Chronic Rumex Patientia Seed Feeding Improves Passive Avoidance Learning and Memory in Streptozotocin-Diabetic Rats

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1. Introduction

Diabetes mellitus (DM) has been associated with neurological complications in both the peripheral and the central nervous system (1). Long-term DM leads to a wide range of peripheral neuronal deficits including reduced motor nerve conduction velocity, impaired nerve regeneration, axonal shrinkage, and deficient axonal transport (2). In streptozotocin (STZ)-diabetic rats, the nerve damage observed parallels in many ways the nerve degeneration seen in human diabetic neuropathy (3). In addition, different kinds of neuropathies are one of the major complications contributing to morbidity in patients with diabetes mellitus. Pathological studies have also suggested that diabetes is one of the risk factors for senile dementia of Alzheimer’s type (4). Although many studies about the relationship between diabetes and peripheral neuropathy have been done to date, however, the effects and consequences of diabetes on the brain itself have not been much studied and no marked structural abnormality has been found in the central nervous system of patients with diabetic neuropathy using routine staining methods (5). Functionally, pas-

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Abstract

Introduction: Diabetes mellitus is accompanied with disturbances in learning, memory, and cognitive skills in the human society and experimental animals. Due to anti-diabetic and antioxidant activity of Rumex patientia (RP), this research study was conducted to evaluate the efficacy of chronic Rumex patientia feeding on alleviation of learning and memory disturbance in streptozotocin-diabetic rats.

Methods: Male Wistar rats were divided into control, diabetic, RP-treated-control and -diabetic groups. For induction of diabetes, streptozotocin (STZ) was administered at a dose of 60 mg/Kg. Meanwhile, RP-treated groups received RP seed powder mixed with standard pelleted food at a weight ratio of 6% for 4 weeks. For evaluation of learning and memory, initial latency (IL) and step-through latency (STL) were determined at the end of study using passive avoidance test.

Results: It was found out that regarding initial latency, there was no significant difference among the groups. In addition, diabetic rats developed a significant impairment in retention and recall in passive avoidance test (p<0.01), as it is evident by a lower STL. Furthermore, RP treatment of diabetic rats did produce a significant improvement in retention and recall (p<0.05).

Discussion: Taken together, chronic RP feeding could improve retention and recall capability in passive avoidance test in STZ-diabetic rats.

Key Words:
Rumex Patientia,
Learning and Memory,
Passive Avoidance Test,
Diabetic Rat

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Assessment

The use of chronic Rumex Patientia seed feeding on learning and memory in streptozotocin-diabetic rats is investigated. The study demonstrates that RP feeding improves retention and recall in the passive avoidance test. This finding suggests a potential therapeutic role of RP in the treatment of diabetic neuropathy-related cognitive deficits.
sive avoidance learning and memory deficits develop in STZ-diabetic rats (6). Impairment of spatial learning in a hippocampus-dependent complex maze has also been reported in such animals (7). Changes in hippocampal synaptic plasticity have been reported in diabetes (8). These findings suggest that untreated diabetes results in deficits across multiple neural systems underlying learning and memory processes.

On the other hand, recent interests are focusing on the use of medicinal plants with antidiabetic and antioxidant potential in reducing the ensuing complications in diabetic patients (9). Plant-based pharmaceuticals have been employed in the management of various mankind diseases (10). They are as essential part of human diet and are present in plant extracts that have been used for centuries in oriental medicine. Antioxidant properties, ROS scavenging and cell function modulation of medicinal plants and their effective substances could account for the large part of their pharmacological activity (11-12). Antioxidant and free radical scavenging activity (13), gastroprotective and anti-ulcerogenic activity in gastric tissue (14), protecting pancreatic B cells against STZ-induced damage (15), and anti-inflammatory effect (16) of Rumex patientia (RP) have already been reported. In addition, Rumex patientia seed (grain) aqueous extract has been used for the treatment of type I diabetes induced by STZ (17). Therefore, this study was undertaken to evaluate the efficacy of chronic RP on alleviation of learning and memory disturbance in streptozotocin-diabetic rats using passive avoidance.

2. Methods

2.1. Animals

Male albino Wistar rats (Pasteur’s institute, Tehran, Iran) weighing 265 ± 13 g (11-13 weeks old) were housed in an air-conditioned colony room on a light/dark cycle (21-23 °C and a humidity of 30-40%) and supplied with standard pelleted diet and tap water ad libitum. Procedures involving animals and their care were conducted in conformity with the NIH guidelines for the care and use of laboratory animals.

2.2. Experimental Procedure

The rats (n = 32) were randomly allocated and similarly grouped into four groups: normal vehicle-treated control, RP-treated control, vehicle-treated diabetic and RP-treated diabetic. The rats were rendered diabetic by a single intraperitoneal injection of 60 mg kg-1 streptozotocin (STZ) (Pharmacia and Upjohn, USA) freshly dis-solved in cold normal saline. Control animals received an injection of an equivalent volume of normal saline and vehicle. Diabetes was confirmed by the presence of hyperglycemia, polyphagia, polydipsia, polyuria and weight loss. One week after STZ injection, blood samples were collected and serum glucose concentrations were measured using glucose oxidation method (Zistshimi, Tehran). Only those animals with serum glucose higher than 250 mg dl-1 were selected as diabetics for the following experiments. The day on which hyperglycemia had been confirmed was designated as day 0. Rumex patientia seed was prepared, dried under shade and finally ground. Plant-mixed food pellet at a weight ratio of 6% was prepared using pellet-making device (Nooran Co., Tehran). This ratio was chosen according to our pilot study. Changes in body weight, food consumption and water intake were regularly observed during the experimental period. Behavioral test (passive avoidance) was performed at the end of study in experimental groups as described below.

2.3. Single-trial Passive Avoidance Test

The apparatus (BPT Co., Tehran) consisted of an illuminated chamber connected to dark chamber by a guillotine door. Electric shocks were delivered to the grid floor by an isolated stimulator. On the first and second days of testing, each rat was placed on the apparatus and left for 5 min to habituate to the apparatus. On the third day, an acquisition trial was performed. Rats were individually placed in the illuminated chamber. After a habituation period (5 min), the guillotine door was opened and after the rat entering the dark chamber, the door was closed and an inescapable scrambled electric shock (1 mA, 1 s once) was delivered. In this trial, the initial latency (IL) of entrance into the dark chamber was recorded and rats with ILs greater than 60 s were excluded from the study. Twenty-four hours later, each rat was placed in the illuminated chamber for retention trial. The interval between the placement in the illuminated chamber and the entry into the dark chamber was measured as step-through latency (STL up to a maximum of 600 s as cut-off).

2.4. Statistical Analysis

All results were expressed as mean ± S.E.M. For behavioral test, parametric one-way ANOVA test was applied. Body weight and serum glucose levels at different weeks were analyzed using repeated measure one-way ANOVA. In all calculations, a difference at p<0.05 was regarded as significant.
3. Results

Body weight and serum glucose measurements (Fig. 1) indicated that before diabetes induction, there were no significant differences among experimental groups. After 4 weeks, the weight of the vehicle-treated diabetic rats was found to be significantly decreased as compared to control rats (p<0.05) and RP-treated diabetics showed a less non-significant decrease as compared to vehicle-treated diabetics. Untreated diabetic rats had also an elevated serum glucose level over those of control rats (p<0.001) and treatment of diabetic rats with RP caused a significant decrease in the serum glucose (p<0.05) only at 2nd week relative to vehicle-treated diabetics. In addition, RP treatment of control rats did not produce any significant change regarding serum glucose level.

Fig. 2 shows the performance of treated-control and diabetic rats in passive avoidance paradigm as indicated by initial and step-through latencies. Regarding initial latency, there was no significant difference among the groups. In addition, diabetic-treated rats developed a significant impairment in retention and recall in passive avoidance test (p<0.01), as it is evident by a lower STL and RP treatment did produce a significant improvement (p<0.05). Furthermore, retention and recall of RP-treated control rats was not affected by RP treatment.

4. Discussion

The main findings of this study were two-fold. First, long-term diabetes was accompanied with disturbances in animal performance in passive avoidance as was evident by a lower STL. Second, 4-week administration of RP improved could prevent retention and recall abnormality in diabetic rats as evaluated by passive avoidance test.

Although the multifactorial pathogenesis of cognitive and memory impairments in diabetes has not yet completely understood, several factors such as metabolic impairments, vascular complications as well as release of free radicals have been implicated (18). First, prolonged hyperglycemia is a primary cause of most complications of diabetes. Indeed, chronic hyperglycemia is thought to lead to cognitive impairments in diabetes (19). Hyperglycemia in type I diabetic patients has also been associated with learning impairments (20).
Therefore, the restoration of some cognitive functions observed in diabetic animals in this study may be partly due to the ability of RP to attenuate hyperglycemia, as observed in this study. Second, brain vascular abnormalities may also contribute to the pathophysiology of cognitive impairment in diabetes (20). Third, oxidative damage is associated with cognitive dysfunction (20), therefore treatment with antioxidants could be a therapeutic approach in various types of neurodegenerative diseases (20). Oxidative stress contributes to increased neuronal damage and death through protein oxidation, DNA damage, and peroxidation of membrane lipids (20). It has been observed that use of antioxidants and neuroprotective agents may decrease the risk of memory deficits (21).

In conclusion, chronic RP feeding could improve retention and recall capability in passive avoidance test in STZ-diabetic rats. Further studies are warranted to investigate the detailed involved mechanisms.

References


