RESEARCH ARTICLE

A comparative study of skeletal muscle fatigue in alcoholic and non-alcoholic sedentary human beings

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ABSTRACT

Background: Physical fatigue, or muscle fatigue, is the temporary physical inadequacy of a muscle to perform adequately and to sustain an intended power generation, occurred from the contraction of muscle against a load with a decrease in both force and speed of shortening. Growing at unprecedented rate, chronic alcoholism is hampering health and well-being of the individuals at small and social and economic loss at large. Even though its effects are seen on every system of the human body, only few studies were done in relation to its effects on skeletal muscles. Aim and Objectives: To find and compare the duration of onset of fatigue and work done in isotonically contracting skeletal muscle in alcoholic and nonalcoholic sedentary healthy subjects. Materials and Methods: A sample size of 100, age and sex-matched sedentary individuals are recruited for the study and are categorized into Group 1 (50 alcoholics) and the Group 2 (non-alcoholic). Duration of the fatigue and work done in isotonically contracting muscle was estimated by Mosso’s ergography and compared using student’s t test. Windostat version 9.2 software was used for all statistical analysis. Throughout the study, the statistical significance was set at $P < 0.05$ using two-sided tests for all analysis. Results: The duration of fatigue was significantly lower in alcoholics than non-alcoholics ($P < 0.05$). The mean duration of fatigue was 2.980 min in alcoholics and 4.210 min in non-alcoholics. The work done was significantly lower in alcoholics than non-alcoholics ($P < 0.05$). The mean work done was 4.363 kgm in alcoholics and 5.913 kgm in non-alcoholics. Conclusion: The work done was significantly lower in alcoholics than non-alcoholics ($P < 0.05$). Hence, chronic alcoholism causes early onset of fatigue in the skeletal muscles and also decreases the amount of work done.

KEY WORDS: Work Done; Alcoholism; Sedentary; Skeletal

INTRODUCTION

Skeletal muscles are capable of conscious movements of bones that help in movement and work output.¹ It is participating in regular metabolic regulation in normal conditions, in fasting states, in disorders, chronic injuries.² Fatigue is a temporary lack of ability to react to an event or execute a function because of excessive action. Physical fatigue, or muscle fatigue, is the temporary physical inadequacy of a muscle to perform adequately and to sustain an intended power generation, occurred from the contraction of muscle against a weight with a decrease in both force and speed of shortening. A decrease in maximum force generation with fatigue caused from a decrease in the active cross-bridges formation and energy originated per cross bridge.³

Metabolic Changes in Fatigue

Metabolic changes that occur during fatigue in a muscle in normal individuals are ATP depletion, lactic acid accumulation, fall in pH, glycogen depletion. As fatigue sets in, Phosphocreatine reduces and ATP will decrease from...
5 mM to <2 mM, mainly at regions of cross-bridge interaction and in the areas of membrane channels, thereby affecting respective ATPase activities. At the same time PO₄, ADP, Mg²⁺, lactate, and H⁺ stores in the sarcoplasm. Inadequacy of the Ca²⁺ pump at SR lengths the Ca²⁺ transient while decreasing the electrochemical driving force for Ca²⁺ output from the SR. At the other side reduction of ATP and the surge in Mg²⁺ can also prevent Ca²⁺ productions through the ryanodine receptor.[3]

**Alcoholism**

The term alcoholism was originally coined in 1849 by Magnus Huss. In the year 1990, The American society of addiction medicine defined alcoholism as “a primary chronic disease with genetic, psychosocial and environmental factors influencing its development and manifestations.” According to the World Health Organization (WHO) in the year 2012 almost 139 million net DALYs (disability-adjusted life years), or 5.1% of the world burden of disease and injury, were attributed to alcoholism. As per the WHO, pattern of drinking score ranges from Score “1” to score “5.” Score “1” is very low-risk pattern of alcohol drinking and “5” is very high risky pattern of alcohol drinking. In India drinking score is “3” (moderate risk). According to the WHO report 2012, the harmful use of alcohol results in 3.3 million deaths every year. It is also estimated that almost close to half the population (38.3%) actually drinks alcohol. Hence, alcoholism is a disease which is progressive in nature and fatal in its outcome. According to Lexicon of alcohol and drugs terms, World Health Organization, Geneva 1994, Standard drink is a volume of beverage alcohol that contains approximately the same amount (in grams) of ethanol regardless of the type of beverage. The term is generally used to create awareness among alcohol users about the identical effects associated with drinking varying alcohol beverages served in standard size glasses or containers. In general, Official “Drinks” or “Units” generally contain between 8 and 14 g of pure ethanol. The WHO (2000) suggests that the thresholds for consumption that results in a high risk of acute adverse outcomes should be set at >100 g of alcohol per day for men and >60 g of alcohol per day for women.

**Effects of Alcoholism on Human Beings**

To understand the causation of short term and long term effects of alcohol on the human body, there is a need to know about the steps of alcohol metabolism, its affects on other metabolisms, and also the balance which exists between alcohol removal and storing up of dangerous byproducts.

The effects of alcohol on different tissues depend on its concentration in the blood (blood alcohol concentration [BAC]) over time. BAC is estimated by how fast does alcohol is absorbed, distributed, metabolized, and excreted. The rate of elimination of alcohol from body changes widely among persons and is dependent on factors such as duration of alcohol consumption, nutrition status, age, habit of smoking, and time of day[4] The various detrimental effects of different kinds of alcohol metabolism in the body will result in tissue damage and diseases seen in alcoholic patients which includes oxygen deficits (i.e., hypoxia) in the liver; interaction between alcohol metabolism byproducts and other cell components, resulting in the origin of harmful products (i.e., adducts); generation of highly reactive oxygen-containing molecules (i.e., reactive oxygen species that can damage other cell components; and changes in the ratio of NADH to NAD⁺. Alcohol through its direct effects (damaging of membrane structures, consequences on signaling proteins) and by its indirect actions (because of alcohol metabolism itself) is able to initiate cellular damage. According to the studies done by Collins and Lapsley, 2008; Rehm et al., 2006; Saar, 2009, it is now understood that harmful alcohol drinking has potential to significantly affect social and economic costs to the working environment, primarily as a result of declined productivity.[5-7]

The Government of India is taking initiative to implement various programs to increase its Gross Domestic Product that ultimately affect the quality of life of every individual. Individual contribution at the level of performance both in quantity and quality is gaining importance in the present time. In India, majority of jobs are of manual work. Hence, their ability to work depends on the skeletal muscle functioning which is affected by number of factors. Out of which, effect of alcohol is interesting concept to be understood. The acute effects of alcohol are different from chronic effects. Especially, long-term effects of alcohol on skeletal muscle are less explored concept. Only few studies are done in this context. The reason may be multiple factors effecting skeletal muscle fatigue. Hence, to study the exclusive effect of alcohol on skeletal muscle is a challenge to accomplish. In India many people who are becoming alcoholic are BPL. The quality of life of these individuals is adversely affected because of alcohol consumption which makes them work less, earns less money, further effect nutrition to self and their family. There are very few studies done in relation to alcohol and its contribution to skeletal muscle fatigue, which may have explained the above problem to some extent. The motivation to carry out the study comes from above-mentioned problems, which need to be prevented as early and effectively as possible.

**Objectives**

To find out and compare the duration of onset of fatigue and amount of work done in isotonically contracting skeletal muscle in alcoholic sedentary subjects (Group 1) and non-alcoholic sedentary healthy subjects (Group 2).
MATERIALS AND METHODS

A sample size of 100 male subjects in the age group of 30–40 years is assessed. The test Group 1 consists of 50 alcoholic sedentary individuals the control group consists of 50 non-alcoholic sedentary volunteers. Subjects were recruited in the study after performing the thorough clinical examination. RAPA questionnaire [Table 1] was used for labeling sedentary individuals and CAGE questionnaire [Table 2] was used in labeling alcoholics.

Inclusion Criteria
- Only Male sedentary individuals subjects aged between 30 and 40 years who are on mixed diet are included in the study
- Group1: Includes 50 alcoholic individuals. Alcoholics who score 2 or more out of 4 points in CAGE questionnaire, who are consuming at least 400 g of pure alcohol in a week for a period of 10 years are included
- Group2 includes non-alcoholic, healthy individuals.

Exclusion Criteria
- Patients with diabetes, hypertension, thyroid dysfunction, malnourishment, anemia, and neuromuscular disorders are excluded from the study
- Trained individuals and yoga practitioners are excluded from the study
- Subjects on medication are excluded from the study
- Smokers and other drug users are excluded from the study
- Social drinkers and who consume less quantity of alcohol are excluded from the study
- Subjects who used to drink earlier and now stopped.

Study Design

It is a casecontrol study (n = 100) conducted in the Department of Physiology, Mediciti Institute of Medical Sciences. The study population consisted of two groups of sedentary male subjects in the age group of 30–40 years. The control group consisted of 50 non-alcoholic volunteers. The test group consisted of 50 alcoholics. The subjects were recruited from the surrounding areas of Ghanpur village, Medchal mandal. Prior to recruitment informed consent was obtained from all the subjects. The study was approved by the MediCiti Ethics Committee [Ref: No: FWA00002084, Dated 31/12/12, MEC/05/12-2012]. All the subjects were instructed not to consume any central nervous system (CNS) stimulants on the day of the experiment. The experiment was conducted with a time lag of 2–3 hours after breakfast.

Table 1: Rapa questionnaire

<table>
<thead>
<tr>
<th>Physical Activities</th>
<th>Does this accurately describe you?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>How physically active are you? (Check one answer on each line)</td>
</tr>
<tr>
<td>I rarely or never do any physical activities.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do some light or moderate physical activities, but not every week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do some light physical activity every week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do moderate physical activities every week, but less than 30 minutes a day or 5 days a week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do vigorous physical activities every week, but less than 20 minutes a day or 3 days a week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do vigorous physical activities every week, but less than 20 minutes a day or 3 days a week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do 30 minutes or more a day of moderate physical activities, 5 or more days a week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do 20 minutes or more a day of vigorous physical activities, 3 or more days a week.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do activities to increase muscle strength, such as lifting weights or calisthenics, once a week or more.</td>
<td>Yes</td>
</tr>
<tr>
<td>I do activities to improve flexibility, such as stretching or yoga, once a week or more.</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Note: If only first answer is yes in from the RAPA questionnaire, then the physical activity level is considered as Sedenta, otherwise it should be considered as non-sedentary.
Mosso’s ergography was used to assess the performance of flexors of the fingers of the non-dominant hand against a load of 2.5 kg.

**Measurement of Muscle Function**

Ergogram is the recording of voluntary contractions of the skeletal muscles of a human being. Mosso’s ergography is done to assess the performance of the flexors of the fingers of the hand. It is also useful to study the phenomenon of fatigue in human skeletal muscle. In Mosso’s ergography, fatigue is affected by the weight to be lifted and the frequency of contractions.

The machine is composed of two parts: The supporting and registering platforms. The forearm and the hand face up when placed within the machine and hold place at the wrist by two metal clamps. The index and the ring finger are placed into finger holders, while the middle finger is attached to a sling by use of a strap connected to the registering apparatus. The middle finger was left free to pull the load. The subject was asked to lift the load by maximal contraction of the flexors of the middle finger. He was asked to repeat lifting the load every 2 s. A stopwatch was provided for this purpose. The subject was asked to continue lifting the load until the load can no longer be lifted.

**Calculations of Indices of Muscle Function**

**Onset of fatigue**

It constitutes the time in minutes from the point the flexors of the middle finger of non-dominant hand start to lift the load by maximal contraction to the point when they cannot lift the load anymore.

**Work done**

The muscle contractions of the flexors of the middle finger are registered on a piece of paper in the form of a graph which is then assessed to calculate the work done. The distance covered in meters (D) is measured using a measuring scale. Force (F) constitutes the load in Kg against which the muscle contracts. Work done in Kg M is then calculated using the formula:

\[
\text{Work done} = \text{Force} \times \text{Displacement}
\]

\[
\text{Force} = \text{Mass} \times \text{Acceleration}
\]

\[
\text{Acceleration} = \text{Gravitational constant i.e 9.8 m/s}^2
\]

<table>
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<tr>
<th>CAGE Questionnaire</th>
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<tr>
<td>Have you ever felt you should Cut down on your drinking?</td>
</tr>
<tr>
<td>Have people Annoyed you by criticizing your drinking?</td>
</tr>
<tr>
<td>Have you ever felt bad or Guilty about your drinking?</td>
</tr>
<tr>
<td>Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (Eye opener)?</td>
</tr>
</tbody>
</table>

**Scoring:**

Item responses on the CAGE are scored 0 or 1, with a higher score an indication of alcohol problems. A total score of 2 or greater is considered clinically significant.

**Statistical Analysis**

Windostat version 9.2 software was used for all statistical analysis. The data are summarized using descriptive statistics (i.e., means, standard deviations). Analysis of variance was used for the comparison of variables between the two study groups. Throughout the study, the statistical significance was set at \( P < 0.05 \) using two-sided tests for all analysis.

**RESULTS**

It is case-control study \((n = 100)\) comprising of sedentary male gender within the age group 30–40 years. Tables 3 and 4 show that the duration of fatigue was significantly lower in alcoholics than non-alcoholics \((P < 0.05)\). Figure 1 shows that the mean duration of fatigue was 2.980 min in alcoholics and 4.210 min in non-alcoholics. Tables 3 and 5 depict that work done was significantly lower in alcoholics than non-alcoholics \((P < 0.05)\). Figure 2 shows that the mean work done was 4.363 kgm in alcoholics and 5.913 kgm in non-alcoholics. Among the calculated parameters duration of onset of fatigue and work done were found significantly lower in alcoholics than non-alcoholics.

**DISCUSSION**

Data from Figures 1 and 2, Table 3 shows that amount of work done \((P < 0.05)\) and duration of onset of fatigue \((P < 0.05)\) are significantly low in alcoholic’s sedentary group when compared to non-alcoholic sedentary group. It is well-known fact that the onset of fatigue and amount of work done by skeletal muscle will depend on the availability of ATP sources. Early depletion of ATP molecules in the alcoholic group is the cause for early onset of fatigue \((2.980 \pm 1.332)\) and decrease in work done \((4.363 \pm 1.386)\).

According to Langh et al., long-term use of alcohol decreases the production of insulin-like growth factor \((IGF)\). Decreased proliferation and maturation of skeletal muscle fibres in alcoholics resulting early onset of fatigue and less amount work done. Alcohol intake also causes impairment of ions across sarcolemma like \(Na^+, K^+, Ca^{2+}\). Alcoholism will result in lactic acidosis that is nothing
but the accumulation of LEWIS factor (Factor “P”) which is nothing but K’ ions. More accumulation of lewis factor will prolong the re-polarization, causing decrease in rate of firing that ultimately brings the early onset of fatigue and less amount work done. Muscle fatigue is the inability of the muscle to further work. The cause of fatigue may be due to exhaustion of source of energy of muscle, accumulation of end products of metabolism such as lactic acid, CO₂, ketone bodies, and decrease of local synthesis of acetylcholine-like substances. O₂ is required for the removal of substances and also for recovery. In physiological exercise, the site of fatigue is in the synapses of CNS, called as central fatigue. It was seen that fatigue after voluntary work, first appears in synapses, neuromuscular junction, and lastly in the muscle itself.

**Effects of Alcohol in Skeletal Muscle**

Chronic Alcohol intake causes atrophy of Type 2 fibers according to Langh *et al.*, Reilly *et al.*, Tiernan *et al.*, [8-10] The atrophy of Type 2 skeletal muscle fibres in alcoholics will decrease skeletal muscle mass. According to Hunter *et al.*, chronic Alcoholism will hamper the synthesis of Titin and Nebulin content.[11] Titin is responsible for stabilized positioning of the thin filaments across thick filaments in hexagonal pattern. Decrease in titin content result in altered stability; result in the early onset of fatigue. Reduced synthesis of NEBULIN causes decreased production of myofibrils. Low levels of myofibrils cause decrease in work done in alcoholics. Table 4 and Figure 2 depicts that in non-alcoholic group the onset of fatigue (4.210 ± 1.340) is longer than alcoholic group and the amount of work done (5.913 ± 1.681) is more than the alcoholic group, respectively. This may be due to normal levels of IGF, titin, nebulin, muscle mass, muscle fiber, and ionic conductance. Long-term use of ethanol might lessen the physiological and morphological changes in skeletal muscle. This could

| Table 3: Comparison of mean values of calculated parameters across two groups |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Variable        | Alcoholic±SD    | SE              | NonAlcoholic±SD | SE              | t test | Probability | Mann whitney Probability |
| Duration of Onset of Fatigue min | 2.980±1.332 | 0.188 | 4.210±1.340 | 0.190 | 4.602 | 0.000 | 621.000 | 0.000*** |
| Work done kgm   | 4.363±1.386 | 0.196 | 5.913±1.681 | 0.238 | 5.032 | 0.000 | 579.000 | 0.000*** |

SD: Standard deviation. ***0.000

| Table 4: ANOVA for the duration of onset of fatigue in min |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Source of variations | df | Sum of squares | Mean squares | F ratio | Probability | h² | hp² | w² |
| Between groups   | 1.000 | 37.822 | 37.822 | 21.178 | 0.000*** | 0.178 | 0.178 | 0.144 |
| Within groups    | 98.000 | 175.025 | 1.786 | 0.000 | 1.000 | 0.000 | 0.000 | 0.000 |
| Total            | 99.000 | 212.848 | 2.150 | *P<0.05 is considered as significant, ANOVA: Analysis of variance |

| Table 5: ANOVA for work done in kgm |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Source of variations | df | Sum of squares | Mean squares | F ratio | Probability | h² | hp² | w² |
| Between groups   | 1.000 | 60.078 | 60.078 | 25.324 | 0.000*** | 0.205 | 0.205 | 0.164 |
| Within groups    | 98.000 | 232.496 | 2.372 | 0.000 | 1.000 | 0.000 | 0.000 | 0.000 |
| Total            | 99.000 | 292.574 | 2.955 | *P<0.05 is considered as significant, ANOVA: Analysis of variance |
be due to alcohol’s effect on the nervous system. Even progressive wasting and the weakness of the muscle groups are seen in alcoholics and may lead to lesion of skeletal muscle, characteristic of myopathy.[12] Sometimes alcohol may bring atrophic changes in human type II fibers[13] and also necrosis.[12] Jackson in the year 1822 might be the first one to explain the damaging effects of ethanol on muscle. Some studies conclude that ethanol can directly affect on skeletal muscle fibers, but most of the studies believe that ethanol effects on skeletal muscle are secondary (indirect). Primary effects of ethanol on the human body include liver damage, undernourishment, and nervous system abnormalities.[14-16] It appears ethanol can profoundly inhibit cell proliferation of skeletal muscle mainly during the initiation of proliferation phase, prolongs differentiation. It is also observed that ethanol is less effective in bringing changes in skeletal muscle DNA, protein content during the proliferation phase. It appears that as the differentiation of cells increases, alcohol effect will be reduced.[17] It is evident that alcohol disturbs the adenylcyclase system.[18] As many proteins are phosphorylated by this system, it plays a key role in both the proliferation and differentiation process.[19] Ethanol also affects intracellular ionic calcium balance and this might be the reason for hampering of certain cellular processes which are linked to Ca\(^{2+}\). It is well-known fact that Ca\(^{2+}\) is an important ion which act as a signal transducer and also takes part in Ca\(^{2+}\)-ATPase system.[20] Consumption of alcohol >100 gm/day for more than a decade is seen in around 45–75% of alcoholics.[21-22] It causes muscle atrophy of legs and arms which is progressive in nature and characterized by reduced muscle strength. Many factors contribute to the adverse effects of alcohol on muscles. One such factor is protein derangements which might be due to the generation of acetaldehyde. Acetaldehyde can lessen the availability of amino acids and also decreases levels of insulin-like growth factors. At the same time, acetaldehyde promotes free radical-induced protein-membrane damage. It is evident that ethanol can significantly reduce protein synthesis by around 30–40%, which affects both the Type I and Type II muscle fibers[10,23-24] and sarcoplasmic proteins.[25] Long-term use of alcohol can decline whole-body protein synthesis from 27% to 15%.[21] The process responsible for mitochondrial dysfunction in alcoholics is deregulation of both oxygen utilization and ATP generation and this might be the cause for slowdown of protein synthesis.[26] All the above-mentioned mechanisms may result in imbalance of energy generation and utilization, decreased oxidation of fatty acids, and triglycerides rise.[27] Ethanol-induced protein content disturbances are also supposed to be mediated by IGF-I. Notably, IGF-I acts as an intermediary hormone which is anabolic in nature induce the production of proteins and amino acids, regulate muscle metabolism especially striated.[28] It seems IGF opposes apoptotic role in myocytes and also plays atrophic role during the process of differentiation of myoblasts into myotubes.[29]

Hence, preventing IGF-I activity might cause many muscle derangements and changes in the Type II b fibers. Long-term use of alcohol causes decreased plasma peptide levels along with less expression of IGF-I mRNA.[30] Moreover, there is parallel rise in IGFBPs (binding proteins) concentrations.[31] It is to be noted that binding proteins such as IGFBPs oppose IGF-I stimulated amino acid synthesis and inhibits IGF-I induced glucose transport in myoblasts. Apart from this, ethanol can raise the levels of certain cytokines such as TNF-α, IL-1, and IL-6. It is to be noted that these cytokines opposes the actions of IGF.[32] It is now evident that chronic alcoholism accentuate the free radicals generation and these free radicals have capability to alter the skeletal muscle structure predominantly Type II fibers.[33,34] Dysfunctioning of sarcolemma because of oxidative stress has been observed in chronic alcoholics. Muscle membrane disturbances in alcoholics are mainly due to faulty electrolyte homeostasis which is mainly due to defective ca\(^{2+}\) movement[35,36] and also Na’ k’ functions.[37] A sustained raise of ca\(^{2+}\) is detrimental to the tissues. This is due to activation of apoptosis secondary to increase in mitochondrial transition pores permeability.[38] It appears that ethanol consumption leads to fall of skeletal muscle weight. Reduction in muscle weight might occur parallel to decrease in DNA and RNA content.[39]

Limitaions of Study
Energy intake data is not available which may not allow for accurate assessment of the role of diet and its mechanism in fatigue in these two groups. Restricted to only one group of muscles and cannot be interpolated to all muscle groups. Alcohol intake assessment and Physical activity assessment were restricted to subjects own interpretation.

CONCLUSION
This study concludes that chronic alcohol intake will damage the work efficiency of skeletal muscles which is substantiated by the early onset of fatigue and less work done in alcoholic group sedentary when compared with non-alcoholic sedentary group. This study strongly suggests that non-consumption of alcohol for normal functioning of skeletal muscles in human beings. Further studies are needed in understanding the exact pathophysiological changes that are taking place at excitation and contraction level. This study leaves a scope for further research on the theme that “will regular exercise training ameliorate or reverse the changes in the skeletal muscles of the chronic alcoholics?”

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