Research Article

Effect of a Carbohydrate-Rich Diet on Rat Detrusor Smooth Muscle Contractility: An Experimental Study

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Objectives. We aimed to investigate the effect of a carbohydrate-rich diet on detrusor contractility in rats. Materials and Methods. Sprague-Dawley rats were randomized into two groups. The control group received regular food and water. The study group received carbohydrate-rich diet for six weeks. The rats’ detrusor muscle was isolated for pharmacological and histopathological examinations. Results. In the control and study groups, mean body weights were 431.5 ± 27.6 g and 528.0 ± 36.2 g, respectively (p < 0.001). Electrical stimulation of the detrusor strips of the control group resulted in gradual contraction. A decreased contractile response was shown in the study group. Acetylcholine in 10-7-10-3 molar concentration produced a decreased contractile response in the study group, compared to the control group (p < 0.01). The study group showed marked subepithelial and intermuscular fibrosis in the bladder. Conclusion. Carbohydrate-rich diet causes marked subepithelial and extracellular fibrosis and changes in contractility in the detrusor within a six-week period. Changes have higher costs in therapeutic choices and correction of these changes remains difficult. Putting an end to carbohydrate-rich diet would seem to be more cost-effective than dealing with the effects of consuming it in high proportions which should be the national policy worldwide.

1. Introduction

An increase in high-energy food intake and the consumption of fat and sugar in foods, along with a sedentary lifestyle, decreased physical activity and lack of exercise, and the development of transportation systems and urbanization all threaten public health around the world. Obesity is a major public health problem affecting populations globally. The worldwide incidence of obesity is increasing significantly. According to the World Health Organization (WHO), 25% of the population are obese and 25% are overweight and prone to obesity [1].

Among the population that falls within the abnormal weight range, 25% are prone to gaining weight genetically. There are more than 400 million obese people and 1.6 billion overweight people living in the world today, and these numbers are predicted to reach 700 million and 2.3 billion, respectively, by 2025. Overweight and obesity are defined as an excessive fat accumulation that presents a risk to health. In recent years, obesity has been declared as one of the four main components of Metabolic Syndrome (MetS) which was first described in 1988 by Reaven [2]. People are considered obese when they have a body mass index (BMI) equal to or above 30. Obesity is known to be associated with many chronic diseases. Morbidity and mortality of the diseases associated with obesity are high. In the urinary tract, renal failure, kidney tumors, kidney stone formation, infertility, and voiding dysfunction have been demonstrated.
in association with obesity [3–5]. The bladder is the most important organ with regard to normal urination. The lower urinary system is also under risk of obesity [6].

It has been reported that obesity may cause urinary incontinence by affecting other organs and systems including neurogenic diseases that may contribute to pelvic floor and urethral dysfunction, delayed median nerve conduction, and likelihood of lumbar intervertebral disc herniation. That study had some limitations: although neuromuscular dysfunction was mentioned, that study was mainly set up on the basis of obesity and stress urinary incontinence. The lack of isolated pharmacological and histological experiments on the detrusor was another limitation [7].

Micturition occurs involuntarily at the beginning of life. After the age of 3 to 5 years, it is regulated voluntarily. The micturition process has complex pathways at several levels, such as the brain, spinal cord, and peripheral nervous system, and it is mediated by multiple neurotransmitters. The urinary control mechanism is sensitive to various disturbances due to its complexity. The role of obesity in bladder dysfunction has gained importance in recent years. A high-fat diet, as well as obesity, may have negative effects on detrusor functions [8]. The food industry’s use of a higher proportion of carbohydrate and the increasing prevalence of obesity may lead to negative effects on detrusor functions.

In this present study, we aimed to investigate the functional and histological effects of a carbohydrate-rich diet on detrusor smooth muscle contractility in rats.

2. Materials and Methods

This experimental animal study was approved by the Ondokuz Mayıs University Animal Care and Use Committee and was carried out in 2016. Mature male Sprague-Dawley rats aged 9–12 weeks were obtained from Gaziosmanpaşa University vivarium sources. All procedures and protocols were conducted in accordance with the Guide for the Care and Use of Laboratory Animals (NIH publication 865-23, Bethesda, MD, USA). Rats were housed in a temperature- and humidity-controlled room (22 ± 1°C). Rats were randomized into two groups, 12h light/dark cycle. Rats were weighed at the beginning of the study, the mean body weights of the control group and study group were 315.1 ± 49.5 g (302–378 g) and 312.5 ± 42.4 g (297–368 g) (p = 0.47), respectively. After a six-week period, in the control and the study group, the mean body weights were 431.5 ± 27.6 g (405–476) and 528.0 ± 36.2 g (476–571) and were found to be statistically significant, respectively (p < 0.001). The functional viability of preparation was assessed by the addition of acetylcholine and electrical field stimulation for the detrusor.

Acetylcholine (Sigma, USA) was administered to assess detrusor smooth muscle contractions in a cumulative manner (10-7-10-3 M) and produced cumulative concentration-response curves. Each incremental concentration was added when the response to the previous concentration reached a plateau and stabilized. The frequency-response curves were constructed as follows: square wave pulses (100 V, 0.5 ms) were delivered for 20 s at increasing frequencies (2–64 Hz) with a 4 min interval between two consecutive frequency steps.

2.2. Statistical Analysis. All data are expressed as the mean ± SD. Data analyses were performed using GraphPad Instat software (v. 3.0) (GraphPad, USA). Following the assurance of a normal distribution of data, one-way analysis of variance (ANOVA) with the Tukey-Kramer post hoc test was used for multiple comparison. Values of p < 0.05 were regarded as significant.

3. Results

Control and study groups’ weights were recorded at the beginning and end of the study after six weeks. At the beginning of the study, the mean body weights of the control group and study group were 315.1 ± 49.5 g (302–378 g) and 312.5 ± 42.4 g (297–368 g) (p = 0.47), respectively.

The solution was continuously gassed with 95% O

2

and 5% CO

2

when the response to the previous concentration reached a plateau and stabilized. The frequency-response curves were constructed as follows: square wave pulses (100 V, 0.5 ms) were delivered for 20 s at increasing frequencies (2–64 Hz) with a 4 min interval between two consecutive frequency steps.
molar concentration caused dose-dependent contractions in
the smooth detrusor muscle strips in the control group, but
no significant dose-dependent response was recorded with
increasing concentration of Ach in the study group ($p < 0.01$)
(Figures 4(a), 4(b), and 4(c)).

4. Discussion
The micturition cycle consists of two different processes:
filling and storing in the bladder and bladder emptying or
voiding. The presence of an adequately coordinated detrusor
contraction, lack of infravesical obstruction, and decrease in
bladder neck pressure are also needed for normal voiding.
Despite an increase in urine volume in the bladder, low
intravesical pressure with appropriate sensation, the absence
of involuntary detrusor contraction, and closure of the
bladder neck are necessary for storage. Relaxation of the blad-
der neck is coordinated by a noradrenergic-noncholinergic
mechanism mediated by nitric oxide. Voiding function is
provided by the inhibitory effect of some neurotransmitters,
such as glycine, gamma-aminobutyric acid (GABA) opioids,
purines, and the noradrenergic system at various levels of
the neural axis. Bladder filling and consequent wall dis-
tention may also result in the release of factors that may
have an influence, such as acetylcholine (Ach), adenosine
triphosphate (ATP), nitric oxide, and prostaglandin. Phar-
macologically, M1, M2, and M3 receptor subtypes have been
found in the human bladder [9]. Stimulation of M3 receptors
by acetylcholine leads to smooth muscle contraction [10].
Obesity is a global health problem that affects multiple organs
and systems with such conditions as hypertriglyceridemia,
type 2 diabetes, hypertension, MetS, coronary heart disease,
stroke, cancers, gallstones, female infertility or menstrual
irregularities, erectile dysfunction, nonalcoholic fatty liver
disease, and osteoarthritis [11–16]. There are a wide variety of
etiological causes of obesity, such as lack of energy balance,
In our study, HFCS was shown to cause marked subepithelial fibrosis within a six-week period and fructose had dual negative effects on detrusor function, including neuromuscular and histopathological aspects. Our opinion is that the lack of flexibility of the fibrotic tissue could adversely affect the neuromuscular mechanism and this could affect voiding behavior. A lack of cystometric evaluation is a limitation of our study. Another limitation is the lack of weekly weight monitoring of the groups. Obesity and marked subepithelial fibrosis are the most significant findings of this study. Oberbach et al. reported that weight loss had no impact on regression of the bladder fibrosis in their experimental study [24], but some advocated that a decrease in BMI caused relief for lower urinary tract symptoms [25].

5. Conclusion

It is obvious that HFCS causes marked subepithelial and detrusor fibrosis and this may cause negative effects on detrusor function and metabolic pathways within a six-week period. Correction of these changes remains difficult and has higher costs in therapeutic choices. Our aim is to create public awareness of high-fructose-caused obesity. Putting an end to fructose-rich diets would seem to be more cost-effective than
dealing with the effects of consuming it in high proportions and this should be the national policy worldwide.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest regarding the publication of this article.

**References**


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