A STUDY OF RELATION OF LOWER LIMB SPASTICITY WITH LIPID PROFILE AND FASTING PLASMA GLUCOSE LEVELS IN CHRONIC MOTOR COMPLETE SPINAL CORD INJURY PATIENTS.

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Abstract

Background: Most common cause of spinal cord injury in India is fall from height followed by road accidents which may lead to incomplete or complete disruption of neural signal transmission across and below the level of injury. Spasticity is a common but not an inevitable complication following spinal cord injury.

Study Objective: The present study tried to explore the correlation between the lower limb spasticity following spinal cord injury and the metabolic markers.

Study design: Hospital-based cross-sectional study.

Material and Methods: Fifty patients recruited from Department of Physical Medicine and Rehabilitation, Sawai Man Singh Hospital, Jaipur (Raj.), were categorized into mild (16), moderate (11), and severe (23) spastic groups based on assessment of ankle/knee extensor muscle group spasticity using the modified Ashworth scale. The metabolic profile markers such as Total Cholesterol (TC), Low-density Lipoprotein (LDL), High-Density Lipoprotein (HDL), Triglyceride (TG) and Fasting Plasma Glucose (FPG) were estimated and compared between the three groups.

Results: The triglycerides, total cholesterol, low density lipoproteins and the fasting plasma glucose level were significantly negatively correlated with the grading of spasticity in lowerlimbs ($P < 0.001$). The high density lipoproteins level was higher in a severe spastic group as compared to the mild and moderate spastic groups; but this result was statistically non-significant ($P = 0.14$).

Conclusion: Spasticity in motor complete SCI may have beneficial effects in preserving glucose homeostasis and defending rise in adiposity, rationalizing the need for its judicious management to maintain the crucial balance between its beneficial and problematic effects.

Keywords: Spasticity, Modified Ashworth score, Spinal cord injury, lipid profile, fasting plasma glucose.

Introduction

Spinal cord injury (SCI) is an incurring insult to the spinal cord resulting in either a temporary or a permanent change in its motor, sensory and autonomic functions. Spasticity is a common complication following spinal cord injury other than respiratory, cardiovascular, neurogenic bladder and bowel, heterotopic ossification, pressure ulcers, deep vein thrombosis, metabolic and endocrinologic changes.

The most common cited definition for spasticity is that published by Lance in 1980¹. "Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex,

as one of the components of the upper motor neuron syndrome.

About 65-70% of persons of spinal cord injury are reported to get affected with spasticity in due course of their life time². Spasticity has likelihood to adversely influence the quality of life (QOL) by inducing pain and exhaustion. In contrast, spasticity may optimize sitting and standing stability, ease some activities of daily living (ADL) and execution of transfers and augment the muscle bulk, thus exhibiting its beneficial effects.³

Nelson MD (2007)⁴ reported that 55% of entities who have spinal cord injury are at risk of developing metabolic syndrome. Gorgey AS et al (2014)⁵ concluded that the major changes in body composition and metabolic profile can lead to comorbidities such as type 2 diabetes mellitus

and cardiovascular diseases after SCI and it is important for a healthcare provider to be aware of the magnitude of these changes.

A hypothesis was made in our study that spasticity could positively affect glucose homeostasis and lessen the deterioration in lipid profile parameters in persons with chronic spinal cord injury by maintaining the free fat mass. Hence the purpose of this study was to explore the consequent effects of lower limb spasticity upon lipid profile and fasting plasma glucose in chronic SCI (≥ 1 year post injury).

The aim of this study was to explore the relation between the lower limb spasticity following spinal cord injury and the metabolic markers such as lipid profile and fasting blood sugar.

Material and Methods

This was a descriptive type of observational cross-sectional study which recruited participants from the Department of PMR, SMS Medical College, Jaipur, Rajasthan (India) from May 2018 to April 2019. Fifty (50) patients of spinal cord injury (≥ 1 year duration of injury) with spasticity in lower limbs, between the age groups of 18-60 years, with ASIA scale A or B, and whose BMI were between 15 and 30 kg/m² were included in the study. The spinal cord injury patients having previous history of other co-morbid medical or surgical condition such as HTN, DM and history of any interventional treatment for spasticity were excluded from the study. An ethical approval was taken from the institute ethical committee and a written informed consent was obtained from all recruited patients before starting the research.

A detailed neurologic assessment was done and the level/completeness of spinal cord injury was determined by using the ASIA impairment scale. The Modified Ashworth Scale (MAS)^{6,7} was used to evaluate spasticity in knee extensors and ankle extensors in the supine position. To evaluate spasticity MAS 1+ was converted to grade 2 and subsequently MAS grade 2, 3, 4 were changed to 3, 4, 5 respectively. The total MAS score (Σ MAS) at knee/ankle extensor muscle was calculated using equations (1) to (3) as done by Jung I-Y et al (2017).⁸

$$\text{Eq.:1. Avg. knee extensor MAS score: } \frac{\text{Right knee extensor} + \text{left knee extensor MAS score}}{2}$$

$$\text{Eq.:2. Avg. ankle extensor MAS score: } \frac{\text{Right ankle extensor} + \text{left ankle extensor MAS score}}{2}$$

$$\text{Eq.:3. Total MAS } (\Sigma\text{MAS}) \text{ score: Avg. knee ext. MAS score} + \text{Avg. ankle ext. MAS Score}$$

The total MAS score (Σ MAS) in extensor muscle groups varies from 0 to 10 and we classified the participants in three groups (mild, moderate and severe) based on their total MAS score. Patients with total MAS score of ≤ 2 were classified as mild spasticity group, score ≥ 4 were classified as severe spasticity group and score between 2 to 4 were

classified as moderate spasticity group, as done by Jung I-Y et al (2017).⁸

Overnight fasting (minimum 8 hours) venous samples of participants were drawn in the morning between 8 to 9 AM. Biochemical Auto Analyzer machine (AU-680) by Beckman Coulter technologies was used to measure metabolic profile (Total Cholesterol, Low-density Lipoprotein (LDL), High Density Lipoprotein (HDL), Triglyceride (TG) and Fasting Plasma Glucose (FPG).

All the three groups of spasticity i.e. mild, moderate and severe spastic were comparable as per age, gender, diet, addiction, socioeconomic status. The study participants of all three spastic groups were undergoing similar exercise regimes, were on same anti spastic medication (Baclofen – at variable doses) and were not on any lipid-lowering drugs (statins).

Statistical Analysis

The Statistical analysis software (SPSS trial version 23.0) was used for statistical analysis. The qualitative data were expressed in proportion and percentages where as the quantitative data expressed as mean and standard deviations. The difference in proportion was analyzed by using the chi-square test. The difference in means among the groups was analyzed using the ANOVA (Analysis of variance test) and post HOC test (Tukey test). Correlation between quantitative outcomes was assessed using the Pearson correlation coefficient. The significance level for tests was determined as 95% ($P < 0.05$).

Results

Demographic profile: –

A total of 50 individuals were recruited in the present study and were divided into mild (16), moderate (11), and severe (23) spastic groups depending upon their total MAS (Σ MAS) scores. Mean Total MAS score was 3.71 ± 1.60 . Majority of patients were males ($n = 42$, 84%; rest females: $n = 8$, 16%), majority belonged to young age group of 21-30 years ($n = 24$, 48%), married ($n = 36$, 72%), either ASIA A ($n = 39$, 78%); or ASIA B ($n = 11$, 22%) and were affected with either cervical spine injury ($n = 32$, 54%) or thoracic spinal injury ($n = 18$, 46%)(Table no: 1).

Correlation of metabolic markers with severity of spasticity:-

The mean total cholesterol (TC) level in severe spasticity group (150.09 ± 20.36 mg/dl) was significantly lower than in mild spastic group (186.44 ± 54.07 mg/dl); ($P = .006$). The mean LDL level in severe spasticity group (86.70 ± 18.91 mg/dl) was significantly lower than the moderate spastic group (111.45 ± 11.21 mg/dl); ($P = .007$). The mean TG level in severe spasticity group (100.83 ± 28.63 mg/dl) was significantly lower than the mild spastic group (160.63 ± 87.91 mg/dl); ($P = .006$). The mean FPG level in severe spasticity group (82.74 ± 12.66 mg/dl) was significantly lower than the mild spastic group

(110.56±18.46mg/dl) ; (P < .001) and moderate spastic group (92.09±16.33mg/dl);(P < .001). The mean HDL level was higher in severe spastic group (39.09±6.07mg/dl) as compared to the moderate (35.00±5.85mg/dl) and mild spastic groups (35.56±7.65mg/dl) but this result was statistically non-significant (P=0.14,r = 0.255)(Table no: 2).

The study observed a significantly negative correlation between the severity of spasticity with the triglycerides (TG) (r = - 0.445), total cholesterol (TC) (r = - 0.426), low density lipoproteins (LDL) (r = -0.323), and fasting plasma glucose (FPG)(r = - 0.577) levels(Figure: 1, 2).

Table 1: Demographic Profile of mild, moderate and severe spastic groups.

PARAMETERS	MILD SPASTICITY (N=16)	MODERATE SPASTICITY (N=11)	SEVERE SPASTICITY (N=23)	P VALUE (LS)
ΣMAS EXT SCORE	1.84±0.30	3.14±0.32	5.28±0.54	<0.001**(S)
AGE MEAN ± SD (years)	35.81±9.34	28.36±4.50	34.04±10.41	0.111**(NS)
GENDER (MALE/FEMALE)	13/3	9/2	20/3	0.870 *(NS)
VERTEBERAL LEVEL (CERVICAL/THORACIC)	11/5	4/7	17/6	0.851*(NS)
ASIA CLASSIFICATION (A/B)	12/4	9/2	18/5	0.915*(NS)

*Chi-square test; ** ANOVA

Table 2: Metabolic markers in mild, moderate and severe spasticity groups

PARAMETERS	MILD SPASTICITY	MODERATE SPASTICITY	SEVERE SPASTICITY	MEAN	P value** r value #
TOTAL MAS SCORE	1.84±0.30	3.14±0.32	5.28±0.54	3.71±1.60	P <0.001
TC(mg/dl)	186.44±54.07	173.09±15.24	150.09±20.36	166.78±37.34	P = 0.007 r = -0.426
LDL(mg/dl)	101.38±28.50	111.45±11.21	86.70±18.91	96.84±23.19	P= 0.007 r = -0.323
HDL(mg/dl)	35.56±7.65	35.00±5.85	39.09±6.07	37.06±6.71	P = 0.14 r = 0.255
TG(mg/dl)	160.63±87.91	126.64±25.69	100.83±28.63	125.64±59.64	P = 0.006 r = -0.455
FPG (mg/dl)	110.56±18.46	92.09±16.33	82.74±12.66	93.70±19.51	P<0.001 r = 0.577

**ANOVA; # Correlation coefficient(r)

Abbreviations: TC: Total cholesterol, LDL: Low density lipoproteins, HDL: High density lipoproteins, TG: Triglycerides, FPG: fasting plasma glucose.

Abbreviations: FPG: fasting plasma glucose, Σ MAS EXT: total spasticity score of knee and ankle extensor muscle group.

Figure: 1. Correlation between Spasticity and Fasting plasma glucose (FPG) Levels.

Figure: 2. Correlation value between spasticity and TC, LDL, HDL, TG, FPG levels.

Abbreviations: TC: Total cholesterol, LDL: Low density lipoproteins, HDL: High density lipoproteins, TG: Triglycerides, FPG: fasting plasma glucose.

Discussion

Albeit, the life expectancy of persons with spinal cord injury has optimized firmly as preventive and treatment approaches have enriched over the past decades still the leading causes of mortality in individuals with long-standing spinal cord injury among SCI persons are cardiovascular complications (46% of all deaths)^{9,10}. The reduction in physical activity paired with the clinical sequel after spinal cord injury often results in deterioration in body composition and metabolic profile.

Spasticity in spinal cord injury is believed to be both problematic and favorable due to its double edged effect. On one hand, the spasticity can cause discomfort, stiffness, pain, pressure sore and difficulty in performing some physical activities such as washing, dressing and sexual activity which can all be affected due to increased muscle tone. Whereas on the other hand, it also has some favorable and beneficial effects on sitting, standing, transfers and the performance of ADLs due to its increase muscle tone.

In the present study, we observed that out of 50 participants, 42(84%) SCI patients were males, which shows that male are more engaged in outdoor activities as compare to female who are more engaged in household activities. Majority of cases in our study belonged to the rural areas, which may be explained that the persons living in rural area are probably unaware or uneducated regarding safety rules or precautions that should be followed in working area. Maximum participants belonged to a young age group i.e. between 21 to 30 years (48%) which suggests the negligence, inattention or unawareness in this population with regards to road safety measures.

In the present study, we observed that the Total Cholesterol (TC), Triglycerides (TG), and Low density Lipoproteins (LDL), and Fasting Plasma Glucose (FPG) levels were significantly negatively correlated with the severity of spasticity. Patients with severe spasticity showed lower plasma Total Cholesterol (TC), Triglycerides (TG), Low density Lipoproteins (LDL), and lower fasting plasma glucose (FPG) as compared to the mild or moderate spastic patients. We reported that the HDL level was higher in a severe spastic group as compared to the mild and moderate spastic groups, but this was statistically non-significant ($P=0.14$). Gorgey AS and Chiodo A.E et al(2010)⁷ also observed similar to our finding that there was a significant negative correlation between knee extensor spasticity with plasma LDL, triglycerides and cholesterol level while a non-significant correlation was observed between the knee extensor spasticity and HDL levels. On the contrary, in an another study conducted by Jung IY et al (2017)⁸, no significant difference was observed in Total cholesterol, LDL, HDL, and TG levels between mild and severe spastic spinal cord injury groups, however they

observed that Fasting plasma glucose levels (FPG) and serum leptin levels were lower in the severe spasticity group as compare to no or mild spasticity groups ($P<0.001$ and $P=0.037$, respectively).Reportedly there has been variable results in literature amid different studies on effects of spasticity on lipid panel which may be attributed to the reason considering that several variables such as genetics, diet, exercise, and smoking, can influence blood profile parameters and a difference in the local skeletal muscle activity owing to spasticity may not lead to a significant difference in the lipid profile.

Spinal cord injury leads to impairment in skeletal muscle oxidative capacity, predisposing individuals with SCI to further weight gain and increased risk for diabetes mellitus.^{11,15} It is unclear how spasticity improves glucose homeostasis; yet here are few possible mechanisms explained in literature such as non-insulin mediated glucose uptake in paralysed spastic muscles is 3 times higher as compared to the abled controls, as suggested by a study done by Bennegard GM et al (2008)¹⁶. This study suggested that these muscles are more metabolically active than resting normally innervated muscles. It is probable that spastic muscle fibers triggers Ca^{+2} release and stimulates translocation of GLUT-4. Spasticity could also help in reducing intramuscular fat, which is a known factor to decrease insulin sensitivity and thus help in maintaining blood glucose levels.^{17,18} The tonic activity associated with the spasticity may defend against deterioration in body composition, energy expenditure, and metabolic profile in individuals with motor complete spinal cord injury as suggested by Kjaer et al¹⁹ who observed that electrically induced exercise in SCI patients increased glucose uptake more than voluntary cycling controls subjects which may be by inducing spasticity during the procedure. Thus spasticity improves glucose and insulin homeostasis as well as lipid profile by primarily maintaining free fat mass and attenuating skeletal muscle atrophy. Our study result was in accordance to above studies where we also observed a negative correlation between severity of spasticity and plasma glucose levels as reported by previous studies.

Elder CP et al²⁰ reported that intramuscular fat(IMF) accounts for 70% reduction in glucose tolerance in individuals with complete SCI. Secondary to spinal cord injury, a high percentage of fast twitch fibers in the paralyzed muscles leads to low aerobic capacity.^{21, 22} The impaired substrate utilization lead to increase in insulin resistance²³ and lead to deterioration of metabolic blood markers such as Triglycerides, Total cholesterol, Low density lipoproteins. Additional to low aerobic capacity, disturbance in autonomic nervous system in SCI impose an atherogenic potential i.e. lower serum HDL and higher serum Total cholesterol, LDL cholesterol and Triglycerides.²⁴ It has been observed that the atherogenic

risk incidence is higher in SCI (228%) as compared to the healthy controls.²⁵

Previous studies observed that spasticity attenuates skeletal muscle atrophy and prevents IMF accumulation in SCI individuals which is proven to impair insulin sensitivity.^{17,18} The current study results observes spasticity to have a benefit on overall picture of lipid profile and decrease atherogenic potential by reducing total cholesterol, LDL, triglycerides and glucose levels. The strength of our study was that all included participants had a motor complete injury, were on similar exercise regimes and were not on any lipid lowering drugs.

Conclusions

In conclusion, severity of spasticity is negatively correlated with total cholesterol, triglycerides, low density lipoproteins and plasma blood glucose levels in motor complete chronic SCI patients whereas there is no significant correlation between severity of spasticity and HDL level. Spasticity after SCI may defend against deterioration in metabolic markers such as glucose and lipid profile, thus preventing the health related long term cardiovascular complications. It may have desirable effects in patients of motor complete SCI with regard to their adiposity and glucose homeostasis. The functional and quality of life issues related to muscle spasticity should be balanced with those related with its soft tissue, metabolic, and long-term cardiovascular outcomes.

Recommendations

This study suggests that severe spasticity in lower limbs could compensate metabolic profile and glucose levels by counteracting the tendency of hyperlipidemia and hyperglycemia in individuals of chronic motor complete SCI. Spasticity might be included as an associated variable in forthcoming considerations on cardiovascular risk factors and co morbidities seen over lifetime of persons living with SCI.

Limitations

In this study the number of patients was small, so before generalization of the results, further studies are required involving large number of patients. The effect of antispastic drugs such as Baclofen on lipid and glucose levels was not observed in this study and need to be investigated in future studies.

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