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PERIOPERATIVE ESSENTIAL AMINO ACID SUPPLEMENTATION IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY: A DOUBLE BLINDED PLACEBO CONTROLLED RANDOMIZED PROSPECTIVE STUDY

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ABSTRACT

Lower-extremity muscle volume and strength decrease after Total Knee Arthroplasty (TKA), leading to complications such as falls and possible readmission. Perioperative essential amino acid (EAA) supplementation in patients undergoing TKA has been shown to reduce these complications. The aim of our study was to know the effects of perioperative EAA supplementation in patients undergoing TKA. Sixty four patients were analyzed in our study in which half received EAA and other half received placebo. In our study we found that patients in EAA group had better functional outcome, quadriceps muscle strength and greater quadriceps muscle diameter than placebo group.

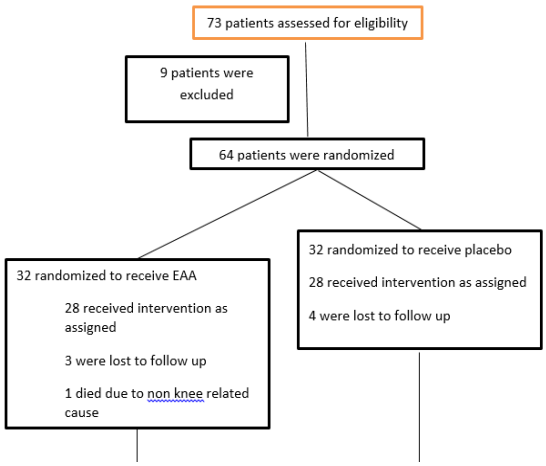
INTRODUCTION

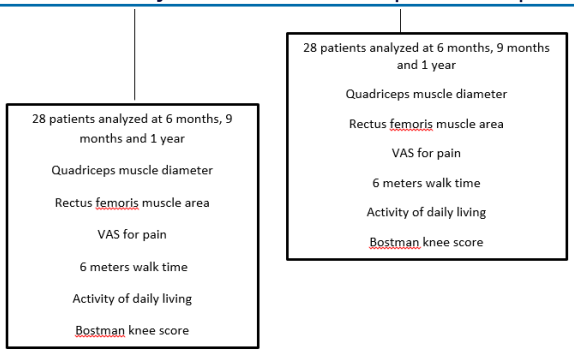
Total knee arthroplasty (TKA) for degenerative arthritis of the knee has demonstrated good clinical results[1]. However, lower-extremity muscle volume and strength decrease after TKA, leading to complications such as falls and possible readmission[2,3]. Functional tasks such as level walking and stair climbing, which is considered a high fall–risk activity, are chronically deficient in patients following TKA as compared with age- and gender-matched adults[4]. Evidence suggests that acute weakness in the nonoperated limb following TKA is related to poorer functional outcomes in the long term[5], and maintaining greater muscle volume in the operated extremity is essential to maximize muscle strength[6,7]. For older adults, acute muscle atrophy and weakness are particularly debilitating, exacerbating underlying issues related to sarcopenia, defined as the chronic loss of muscle mass and function associated with normal again[8,9]. Sarcopenia is related to physical disability[10] and increased risk of home care[11], nursing home placement[12], and hospitalization[13]. Preoperative preparation of patients before surgery is paramount to avoidance of adverse events[14]. Nutritional assessment is part of the routine preoperative assessment of patients undergoing elective total joint arthroplasty. Although hypoalbuminemia has been shown to be predictive of postoperative complications, including infection[15-17], the effects of protein supplementation on postoperative recovery are less well-established. Perioperative essential amino acid (EAA) supplementation in patients undergoing TKA has been shown to reduce rectus femoris muscle atrophy in the first 4 weeks after TKA[18]. There are limited data evaluating protein and amino acid supplementation following orthopaedic injuries. Aminoacids have commonly been used as nutritional supplements to stimulate anabolism[19]. The aim of this study was to know effect on the recovery of lower-limb muscle volume and strength of Essential Amino Acids (EAA) supplementation in perioperative period.

MATERIALS AND METHODS

This was a double blinded, prospective, hospital based, parallel trial with 2 groups (EAA and placebo group) conducted in Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal for a period of 1 year (Jul 2022 to Jun 2023). Ethical committee approval was taken, written and informed consent was taken from all patients. Seventy three patients who underwent unilateral TKA for knee osteoarthritis were potentially eligible for the study. Exclusion criteria were (1) an etiology other than knee osteoarthritis, (2) severe hepatic or renal disease or other conditions that could affect the metabolism of nutrients, and (3) scheduled TKA of the contralateral knee. After applying exclusion criteria 64 patients were enrolled. All patients were hospitalized from a week prior to until 4 weeks after TKA; during hospitalization, the same nutritional and physical therapies were provided, with exception of the EAA supplementation. Patients were given 3g of EAA or 3g of placebo (lactose powder) thrice daily after meals from 1 week before surgery to 3 weeks after surgery.

Threonine	405mg, 4.5%
Lysine	756mg, 8.4%
Isoleucine	603mg, 6.7%
Leucine	684mg, 7.6%
Valine	603mg, 6.7%
Methionine	603mg, 6.7%
Tryptophan	207mg, 2.3%
Phenylalanine	405mg, 4.5%
Histidine	315mg, 3.5%
Arginine	630mg, 7%
Glycine	1089mg, 12.1%
Starch	2700mg, 30%





Baseline measurements were obtained 1 month before surgery. Outcomes such as rectus femoris muscle area as assessed by ultrasonography, diameter of the quadriceps muscle, knee pain on a visual analogue scale (VAS), 6-meter walk time, activity of daily living, Bostman knee score were measured at baseline and at 3 weeks at time of discharge, 3months, 6 months and 1 year postoperatively.

RESULTS

Sixty four patients were enrolled in the study, 28 patients received intervention as assigned in each group, 3 patients and 4 patients were lost to follow up in EAA and placebo group respectively and 1 patient died due to accident in EAA group.

Table 1 Patient demographics

Parameters	EAA group(n= 28)	Placebo group(n= 28)	p value
Age of patient	69.3 ± 7.6	71.2 ± 6.8	0.57
Sex Male Female	 9(32.1%) 19(67.8%)	 7 (25%) 21 (75%)	 0.36
BMI	24.7 ± 4.2	25.1 ± 3.6	0.57
Comorbidities Diabetes Hypertension Osteoporosis	 9 (32.1%) 5 (17.8%) 11(39.2%)	 7 (25%) 6(21.4%) 13(46.4%)	 0.65 0.74 0.54
Operative time	85 ± 9 min	86 ± 8	0.53
*Values are given as mean ± standard deviation. EAA = Essential Amino Acid, BMI = Body Mass Index , p value < 0.05 was considered significant			

The relative changes in the outcomes at 3 months, 6 months, and 1 year after TKA are shown in Table 2. The relative changes in the rectus femoris muscle area (p value 0.03), quadriceps muscle diameter (p value 0.008), quadriceps muscle strength (p value 0.01), Bostman knee score (p value 0.04) were significantly better in the EAA group than in the placebo group at 1 year.

Table 2 Relative values of parameters at 3 months, 6 months and 1 year

Parameters	EAA group (n = 28) (%)	Placebo group (n= 28) (%)	p value
At 3 months Quadriceps muscle diameter	 115.3 ± 18.2	 100.4 ± 20.1	 0.54
Rectus femoris muscle area(mm^2)	103.4 ± 18.7	96.8 ± 19.2	0.34
VAS for pain	42.0 ± 36.0	39.0 ± 32.0	0.76
Quadriceps muscle strength	112.4 ± 47.3	98.8 ± 40.5	0.24
Bostman knee score	106.4 ± 13.8	100.8 ± 12.7	0.48
At 6 months Quadriceps muscle diameter	 123.4 ± 19.4	 105.7 ± 21.3	 0.03
Rectus femoris muscle area(mm^2)	123.4 ± 17.3	102.5 ± 20.4	0.004
VAS for pain	43.7 ± 47.2	38.4 ± 27.6	0.65
Quadriceps muscle strength	139.3 ± 44.2	115.7 ± 38.4	0.06
Bostman knee score	113.5 ± 14.7	103.4 ± 11.4	0.26
At 1 year Quadriceps muscle diameter	 127.7 ± 21.5	 108.3 ± 22.4	 0.008
Rectus femoris muscle area(mm^2)	135.2 ± 19.6	109.7 ± 21.0	0.03
VAS for pain	31.4 ± 25.6	29.8 ± 23.1	0.62
Quadriceps muscle strength	158.2 ± 53.3	127.3 ± 39.7	0.01
Bostman knee score	124.3 ± 15.3	112.2 ± 13.7	0.04
*The baseline value was taken as 100%, and values relative to it are given. The values are shown as the mean ± standard deviation. EAA=essential amino acid, VAS=Visual Analogue Scale. Significant (p<0.05).			

DISCUSSION

In our study, the rectus femoris muscle area, quadriceps muscle diameter, Quadriceps muscle strength, Bostman knee score were significantly improved from baseline in the EAA group 1 year after TKA. Risk of falls, cost of patient care, and readmission rate after TKA are higher for patients with weak quadriceps muscles[3]. EAA supplementation helps to resolve these issues through accelerated postoperative muscle recovery. Human models of muscle disuse and immobilization have been shown to decrease muscle cross-sectional area by 0.3% to 0.8% per day within 4 weeks, likely because of reductions in resting muscle protein synthesis of approximately 60% and a blunted anabolic response to EAA ingestion of approximately 50%[20]. Any major surgery results in a short-term increase in catabolism, its metabolic impact has been demonstrated to persist in the long term[21]. In this study nutritional supplementation with EAA has been shown to mitigate these effects in the perioperative period and continue to have favorable effect on muscle mass and strength after TKA. Estrogen in women has been demonstrated to have a positive effect on the recovery of muscle volume and strength, but it has less effect on muscle metabolism in older women in whom estrogen has decreased due to menopause[22], most of the patients in our study were postmenopausal females which might have affected muscle recovery. Quadriceps muscle strength has been reported to recover to preoperative levels in approximately 6 months after TKA[23]. In our study quadriceps muscle strength continued to increase beyond 6 months in both groups suggesting that TKA also permits the eventual recovery of muscle strength that had been lost preoperatively due to osteoarthritis[24]. Functional outcome at 1 year measured using Bostman knee score was comparably better in EAA group then placebo group.

The strengths of this study include a robust design with randomization, double blinding, and a placebo control. Limitations of this study include relatively small sample size, all cases were not operated by same surgeons, differences in BMI may alter the response to surgery, rehabilitation, and EAA supplementation.

CONCLUSION

Perioperative essential amino acid supplementation improves quadriceps muscle strength and volume and clinically improved functional outcome at 1 year after Total Knee Arthroplasty.

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