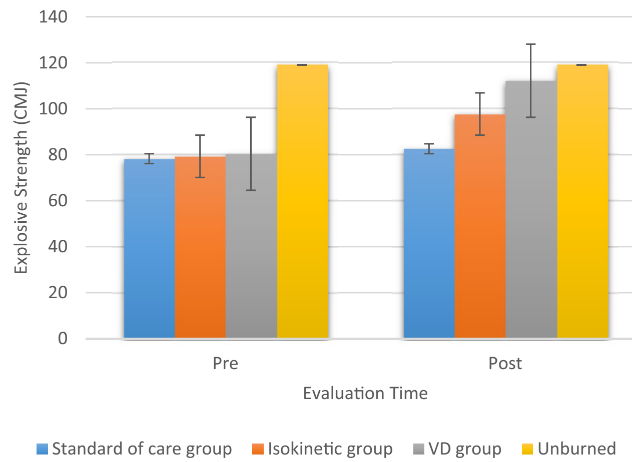

Fig. 3 – Mean values of ES for burned and unburned control.

3.5. Gait parameters

In all three groups, the gait parameters increased significantly, but to varying degrees after 12 weeks of intervention versus baseline ($p<0.0001$); the largest improvement was observed in the VD group. The percent improvement for the standard of care, isokinetic and VD groups were: stride length (7.92%,

Table 3 – Mean values of gait parameters and explosive strength for burned and unburned control.

Mean values of gait parameters and explosive strength

	Burned						Unburned (N=20)
	Standard of care group (N=16)		Isokinetic group (N=17)		VD group (N=15)		
	Baseline	12 weeks	Baseline	12 weeks	Baseline	12 weeks	
Stride length (cm)	87.10±2.34	94.00±2.69	88.00±2.09	110.60±2.87	87.00±2.08	139.56±2.57	149.50±1.56
p Value	p<0.0001*		p<0.0001*		p<0.0001*		
% of improvement	7.92%		25.68%		60.41%		
p Value (between groups after 12 weeks)			p<0.0001*				
Step length (cm)	37.00±1.83	43.76±1.34	38.62±1.32	55.25±2.49	39.00±1.83	67.26±2.45	74.60±1.35
p Value	p<0.0001*		p<0.0001*		p<0.0001*		
% of improvement	18.27%		43%		72%		
p Value (between groups after 12 weeks)			p<0.0001*				
Velocity (cm/s)	74.70±1.53	80.11±1.91	73.93±1.38	99.94±1.65	73.34±1.48	133.94±1.65	137.60±1.20
p Value	p<0.0001*		p<0.0001*		p<0.0001*		
% of improvement	9%		35%		82%		
p Value (between groups after 12 weeks)			p<0.0001*				
Cadence (step/min)	82.88±1.53	90.35±1.32	83.50±1.55	132.63±1.36	83.43±1.65	140.63±1.36	148.35±1.38
p Value	p<0.0001*		p<0.0001*		p<0.0001*		
% of improvement	9%		58%		68%		
p Value (between groups after 12 weeks)			p<0.0001*				
Explosive strength (CMJ)	78.3±10.3	82.6±9.3	79.3±11.3	97.7±10.5	80.4±9.3	112.2±11.5	119.1±13.8
p Value	0.2248**		p<0.0001*		p<0.0001*		
% of improvement	5.49%		23.20%		39.55%		
p Value (between groups after 12 weeks)			p<0.0008*				

Values are mean±SD.
* Significant.
** Non significant.

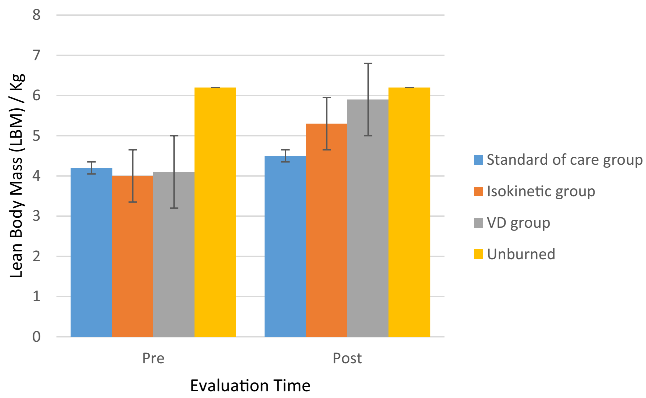

Fig. 4 – Mean values of LBM for burned and unburned control.

25.68% and 60.41%), step length (18.27%, 43% and 72%), velocity (9%, 35% and 82%) and cadence (9%, 58% and 68%), respectively. The gait parameter data are shown in Table 3 and Fig. 5.

3.6. *VD group versus isokinetic group*

The data concerning the magnitude of difference between VD and isokinetic group are shown in Tables 2 and 3. There was a significant difference between VD and isokinetic group in quadriceps strength, VD level, ES and gait after 12 weeks, and there was no significant difference between VD and isokinetic groups regarding LLM after 12 weeks.

4. Discussion

The quadriceps muscle strength, ES, TLBM and gait were significantly increased after treatment in the VD and isokinetic groups versus the unburned subjects. This is consistent with previous reports of strength gains in burned and unburned children after resistance training [20,28,29]. The increased muscle strength and improved gait in the treatment groups in this study supports our previous report [28], and others reports about the benefits of exercise on LBM and muscle strength in children after burn [30,31].

Our results showed a significant difference in TLBM at baseline and after 12 weeks in VD and isokinetic groups due to

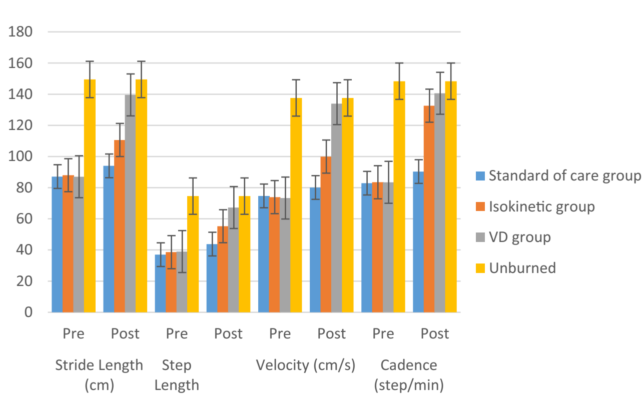

Fig. 5 – Mean values of gait parameters for burned and unburned control.

the profound effect of isokinetic exercise and VD on increasing non-LLM relative to exercise alone. Although exercise improves muscle strength when used alone during rehabilitation of children recovering from burns, it is insufficient to produce a long-term effect against muscle weakness. Our findings suggest that the use of VD in conjunction with isokinetic exercise significantly improves muscle strength, VD level, TLBM, muscle mass, and gait in burned children.

Muscle breakdown in burn patients was observed for up to 9 months after discharge from hospital and wound healing. During this time, anabolic steroids as oxandrolone were used to increase muscle strength and body mass by decreasing muscle breakdown [5].

After burn, the burn scar and normal skin close to the wound demonstrates a decreased ability of the skin to transform 7-dehydrocholesterol into pre-VD3 by about 5-fold. Children with a severe burn might present with VD deficiency due to decreased endogenous production of VD inside the body and hypovitaminosis D; these are both relatively common in children [32].

Burn impairs VD metabolism with a decrease in 25-hydroxy VD levels and decreased formation of bone in children and adults with burn trauma. Thus burned patients require VD supplementation to counteract these deficits. Furthermore, sufficient calcium and VD are important for burned patients to decrease the risk of fractures after discharge [33–35].

VD has a direct effect on muscle tissue via VD receptors in muscle. There is a positive relationship between muscle function and VD levels in blood [15]. This supports our results describing significantly improved muscle strength, mass, TLBM, VD level and gait in the VD group. VD deficiency can lead to weakness of proximal muscle with type 2 muscle fiber reduction as well as diffuse muscle pain and gait impairments [36–39]. In addition, a deficiency in VD reduces nerve conduction velocity. Reports have concluded that VD regulates transmission in the nervous system by acting as a neurosteroid hormone [40]. It has also been demonstrated that VD improves physical performance measures such as muscle strength, muscle power and contraction speed. In addition, VD affects neural coordination and control on the neuromuscular system, and there is growing evidence showing that VD has a neurotrophic effect on body systems [41].

To the best of our knowledge, there has been no previous report regarding the effect of combining VD supplementation with isokinetic training in the rehabilitation of burned children. However, a pilot randomized controlled trial for one-year conducted on burned adults concluded that VD supplementation facilitates the correction of hypovitaminosis D in burned adults and increases quadriceps muscle strength [42], this is consistent with our data from burned children.

A previous review regarding the effects of VD on level of physical performance, muscle strength, and risk of falls in elderly individuals concluded that VD should be combined with other modalities and cannot be recommended alone for use in clinical practice [43]; however, another review suggested that higher doses of VD (800 IU daily) were necessary to increase muscle strength, gait, balance and physical performance-related outcomes in older adults [44]. Only one study incorporated a muscle fiber analysis. It concluded that the stretch and cross-sectional area of type 2 fibers in the vastuslateralis muscle increased significantly in response to VD treatment [45].

Resistance training leads to normal physiological responses such as an increased activation and adaptation of the nervous system, which was predominant after a short period of training and hypertrophy of skeletal muscle. This developed in the late stage of exercise training. We also know that neural factors are important determinants in strength gains after training protocols [20,46,47]. The combined effect of isokinetic training and VD supplementation on neural and neuromuscular function results in improved muscle strength, VD level, TLBM, gait and physical function in burned children.

Age and inactivity lead to muscle wasting which were prevented and treated by exercise. Thus, prevention and rehabilitation of muscle wasting and deconditioning are excellent areas for research in the field of burns [48]. Isokinetic training protocol are safer and more effective for torque gain and strength of skeletal muscle after burn relative to other types of strength training. This is because isokinetic exercise training stimulates different enzymatic activity pathways and neural factors/mechanisms this leads to better muscle action and increases resistance to fatigue during the training [49].

Our findings indicate that isokinetic training combined with the VD improves muscle strength, VD level, muscle mass, ES and enhance gait, some of these values are still lower than the values seen in unburned controls and other values nearly reached the unburned controls [24]. Thus, VD supplementation is indicated in burned patients.

During rehabilitation, the musculoskeletal status of burn patients must be determined as soon as possible using qualitative and quantitative techniques to provide targeted therapeutic strategies. Further studies are recommended to identify patients who will need aggressive support to treat and prevent musculoskeletal complications. The ultimate goal of burn care goes beyond survival to the improvement of the quality of life. This goal requires a comprehensive and aggressive but also targeted and individualized rehabilitation approach.

Study limits include the relatively small number of patients in our study as well as the lack of re-evaluation at follow-up (weeks or months after completion of the study). These potential sources of bias should be controlled in future studies to provide a better understanding and overview about the therapeutic effect and benefits of VD supplementation combined with exercise in the rehabilitation of pediatric burned patients.

5. Conclusion

VD supplementation combined with an isokinetic training program significantly increase quadriceps muscle strength, VD level, ES, TLBM and gait in severely burned pediatric subjects.

Conflicts of interest

All authors declare no conflicts of interest.

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REFERENCES

[1] Disseldorp LM, Mouton LJ, Takken T, Brussel MV, Beerthuizen G, Van der Woude L, et al. Design of a cross-sectional study on physical fitness and physical activity in children and adolescents after burn injury. BMC Pediatr 2012;12:195.

[2] Bayat A, Ramaiah R, Bhananker SM. Analgesia and sedation for children undergoing burn wound care. Expert Rev Neurother 2010;10:1747–59.

[3] Heath K, Timbrell V, Calvert P, Stiller K. Outcome measurement tools currently used to assess pediatric burn patients: an occupational therapy and physiotherapy perspective. J Burn Care Res 2011;32:600–7.

[4] Herndon DN, Tompkins RG. Support of the metabolic response to burn injury. Lancet 2004;363:1895–900.

[5] Hart DW, Wolf SE, Mlcak R, Chinkes DL, Ramzy PI, Obeng MK, et al. Persistence of muscle catabolism after severe burn. Surgery 2000;128:312–9.

[6] Branski LK, Herndon DN, Barrow RE, Kulp GA, Klein GL, Suman OE, et al. Randomized controlled trial to determine the efficacy of long-term growth hormone treatment in severely burned children. Ann Surg 2009;250:514–23.

[7] Lee P. Vitamin D metabolism and deficiency in critical illness. Best Pract Res Clin Endocrinol Metab 2011;25:769–81.

[8] Klein GL, Chen TC, Holick MF, Langman CB, Price H, Celis MM, et al. Synthesis of vitamin D in skin after burns. Lancet 2004;363:291–2.

[9] Boonen S, Bischoff-Ferrari HA, Cooper C, Lips P, Ljunggren O, Meunier PJ, et al. Addressing the musculoskeletal 464 components of fracture risk with calcium and vitamin D: a review of the evidence. Calcif Tissue Int 2006;78:257–70.

[10] Dawson-Hughes B. Serum 25-hydroxyvitamin D and functional outcomes in the elderly. Am J Clin Nutr 2008;88:537S–40S.

[11] Murphey ED, Chattopadhyay N, Bai M, Kifor O, Harper D, Traber DL, et al. Up-regulation of the parathyroid calcium-sensing receptor after burn injury in sheep: a potential contributory factor to post-burn hypocalcemia. Crit Care Med 2000;28:3885–90.

[12] Klein GL, Xie Y, Qin YX, Lin L, Hu M, Enkhbaatar P, et al. Preliminary evidence of early bone resorption in a sheep model of acute burn injury: an observational study. J Bone Miner Metab 2014;32(2):136–41.

[13] Klein GL, Nicolai M, Langman CB, Cuneo BF, Sailer DE, Herndon DN. Dysregulation of calcium homeostasis after severe burn injury in children: possible role of magnesium depletion. J Pediatr 1997;131:246–51.

[14] Amrein K, Venkatesh B. Vitamin D and the critically ill patient. Curr Opin Clin Nutr Metab Care 2012;15:188–93.

[15] Bischoff HA, Borchers M, Gudat F, Duermueller U, Theiler R, Stahelin HB, et al. In situ detection of 1,25-dihydroxyvitamin D3 receptor in human skeletal muscle tissue. Histochem J 2001;33:19–24.

[16] Ziambaras K, Dagogo-Jack S. Reversible muscle weakness in patients with vitamin D deficiency. West J Med 1997;167:435–9.

[17] Rousseau AF, Damas P, Ledoux D, Cavalier E. Effect of cholecalciferol recommended daily allowances on vitamin D status and fibroblast growth factor-23: an observational study in acute burn patients. Burns 2014;40:865–70.

[18] Gripp CL, Salvaggio J, Fratianne RB. Use of burn intensive care unit gymnasium as an adjunct to therapy. J Burn Care Rehabil 1995;16:160–1.

[19] Tang SC, Blecker U. Inclusion of resistive exercise in a multidisciplinary outpatient treatment program for preadolescent obese children. South Med J 1999;92:585–92.

[20] Suman OE, Spies RJ, Celis MM, Mlcak RP, Herndon DN. Effects of a 12-week resistance exercise program on skeletal muscle strength in children with burn injuries. J Appl Physiol 2001;91:1168–75.

[21] Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008;(Suppl. 87):1080S–6S.

[22] Avila MA, Brasilerio JS, Salvini TF. Electrical stimulation and isokinetic training: effects on strength and neuromuscular properties of healthy young adults. Rev Bras Fisoter Sao Carlos 2008;12:435–40.

[23] Huang MH, Lin YS, Yang RC, Lee CL. A comparison of various therapeutic exercises on the functional status of patients with knee osteoarthritis. Semin Arthritis Rheum 2003;32:398–406.

[24] Suman OF, Herndon DN. Effects of cessation of a structured and supervised exercises conditioning program on lean mass and muscle strength in severely burned children. Arch Phys Med Rehabil 2007;88(12 Suppl. 2):S24–9.

[25] Markovic G, Dizdar D, Jukic I, Cardinale M. Reliability and factorial validity of squat and countermovement jump tests. J Strength Cond Res 2004;18:551–5.

[26] McDonough AL, Batavia M, Chen FC, Kwon S, Ziai J. The validity and reliability of the GAITRite system's measurements: a preliminary evaluation. Arch Phys Med Rehabil 2001;82:419–25.

[27] Thorpe DE, Dusing SC, Moore CG. Repeatability of temporo-spatial gait measures in children using the GAITRite electronic walkway. Arch Phys Med Rehabil 2005;86:2342–6.

[28] Ebid AA, El-Shamy SM, Draz AH. Effect of isokinetic training on muscle strength, size and gait after healed pediatric burn: a randomized controlled study. Burns 2014;40:97–105.

[29] Faigenbaum AD, Westcott WL, Loud RL, Long C. The effects of different resistance training protocols on muscular strength and endurance development in children. Pediatrics 1999;104:e5.

[30] Disseldorp LM, Nieuwenhuis MK, Van Baar ME, Mouton LJ. Physical fitness in people after burn injury: a systematic review. Arch Phys Med Rehabil 2011;92:1501–10.

[31] Porter C, Hardee JP, Herndon DN, Suman OE. The role of exercise in the rehabilitation of patients with severe burns. Exerc Sport Sci Rev 2015;43:34–40.

[32] Docio S, Riancho J, Perez A, Olmos J, Amado J, Gonzalez-Macias J. Seasonal deficiency of vitamin D in children: a potential target for osteoporosis-preventing strategies. J Bone Miner Res 1998;13:544–8.

[33] Klein GL, Herndon DN, Goodman WG, Langman CB, Phillips WA, Dickson IR, et al. Histomorphometric and biochemical characterization of bone following acute severe burns in children. Bone 1995;17:455–60.

[34] Wray CJ, Mayes T, Khoury J, Warden GD, Gottschlich M. The 2002 Moyer Award. Metabolic effects of vitamin D on serum calcium, magnesium, and phosphorus in pediatric burn patients. J Burn Care Rehabil 2002;23:416–23.

[35] Edelman LS, Mc Naught T, Chan GM, Morris SE. Sustained bone mineral density changes after burn injury. J Surg Res 2003;114:172–8.

[36] Simpson RU, Thomas GA, Arnold AJ. Identification of 1,25 dihydroxyvitamin D3 receptors and activities in muscle. J Biol Chem 1985;260:8882–9.

[37] Ceglia L. Vitamin D and skeletal muscle tissue and function. Mol Asp Med 2008;29:407–14.

[38] Annweiler C, Beauchet O, Berrut G, Fantino B, Bonnefoy M, Herrmann FR, et al. Is there an association between serum 25-hydroxyvitamin D concentration and muscle strength among older women? Results from baseline assessment of the EPIDOS study. J Nutr Health Aging 2009;13:90–5.

[39] Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006;84:18–28.

[40] Buell JS, Dawson-Hughes B. Vitamin D and neurocognitive dysfunction: preventing decline. Mol Asp Med 2008;29:415–22.

[41] Annweiler C, Schott AM, Berrut G, Chauviré V, Le Gall D, Inzitari M, et al. Vitamin D and ageing: neurological issues. Neuropsychobiology 2010;62:139–50.

[42] Rousseau AF, Foidart-Desalle M, Ledoux D, Remy C, Croisier JL, Damas P, et al. Effects of cholecalciferol supplementation and optimized calcium intakes on vitamin D status, muscle strength and bone health: a one-year pilot randomized controlled trial in adults with severe burns. Burns 2015;41(2):317–25.

[43] Latham NK, Anderson CS, Reid IR. Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: a systematic review. J Am Geriatr Soc 2003;51:1219–26.

[44] Montero-O dasso M, Duque G. Vitamin D in the aging musculoskeletal system: an authentic strength preserving hormone. Mol Asp Med 2005;26:203–19.

[45] Sato Y, Iwamoto J, Kanoko T, Satoh K. Low-dose vitamin D prevents muscular atrophy and reduces falls and hip fractures in women after stroke: a randomized controlled trial. Cerebrovasc Dis 2005;20:187–92.

[46] Ozmun JC, Mikesky AE, Surburg PR. Neuromuscular adaptations following prepubescent strength training. Med Sci Sports Exerc 1994;26:510–4.

[47] Ramsay JA, Blimkie CJR, Smith K, Garner S, MacDougall JD, Sale DG. Strength training effects in prepubescent boys. Med Sci Sports Exerc 1990;22:605–14.

[48] Borst SE. Interventions for sarcopenia and muscle weakness in older people. Age Ageing 2004;33:548–55.

[49] Esselman PC, de Lateur BJ, Alquist AD, Questad KA, Giaconi RM. Torque development in isokinetic training. Arch Phys Med Rehabil 1991;72:723–8.