

Effect of Clopidogrel on the Levels of Adropin and Adiponectin in Serum of Female Albino Rats

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Abstract—Clopidogrel is an antiplatelet drug. It helps hold blood flowing smoothly in body, used to save you coronary heart attacks and strokes in individuals with heart disease, recent stroke, or blood movement disease. It is also used to keep blood vessels open and prevent blood clots after sure processes. Adropin is a unique hormone encode via the electricity homeostasis-associated. Adropin is produce within the liver and brain, and additionally in peripheral tissues inclusive of inside the heart and gastrointestinal tract. Furthermore, adropin is present inside the circulatory machine. Adiponectin is a hormone and an adipokine protein that influences several metabolic tactics and is specially recognised for its insulin-sensitizing and anti-inflammatory results. Adipose tissue is specially responsible for generating adiponectin, though other tissues in frame crop it as properly. The relationship between the Glolidogrel and adropin, adiponectin is still not clear. The aim of the study is to determine adropin and adiponectin attentiveness in serum male rats that treated with Clopidogrel, and to examine the relationship amid serum adropin and adiponectin. Materials and strategies: fifteen healthy adult female albino rats have been used for this examine. The rats had been randomly and equally alienated into three businesses. Group-A; control group, group-B; given 15mg/kg Glolidogrel, and group-C; given 20mg/kg Glolidogrel. Results: this study revealed rats which treated with Glolidogrel showed significantly increased in serum adropin and adeponectin levels comparison with control group.

Keywords— Clopidogrel, Adropin, Adiponectin, antiplatelet drug, Insulin resistance.

I. INTRODUCTION

Clopidogrel is utilized in sufferers with coronary artery syndromes who are liable to thrombosis or who are receiving percutaneous coronary intervention to lessen coronary heart attack and stroke [1]. Clopidogrel stays the maximum broadly prescribed antiplatelet drug in the United States and Canada. Clopidogrel is a prodrug that, after oral management, clopidogrel is swiftly absorb. Because of its great metabolism, clopidogrel is not noticed in human plasma. Clopidogrel is a prodrug that is absorbe inside the intestine and activate within the liver and calls for cytochrome P450 (CYP) enzymes for biotransformation into the energetic thiol metabolite [4]. Despite the preliminary promise of clopidogrel pharmacogenetics and the Food and Drug Administration (FDA) black container caution encouraging recurring genotyping exercise to direct antiplatelet therapy with a P2Y12 inhibitor, this technique has now not been embraced via the cardiovascular network [5].

Adropin is a singular peptide of seventy six amino acids this is spoken in diverse tissues and cells consisting of the liver, heart, pancreas, blood vessels, kidneys, milk, serum, plasma and numerous part of the brain. Adropin, encode by using the Enho gene, theaters a vital function in electricity homeostasis. A evaluate of the literature indicates that adropin attenuates the grade of insulin resistance by means of decreasing endogenous hepatic glucose manufacture. Adropin recovers glucose metabolism with the aid of improving glucose usage in mice, together with sensitization of insulin gesturing trails inclusive of Akt (a serine/threonine kinase that plays a significant part in cell proliferation, existence, increase, and glucose metabolism) Phosphorylation and

activation of glucose transporter receptor 4 [6]. Adropin is a hormone that changed into recognized by using Kumar et al in 2008 [7]. Notably, the amino acid collection of adirubin is especially preserved between class and is equal in rat, human, mouse, and swine, furthermore, the adirubin protein is current inside the cardiovascular device of animals and humans [7]. Inappropriately, the plasma half of-existence of adropin is motionless unidentified and leftovers to be strong-minded. Adropin is encoded via the electricity homeostasis-related gene (Enho), which is usually spoken within the mind and liver. Though, it's too noticed in peripheral tissues consisting of coronary heart, lung, kidney, muscle, blood mononuclear cells, and breast cancer cells [8].

Adiponectin is a hormone and an adipokine protein that effects on many which included metabolic procedures and is mostly known for its insulin sensitivity and anti-inflammation belongings. Adipose tissue have mainly responsible for formation adiponectin, and other tissues in the body produce it as well [9]. Adiponectin regulated metabolism process through fatty acid oxidation and blood glucose control, on other hand, Mediated in component by using downstream outcomes of adiponectin gesturing in skeletal muscle. Now, skeletal muscle has been regarded to be a supply of adiponectin look, powering hobby inside the roles of adiponectin as a mingling adipokine and a domestically spoken paracrine/autocrine issue. In adding to existence metabolically receptive, skeletal functional volume, calcium dealing with, boom and law, reformative potential, and vulnerability to persistent infection are altogether powerfully tormented by adiponectin. Thus, the part of adiponectin gesturing in skeletal muscle may make bigger skeletal muscle characteristic and maintain muscle fitness. [10]. In adding to its valuable results on insulin compassion and lipid metabolism, adiponectin uses its

angiogenic protecting impact via its directed movements on endothelial cells, macrophages, monocytes, different platelets, inflammatory cells, and easy muscle cells, thereby initiating and progressing atherosclerosis. Adiponectin increases endothelial nitric oxide production [11,12,13] which inhibits endothelial ROS formation brought about with the aid of LDL [14]. , inhibits the expression of endothelial adhesion molecules [15], protects white cellular–endothelium connections [16] and defends endothelial cells from apoptosis [17]. Moreover, adiponectin reduced macrophage start [18, 19] and foam mobile formation [20], and promotes permission of primary apoptotic cells with the aid of macrophage cells [21], and prevented smooth muscle cell proliferation. Because there is no study showing the association amid antiplatelet drugs (Clopidogrel), adropin and adiponectin, this study aims to control the result of clopidogrel on adropin and adiponectin in serum.

II. MATERIAL AND METHOD

Fifteen healthy adult female Wistar albino rats were weighted 180-200g , Obtained from the Animal House of the College of Veterinary Medicine - Tikrit University. Rats were housed in steel wire cages (70 cm x 50 cm x 30 cm - five rats/cage) below regular circumstances. They had been fed business rodent food with unfastened get right of entry to to water, stored at room temperature and maintain on an everyday light/darkish cycle. Mice had been adapt to the new environment for one week prior to the trial. The rats have been randomly divided into 3 equal agencies: Group A: the ordinary manipulate institution: the rats have been fed a ordinary weight loss program. for month. Group-B: animals conventional single oral dose 15 mg/kg from Clopidogrel daily for month. Group-C: animals received single oral dose 20mg/kg from Clopidogrel daily for month. And after finish the experiment the blood sample were collection for laboratory analysis.

Measurement level of Adropine in serum was analyze by rat adropine ELISA kit (Sun Red Biotechnology, China) and level of Adiponectin in serum was analyze with rat adiponectin ELISA kit (Sun Red Biotechnology, China). *Statistical Analysis:* Results were presented by analyze using One method Analysis of variance (ANOVA) inside the statistically considerable variations test became used to compare statistical differences between organizations. A P cost of much less than 0.05 became taken into consideration to be big.

III. RESULTS

The result of this study presented that increased of adropin serum levels in group B and group C that treated by Clopidogrel comparison with control group A, table (1) and fig (1) also the result presented that increased of adiponectin serum levels in group B and group C that treated by Clopidogrel comparison with control group A. significantly increased of adropin and adeponectin levels in serum levels in group B and group C comparison with control group, table (1).

TABLE (1) Adropin and Adiponectin serum levels in female rats treated with Clopidogrel. (The different characters indicate that found moral difference ($P \leq 5$).

Factor	Adropin mean±SD	Adiponectin mean±SD
Group B	28.83 b ± 3.04	1333.4 b ± 139.3
Group C	31.33 a ± 4.44	1690.4 a ± 119.9
Group A	27.62 b ± 0.79	1209.4 c ± 210.7

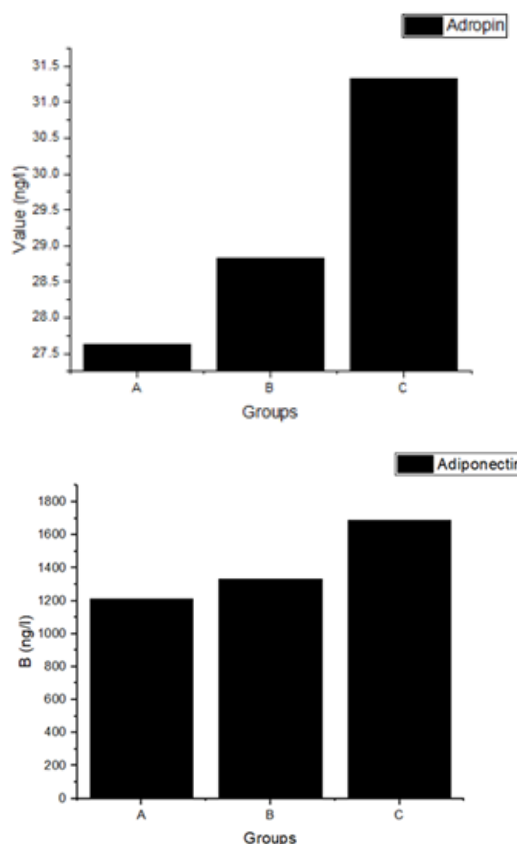


Figure (1) shows the difference in the serum Adropin and Adeponectin levels between the groups.

IV. DISCUSSION

In this study, we chose Clopidogrel, an antiplatelet drug that help keep blood graceful smoothly in the body. It is use to stop heart attack and stroke in individuals with heart illness. The aim of our study was to elucidate the effect of Clopidogrel on the heights of Adropin and Adiponectin, which are known to be related with glucose metabolism, insulin confrontation, and lipid metabolism. We hypothesized that Clopidogrel treatment may ameliorate these metabolic parameters and inhibit hepatocyte inflammation, coronary artery disease, and coronary lesion complexity. We conducted an experiment using animal models and measured the serum heights of Adropin in different groups, comparing those treated with Clopidogrel to the control group.

Our findings demonstrated that the level of Adropin increase meaningfully in the group treat with Clopidogrel likened to the control group. These result provision the hypothesis that Clopidogrel treatment can elevate Adropin levels. Previous studies by Wei et al. have also indicated that

high level of Adropin in the serum are associated with a reduced risk of cardiovascular disease and carotid atherosclerosis in patient by type 2 diabetes [22]. And the high levels of adropin in the serum also been linked to a abridged danger of circulatory disease have been associated with improved insulin sensitivity and glucose metabolism, which can be beneficial for people by type 2 diabetes and a lower incidence of metabolic syndrome.[23], This promotes the use of clopidogrel as an antiplatelet agent and to prevent blood clot formation. whereas Danoli'c, *et al* in 2021, indicated that Serum adirobin degrees extended in sufferers with primary Sjogren's syndrome and showed a negative association amid adirubin ranges and the degree of primary harm of Sjogren's syndrome. These findings propose that greater release of adropenia may be worried in the pathogenesis of number one Sjogren's syndrome, however whether adropenia has a protective or damaging position on this putting remains elusive. Increased serum adropenic stages can be predicted in continual inflammatory disorder [25]. The degree of adropen in myocardial ischemia has proven some controversy making the capacity function of adropen as a biomarker for analysis and comply with-up in a few cardiovascular issues including coronary heart failure and ischemic coronary heart sickness a place of super interest and certain report have claimed that serum adropen is expanded in acute myocardial infarction [26]. And the level of adirobin in the blood increases in the initial length of ST promotion myocardial infarction [27]. In an examine by way of Lian et al. In 2011, comparing heart failure patient and healthful people, it become strong-minded that the level of adropenia elevated in proportion to the harshness of heart failure, while the extent of adropenia became little in the healthy manage organization [28]. They recommended that a high blood level of adropenia plays a function in inflicting heart failure. In an animal have a look at carried out by means of Aydın et al. In 2017 on rats, it become determined that blood ranges of adirubin elevated 1 hour after an experimentally brought about myocardial infarction [29]. On the alternative hand, within the take a look at carried out with the aid of Yu et al in 2014, they located that the blood stage of adropenia reduced in sufferers with acute myocardial infarction [30]. Low levels of Adropin in serum were associated with obesity, metabolic issues, and cardiovascular disease. Low adropen tiers have additionally been connected to a better occurrence of kind 2 diabetes and an increased hazard of cardiovascular disease, consisting of heart attack and stroke [31]. While adropenia reduced inside the blood in sufferers with osteoporosis [32]. Adropin may also improve fat metabolism, reduce insulin resistance, and prevent infection of hepatocytes. Thus, atropine had vast healing advantages and will be proposed as a potential candidate agent in opposition to hyperlipidemia [33]. Semak et al. In 2023 determined that blood tiers of adropenia are low in sufferers with rheumatoid arthritis [34].

Furthermore, we observed a similar pattern with Adiponectin levels, findings demonstrated that Adiponectin levels significantly increased in the groups that treated with Clopidogrel compared with control group. Adiponectin is known to possess anti-thrombotic properties and can inhibit

platelet activation and aggregation, thereby preventing excessive blood clotting. This mechanism helps maintain normal blood flow and prevents the formation of harmful clots [35]. Increased adiponectin levels have also been associated with greater physical activity and improved insulin sensitivity [36]. Signifying that the pathophysiological part of Clopidogrel may be prevent coronary artery disease and coronary lesion complexity and Our data provision the idea that adiponectin is an significant for safety coronary artery and heart.

Gamberi et al in 2019 speak the contemporary information about adiponectin in myopathies that a few myopathies are characterised by way of a decreased degree of circulating adiponectin and that regeneration of the hormone induces beneficial results in diseased muscle mass [37]. Studies on the involvement of adiponectin in most cancers have accelerated in latest years, as Parida et al, in 2019, mentioned how weight problems and weight problems are intently associated with the development of most cancers in numerous sorts of tumors, and obesity works by dysregulating adipokin manufacturing, which results in an upregulation of Oncogenic adipokines, along with leptin, down-alter adiponectin, which theaters a defensive role in obesity-associated cancers [38]. Advanced adiponectin expression is related with more physical interest whilst decrease ranges of adiponectin are discovered in inactive topics who are obese, prediabetic, and prediabetic [39]. Elevated degrees of serum adiponectin had been related to an improved threat of detrimental cardiovascular and cerebrovascular events and mortality unbiased of conventional threat factors in sufferers with ischemic stroke [40]. In 2023, Kim et al. Stated that adiponectin is associated with age-related infection and salivary gland lipid accumulation [41]. And adiponectin attenuates inflammatory signals [42].

Adiponectin seems to production a part in adaptable muscular tissues, with latest mechanistic studies representative that it is a crucial sign for muscle renewal and conquest of proteolysis [43]. Its significance to the everyday physiological purpose of skeletal muscle has been established in research of muscle increase, renewal, protein turnover, and rule of inflammatory gesturing, while decreased plasma adiponectin stages had been related to diverse diseases, which include obesity and kind 2 diabetes [44]. Little adiponectin degrees are an self-governing predictor of blended and non-calcified coronary artery sclerotic plaques [45]. In comparison, different research have shown an affiliation among adiponectin and event coronary coronary heart disease in addition to secondary cardiovascular events in sufferers with acknowledged coronary artery disease. Low ranges of adiponectin have been associated with lipid-wealthy however non-calcified coronary artery plaques in non-diabetic sufferers in a bivariate. Analysis as decided by IVUS [46-47]. Suggesting that adiponectin is an essential marker inside the pathogen of atherosclerosis.

V. CONCLUSION

this study provides evidence that Clopidogrel treatment can increase the levels of Adropin and Adiponectin. These findings suggest potential therapeutic benefits of Clopidogrel in improving metabolic parameters and preventing

cardiovascular complications. However, further studies on animal species to see the effect of this drug and needed to fully understand the fundamental mechanisms and confirm the clinical implications of these findings

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