

Nutrient Supplementation Post Ambulation in Persons With Incomplete Spinal Cord Injuries: A Randomized, Double-Blinded, Placebo-Controlled Case Series

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ABSTRACT. Nash MS, Meltzer NM, Martins SC, Burns PA, Lindley SD, Field-Fote EC. Nutrient supplementation post ambulation in persons with incomplete spinal cord injuries: a randomized, double-blinded, placebo-controlled case series. *Arch Phys Med Rehabil* 2007;88:228-33.

Objective: To examine effects of protein-carbohydrate intake on ambulation performance in persons with incomplete spinal cord injury (SCI).

Design: Double-blinded treatment with washout and placebo crossover.

Setting: Academic medical center.

Participants: Three subjects aged 34 to 43 years with incomplete SCI at C5-T4.

Interventions: Subjects walked to fatigue on 5 consecutive days. On fatigue, participants consumed 48g of vanilla-flavored whey and 1g/kg of body weight of carbohydrate (CH₂O). Weekend rest followed, and the process was repeated. A 2-week washout was interposed and the process repeated using 48g of vanilla-flavored soy.

Main Outcome Measures: Oxygen consumed ($\dot{V}O_2$; in L/min), carbon dioxide evolved ($\dot{V}CO_2$), respiratory exchange ratio (RER: $\dot{V}CO_2/\dot{V}O_2$), time (in minutes), and distance walked (in meters) were recorded. Caloric expenditure was computed as $\dot{V}O_2$ by time by 21kJ/L (5kcal/L) of oxygen consumed. Data were averaged across the final 2 ambulation sessions for each testing condition.

Results: Despite slow ambulation velocities (range, .11–.34m/s), RERs near or above unity reflected reliance on CH₂O fuel substrates. Average ambulation time to fatigue was 17.8% longer; distance walked 37.9% longer, and energy expenditure 12.2% greater with the whey and CH₂O supplement than with the soy drink.

Conclusions: Whey and CH₂O ingestion after fatiguing ambulation enhanced ensuing ambulation by increasing ambulation distance, time, and caloric expenditure in persons with incomplete SCI.

Key Words: Ambulation; Dietary supplements; Energy metabolism; Fatigue; Nutrition; Rehabilitation; Spinal cord injuries.

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INCOMPLETE SPINAL CORD injuries (SCI) and diseases bring about varying degrees of muscle paralysis and diminished locomotor function.¹ Lost or diminished motor function occurring after SCI impairs performance of daily activities,² fosters physical deconditioning,³ and hastens multisystem decline that accompanies aging with a physical disability.⁴ In doing so it decays the quality and longevity of life for many persons with SCI.

Reconditioning exercises undertaken by persons with SCI often reverse unhealthy and diminished functional states imposed by paralysis,⁵ mirroring exercise benefits attained by those without disability. Unfortunately, altered contractile properties of muscle after SCI often limit the ability of weakened muscle to undergo aggressive exercise and satisfy vigorous functional performance needs.⁶ These muscle alterations include transformation to fibers having fast contractile properties and favored use of glycolytic energy substrates. In such cases the relative intensity of muscle actions increases to the point of early fatigue while still performing relatively little physical work.⁷ The mixture of muscle fuels can be examined during exercise by monitoring the respiratory exchange ratio (RER), an index of fuel use derived from the quotient of carbon dioxide evolved ($\dot{V}CO_2$) to oxygen consumed ($\dot{V}O_2$), which increases as proportional use of muscle fuel shifts from low-intensity use of fatty fuels to high-intensity use of carbohydrates. Unity of the RER (ie, 1.0), and values above this level, indicate an increasing reliance on carbohydrate substrates (ie, muscle glycogen and blood glucose), and generally forecasts impending fatigue.

Considerable research and clinical effort has focused on locomotor rehabilitation of persons with incomplete SCI as a pathway to improved function and enhanced health.^{8,9} To date, however, dietary, pharmacologic, and nutrient modification that optimize physical performance for those with SCI have met with limited scrutiny, compared with the extensive research base and well-established benefits of immediate postexercise nutrient supplementation in persons without disability. In many cases of intense exercise the combined intake of carbohydrate (CH₂O) and protein immediately after muscle fatigue hastens recovery from intense physical activity, and improves performance during ensuing exercise bouts.¹⁰ The most effective supplement combination for achieving this benefit in persons without disability is whey protein and CH₂O,^{11,12} which serves as the basis for testing of potential benefits in persons with SCI. The purpose of this case series was to examine whether postexercise nutrient supplementation with whey protein and CH₂O administered immediately after fatiguing ambulation enhances locomotor performance over a 2-week period.

Table 1: Descriptive Characteristics of the Study Participants

Participant	Age (y)	Duration of Injury (y)	Level of Injury/ASIA Grade	Sex	Assistive Device(s)
1	43	21.8	C4-5 ASIA C	F	Bilateral AFO
2	39	5.6	C5-6 ASIA C	M	None
3	34	6.5	T4 ASIA D	M	Left AFO
Mean	38.7	11.3			

Abbreviations: AFO, ankle-foot orthosis; F, female; M, male.

METHODS

Participants

Study participants were 3 people aged 34 to 43 years with incomplete SCI (American Spinal Injury Association [ASIA] grades C and D) at the C5-T4 levels. The International Guidelines for Classification of Neurological Injury (revised 2000) served as the standard for participant classification. Participants were in good health and free of infection or illness at the time of testing. They refrained from ingestion of food and caffeine for 4 hours before and 3 hours after testing sessions. Participants consented to undergo study with the approval of the Medical Sciences Committee for the Protection of Human Subjects. Descriptive characteristics of the study participants are shown in table 1.

Ambulation Testing and Supplementation

Study participants were experienced in overground locomotion through participation in an earlier research study, but were not actively ambulating when studied. More than 3 months had passed since they had participated in these studies. They were not enrolled in concurrent studies, undergoing structured therapy, or independently exercising in a home-based program. They wore a safety harness and used a rolling walker during testing, but were not provided additional body weight support. Assistive devices used during ambulation are shown in table 1 and were kept constant throughout all testing.

Ambulation was performed to fatigue over a 24-m (80-ft) long indoor oval track on 5 consecutive days. Fatigue was determined by the inability of participants to take additional steps. Weekend rest followed, and the process was repeated for another 5 days. Within 5 minutes of experiencing fatigue participants consumed a blended drink containing 48g of vanilla-flavored whey^a and 1g/kg of body weight CH₂O (maltodextrin^b). This combination drink, given immediately after fatiguing exercise, is known to rapidly replete muscle glycogen. A 2-week washout period was interposed and the process repeated using 48g of vanilla-flavored soy protein^c to which 2 packets of a commercial non-nutritive sweetener (Splenda^d) were added. By contrast, soy protein is slowly absorbed by the body and is not recognized as an aid in recovery from fatiguing exercise. Supplements had similar vanilla flavor, were blended to form similar liquid volumes, and were equally sweetened. There was a slight difference in texture that alerted participants to their difference, but not their identity. The order of supplementation was determined by chance, and the drink composition was unidentified for participants and investigators involved in data collection.

Metabolic Monitoring

Participants wore a Hans-Rudolph soft mask^e over their nose and mouth during each session. Oxygen consumed ($\dot{V}O_2$; in L/min), carbon dioxide evolved ($\dot{V}CO_2$), and RER ($\dot{V}CO_2/\dot{V}O_2$) were assessed by open-circuit spirometry using a portable

metabolic analyzer carried on body harness (fig 1) and set to average responses over a 1-minute time interval. After preparation for metabolic monitoring participants sat quietly for 5 minutes while baseline data were collected. They then walked

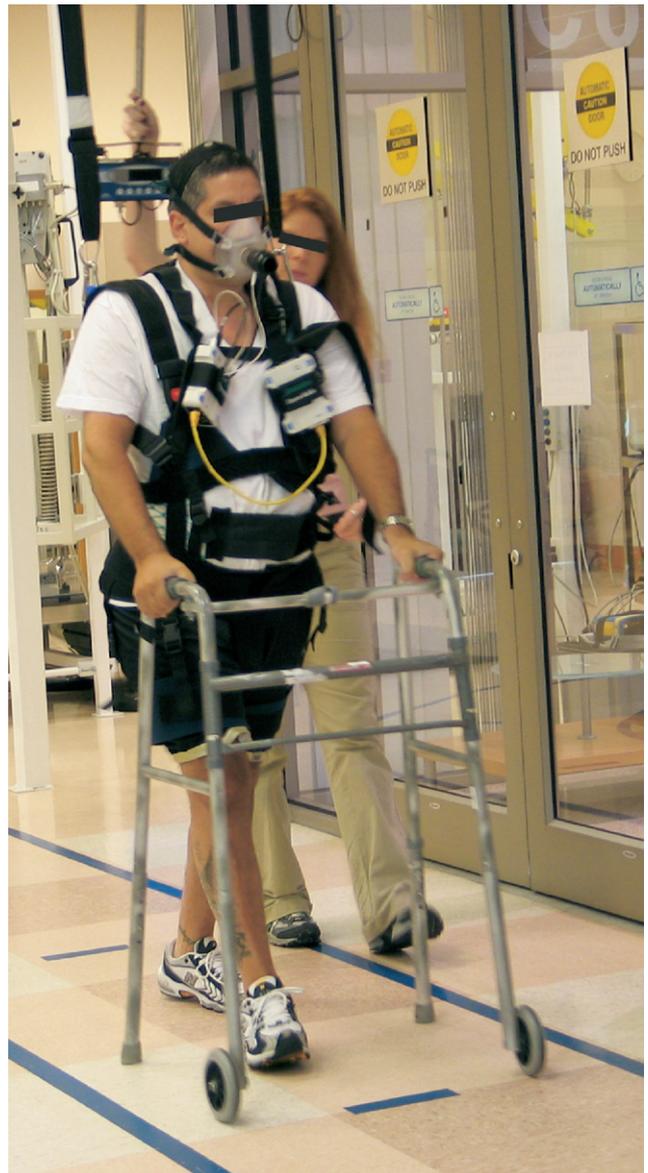


Fig 1. A test participant wearing a metabolic monitor while walking on an indoor oval track. The participant is wearing a harness for safety, but is not being assisted with body weight support.

Table 2: Individual Performances of Participants Under the 2 Test Conditions

Participant	Time (min)	Distance (m)	Expended Energy (kJ)
Participant 1			
Whey and CH ₂ O	13.5	1219	215
Soy	10.5	853	148
Participant 2			
Whey and CH ₂ O	23.0	127	372
Soy	20.5	121	296
Participant 3			
Whey and CH ₂ O	59.5	85	1610
Soy	50.5	49	1514
Average difference (%)	+17.8	+12.2	+37.9

NOTE. One kilojoule equals .238kcal.

to fatigue, accompanied by an investigator. Time (in minutes) and distance walked (in meters) were recorded. Caloric expenditure was computed as the product of $\dot{V}O_2$, time, and a constant reflecting 21kJ (5kcal) burned per liter oxygen consumed.¹³

Data Management

Data for each test condition were averaged across the final 2 days of ambulation and expressed both as individual participant responses and pooled data. The use of an average expressed over the last 2 days decreased the likelihood of bias imposed by factors that might enhance or limit performance on a single day. Differences between test conditions (whey and CH₂O vs soy) were computed as percentage differences.

RESULTS

Participants consumed the study drinks without stomach upset or changes in bowel habits. They noted a slight taste difference between drinks, but were unable to identify the composition.

Responses to walking for individual participants are shown in table 2. Despite slow ambulation velocities (range, .11–.34m/s), RERs near or above unity (RER=1) reflected reliance on CH₂O fuel substrates (fig 2). Irrespective of testing order, average ambulation time was 17.8% longer (32.0min vs 27.1min); distance walked 37.9% longer (470m vs 341m), and

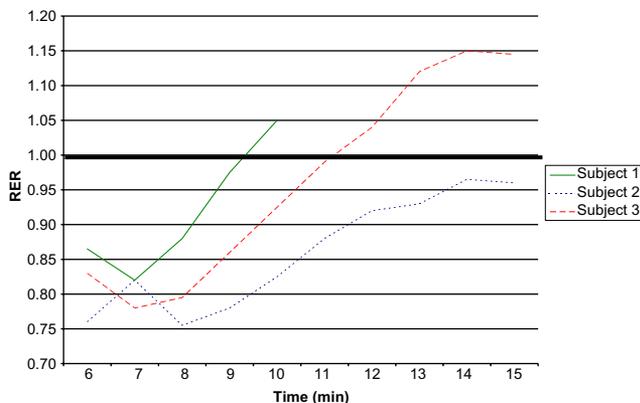


Fig 2. RERs ($\dot{V}CO_2/\dot{V}O_2$) reflecting reliance on glycolytic substrates during locomotion. Increasing RER identifies an increasing proportional use of carbohydrate as a substrate to fuel muscle metabolism.

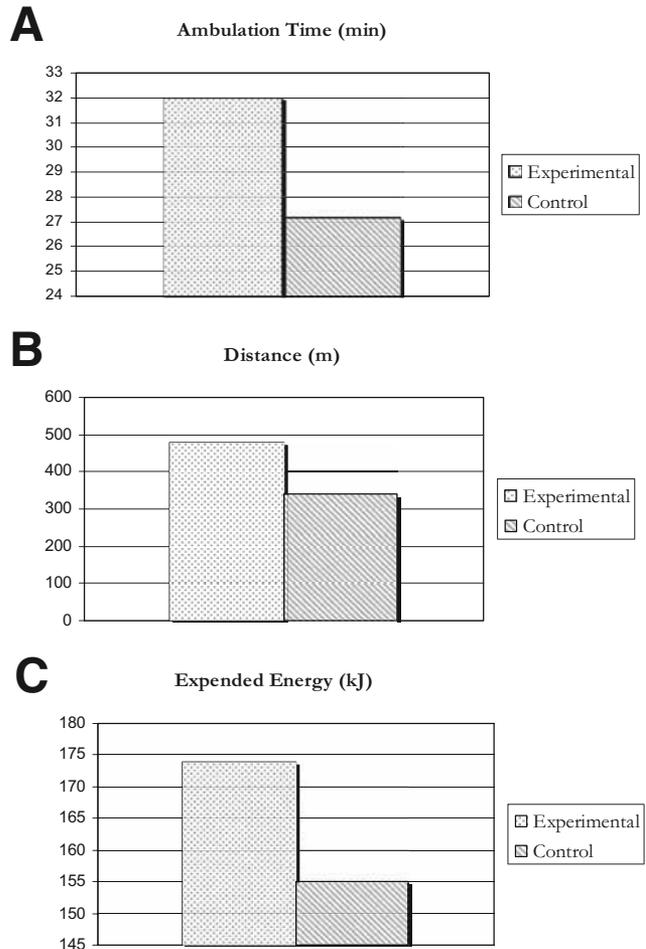


Fig 3. Pooled averages for locomotor and metabolic performance for (A) ambulation time, (B) distance, and (C) energy expenditure.

energy expenditure to fatigue 12.2% greater (731kJ [174kcal] vs 651kJ [155kcal]) with the whey and CH₂O supplement than soy (fig 3).

DISCUSSION

The key observation of this study is that 3 persons with incomplete injuries walked longer distances and at greater caloric expenditure before sustaining fatigue after 2 weeks of whey and CH₂O supplementation, whereas a blinded control condition failed to bring about this change. Although the specific benefit to muscle was not studied, the short duration of testing would argue against muscle strengthening known to accompany longer-term supplementation with whey protein,^{10,14} and favor enhanced repletion of muscle glycogen typically depleted during repeated exhaustive exercise.

Most studies of sublesional muscle after SCI in humans report fibers that are smaller than those above lesion, and than those of persons without SCI.¹⁵⁻¹⁷ These fibers have less contractile protein,¹⁵ produce lower peak contractile forces,¹⁸ and transform toward fast phenotypic protein expression.^{17,19,20} By increasing their fast myosin heavy chain isoforms,^{20,21} muscles located below lesion level increase their reliance on glycogen fuels and decrease their resistance to fatigue.^{17,22} This reliance was seen in study participants who walked at slow speeds but

had RERs that rapidly approached or exceeded unity (1.0), indicating that despite slow walking the work is challenging.

Muscle glycogen is an obligate fuel normally used to support moderate to high intensity contraction of innervated muscle,²³ and it is the preferred fuel for both innervated and paralyzed muscle undergoing fatiguing contraction.²⁴⁻²⁶ Glycogen breakdown is greater in paralyzed than in innervated muscle when undergoing contraction.^{19,22} When glycogen is depleted from innervated or paralyzed muscle the capacity to perform additional voluntary or involuntary activity at moderate and higher work intensities is either completely lost or severely limited.^{10,27} This makes rapid replenishment of depleted or exhausted glycogen stores critical if, and when, additional bouts of work are performed.^{10,12,28}

Enhanced recovery from glycogen-depleting exercise in persons without disability is readily achieved by immediate CH₂O administration, which is superior to both no supplementation and supplementation with electrolytes in water.^{10,12,29} Immediate postactivity ingestion of this nutrient appears critical for successful glycogen repletion.^{10,30} This generally rules out ingestion of bulk food to achieve the same benefit, because the immediacy of muscle CH₂O uptake is stalled by time required for nutrient digestion, intestinal transit, and blood-borne transport. Addition of protein to the supplement mix increases the glycogen resynthetic capacity of ingested carbohydrates by stimulating an insulin response considered permissive for rapid glycogen repletion.³¹ It also provides an amino acid reservoir that delays postexercise protein catabolism and enhances protein anabolism.^{29,32} Whey protein generally satisfies this need, because it is easily digested, contains high concentrations of branch-chain amino acids used for muscle repair, and rapidly crosses from the intestinal tract into the circulation. By contrast, soy is slowly ingested, and its uptake exceeds the critical timing need for protein uptake, which explains its selection as a control condition for this study.

The incorporation of locomotor training in rehabilitation of persons with incomplete SCI has received widespread research attention and has achieved diverse performance outcomes.^{1,8,33-37} Not all persons who undergo the process become functional ambulators, because walking requires greater muscle forces and more prolonged endurance than many persons can achieve before experiencing fatigue.

Surprisingly, no studies have mentioned dietary enhancements or nutrient supplementation as tools to improve performance outcomes, even though enhanced strength, endurance, ambulation time and speed, and motor efficiency have been primary experimental goals of treatment.^{1,8,35-39} By contrast, considerable success has been achieved in enhancing exercise performance of healthy persons without disability, the frail elderly, and people with chronic infections through use of postexercise nutrient supplementation.^{10,40} The performance-enhancing effects of these supplements underpin a joint position of the American Dietetic Association, Dietitians of Canada, and American College of Sports Medicine that "... physical activity, athletic performance, and recovery from exercise are enhanced by optimal nutrition ...",^{41(p2130)} and who jointly "... recommend appropriate selection of food and fluids, timing of intake, and supplement choices for optimal health and exercise performance."^{42(p1543)} To our knowledge none of these recommendations have been incorporated or examined for efficacy in persons with SCI undergoing locomotor training. Several studies on persons with SCI have examined pharmacologic approaches to increasing ambulation time and efficiencies, with most efforts focusing on antispasmodic medications having adrenergic, serotonergic, and γ -aminobutyric acid agonist properties,⁴³ although responses to these

drugs have been mixed and their universal use limited. Benefits on muscle strengthening have been reported for the β_2 -selective adrenergic agonist metaproterenol.⁴⁴ The nutritional food supplement creatine monohydrate has been used for short periods of time to increase motor function of weakened upper muscles in persons with tetraplegia, but with mixed outcomes^{45,46}; however, no evidence suggests that activity-induced creatine deficiency is a cause of muscle weakness or premature fatigue in persons with SCI. The α_1 sympathomimetic agent midodrine reportedly enhances exercise performance in persons with tetraplegia,⁴⁷ although the benefits of treatment have been attributed to enhanced pressor responses in persons having cardiovascular autonomic dysfunction from injuries above the T1 level. Again, no evidence suggests that ambulation deficiencies in those with SCI are caused by circulatory dysregulation or are corrected by use of α_1 selective adrenergic agonists.

Study Limitations

We note a number of study limitations. The study population is a small case-series and therefore subject to selection bias. In this first study examining this topic, we did not control for dietary intake, but instructed participants to maintain their habitual food choices. A treatment group for CH₂O alone was not included, and thus, the extent to which they enhanced the postulated effect of CH₂O ingestion cannot be determined. Instead, we elected to examine whether the combination of whey and CH₂O appeared beneficial, and then backtrack through its nutritional elements. Whereas protein content was matched in the two study supplements, the CH₂O was not, which makes room for the possibility that CH₂O alone was responsible for the case observations. No muscle biopsies were taken to confirm glycogen depletion after fatiguing exercise, or greater glycogen storage after treatment. Participants were studied without body weight support, which differs from the partially unloaded state commonly used to train persons with incomplete SCI. We note that postural hypotension and other circulatory dysfunction accompanying SCI may have contributed to the fatigue patterns.⁴⁸ Despite these limitations, the magnitude of change observed under blinded placebo-controlled conditions is encouraging; it exceeds in magnitude and speed of change the benefits provided by other ergogenic aids tested for those with SCI and provides a basis for more systematic study in a larger test population.

CONCLUSIONS

Intake of whey and CH₂O after fatiguing ambulation enhanced ensuing ambulation by persons with incomplete SCI. Apparent reliance on CH₂O substrates, and known benefits of whey and CH₂O in postactivity CH₂O repletion, suggest a mechanism of action. Ease of digestion and minimal adverse effects were noted. Future research directions could reasonably include studies examining mechanisms of total or subtotal fatigue during locomotor training, as well as investigations of anticatabolic effects of protein supplementation during exhaustive exercise. Confirmation of this benefit requires investigation in a larger study population.

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Suppliers

- a. Solgar Vitamin and Herb, 500 Willow Tree Rd, Leonia, NJ 07605.
- b. Now Foods, 395 S Glen Ellyn Rd, Bloomingdale, IL 60108.
- c. Nutrition S'mart, 4155 Northlake Blvd, Palm Beach Gardens, FL 33410.
- d. McNeil Nutritionals, 501 George St, New Brunswick, NJ 08903.
- e. Hans-Rudolph Inc, 7200 Wyandotte, Kansas City, MO 64114.