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Pioglitazone as an Insulin Sensitizing Agent in Metabolic Syndrome Management

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ABSTRACT

Metabolic syndrome (MetS) has emerged as a global metabolic epidemic driven by rapid urbanization, sedentary lifestyles, and rising obesity rates, substantially increasing the risk of type 2 diabetes mellitus and cardiovascular disease. Insulin resistance is the central pathophysiological hallmark of MetS, linking impaired glucose utilization, dyslipidemia, chronic low-grade inflammation, and endothelial dysfunction. Targeting insulin resistance therefore represents a pivotal strategy for comprehensive management of MetS, extending beyond simple glycemic control.

Pioglitazone, a thiazolidinedione class drug, functions as a potent agonist of peroxisome proliferator-activated receptor-gamma (PPAR-γ), a nuclear receptor that regulates genes involved in glucose and lipid metabolism. Through activation of PPAR-γ, pioglitazone enhances insulin sensitivity in adipose tissue, skeletal muscle, and liver, resulting in improved peripheral glucose uptake and reduced hepatic glucose production.

Beyond its glucose-lowering action, pioglitazone exerts favorable effects on lipid metabolism by decreasing triglyceride levels and increasing high-density lipoprotein cholesterol. Additionally, it demonstrates pleiotropic benefits by modulating adipokine secretion, suppressing pro-inflammatory cytokines, reducing oxidative stress, and improving endothelial function, thereby contributing to attenuation of cardiovascular risk.

Clinical evidence indicates that pioglitazone can simultaneously improve multiple components of MetS, positioning it as a disease-modifying insulin-sensitizing agent. However, its clinical utility is limited by safety concerns such as weight gain, fluid retention, potential heart failure exacerbation, and increased fracture risk, necessitating careful patient selection and ongoing monitoring. In appropriately selected individuals, pioglitazone remains a valuable therapeutic option. Future perspectives emphasize personalized treatment strategies, optimized combination therapies, to maximize benefits while minimizing adverse effects safely.

Keywords: Pioglitazone; Metabolic syndrome; Insulin resistance; PPAR-γ; Type 2 diabetes mellitus

1. Introduction

Metabolic syndrome (MetS) is a multifactorial metabolic syndrome, a combination of inter-relationship cardiometabolic risk factors, that combine to increase the risk of contracting type 2 diabetes mellitus and cardiovascular diseases. The most prominent diagnostic aspects of MetS are central or abdominal obesity, impaired glucose tolerance/high level of fasting glucose in the blood, dyslipidemia with high percentage triglyceride and low percentage of high-density lipoprotein cholesterol, high blood pressure [1]. The world has taken a huge stride in the morbidity and mortality through the rapid urbanization, sedentary lifestyle, caloric overload and genetic susceptibility, which has led to the emergence of metabolic syndrome [2].

The most important pathophysiological process of metabolic syndrome is insulin resistance. It is characterized by defective insulin sensitivity of insulin sensitive body tissues such as skeletal muscle, adipose tissue and liver to normal insulin levels in the circulation [3]. It leads to the development of compensatory hyperinsulinemia that causes the inability to absorb glucose, high gluconeogenesis in the liver, lipid metabolic disorders, and release of pro-inflammatory cytokines. This metabolic dishomeostasis augments endothelial pathology, oxidative stress and chronic low-grade inflammation thereby augmenting the emergence of metabolic and cardiovascular issues [4].

The conventional antidiabetic interventions are primarily hypoglycemic but not insulin insensitivity that is the cause of the metabolic syndrome. In addition, several glucose-lowering drugs may be associated with adverse effects, including hypoglycemia, weight gain, or reduced effectiveness in terms of connected abnormalities, including dyslipidemia and inflammation [5].

More holistic approach to treatment is greater efficacy of insulin insensitizers: it increases insulin responsiveness and restores a metabolic balance. The thiazolidinedione class drug has been selected to be the one that carries the formation of a clinically significant agent because it has a high activation of peroxisome proliferator-activated receptor-gamma (PPAR- gamma) [6]. This mechanism amplifies the insulin sensitivity, lipid metabolism, and the anti-inflammatory activity of the pioglitazone, hence, highlighting the clinical importance of the latter to the combination of metabolic syndrome [7].

2. Literature Search Methodology

The literature search was done in a systematic and comprehensive way; published studies were gathered and analyzed associated with the role of pioglitazone as an insulin-sensitizing agent in the management of metabolic syndrome. Several electronically accessible databases such as PubMed, Scopus, ScienceDirect, and Google Scholar were used to guarantee the wide-ranging coverage of peer-reviewed scientific literature and reduce the chances of having to skip pertinent studies [8].

The search strategy was narrowed down by using relevant keywords separately and in combination with Boolean operators, including “AND” and “OR”. The major search keywords comprised metabolic syndrome, insulin resistance, pioglitazone, PPAR- g agonist, thiazolidinediones, glucose metabolism, lipid profile, inflammation, and cardiovascular risk. These keywords were effectively pooled to get the studies that focused specifically on both the mechanistic and clinical aspects of the pioglitazone therapy in metabolic syndrome [9].

The selection criteria included original studies, clinical trials and review studies against the pharmacological effects, mechanisms of action, therapeutic efficacy and safety profile of pioglitazone relative to the metabolic syndrome or insulin resistance. Preclinical studies (in vitro and in vivo) as well as clinical studies involving human subjects were all deemed to carry a complete picture of the therapeutic potential of the drug [10].

The exclusion criterion consisted of duplicate publications, abstracts of the conferences, articles in other languages, studies that do not present any clear methodology, and studies that are not relevant to metabolic syndrome. The literature used was critically analyzed, organized and synthesized in order to come up with a coherent and evidence-based review [11].

3. Metabolic Syndrome: Pathophysiology and Clinical Implications

Metabolic syndrome (MetS) is a multi-factorial metabolic complication that results as a product of genetic, environmental, and lifestyle-related influences and has insulin resistance as its pivotal pathophysiological characteristic. The development of skeletal muscle resistance, liver resistance and adipose tissue resistance causes a decrease in glucose uptake and an enhancement in the production of glucose in the liver [12]. The dysfunctional adipose tissue especially excess visceral fat is important because it is an active endocrine organ and releases free fatty acids and inadequately regulated adipokines. This changes the adipokine profile to a reduced insulin sensitivity, lipotoxicity and abnormal metabolic homeostasis [13].

The commonly occurring chronic low-grade inflammation and oxidative stress are the main factors in the formation and progression of metabolic syndrome. The insulin-resistant adipose tissue releases more pro-inflammatory cytokines, including tumor necrosis factor-alpha and interleukin- 6 and reduced anti-inflammatory adipokines like adiponectin. Through this inflammatory environment, oxidative stress increases excessively through overproduction of reactive oxygen species, resulting in dysfunction of endothelium, disruption of insulin signaling, and subsequent worsening of metabolism [14].

Another symptom of metabolic syndrome is dyslipidemia, which is marked by a high level of triglyceride, high small dense low-density lipoprotein levels, and low levels of the high-density lipoprotein cholesterol. These lipid disorders place a great burden on cardiovascular risks over faster atherosclerosis and vascular inflammation promotion. Consequently, people having MetS are significantly exposed to the risk of developing hypertension, coronary artery diseases, and cerebrovascular incidents [15].

Unattended, the metabolic imbalances that accompany metabolic syndrome gradually deteriorate to cause dysfunction and subsequent failure of the pancreatic 8 cells. This change is the shift between insulin resistance and impaired glucose tolerance to overt type 2 diabetes mellitus that increases cardiovascular morbidity and mortality [16].

Table 1: Key Features of Metabolic Syndrome[17]

Sr. No.	Parameter	Description
1	Central obesity	Excess accumulation of visceral fat, commonly assessed by waist circumference
2	Waist circumference	Increased waist size indicating abdominal obesity
3	Insulin resistance	Reduced responsiveness of peripheral tissues to insulin
4	Fasting plasma glucose	Elevated fasting blood glucose levels
5	Impaired glucose tolerance	Reduced ability to regulate postprandial glucose levels
6	Hyperinsulinemia	Compensatory increase in circulating insulin levels
7	Elevated triglycerides	Increased plasma triglyceride concentration
8	Reduced HDL cholesterol	Decreased cardioprotective high-density lipoprotein levels
9	Increased LDL particles	Presence of small dense LDL associated with atherogenesis

Sr. No.	Parameter	Description
10	Hypertension	Elevated systolic and/or diastolic blood pressure
11	Pro-inflammatory state	Increased levels of inflammatory cytokines (e.g., TNF-α, IL-6)
12	Oxidative stress	Excess generation of reactive oxygen species
13	Endothelial dysfunction	Impaired vascular relaxation and nitric oxide bioavailability
14	Prothrombotic state	Increased risk of thrombosis due to altered coagulation factors
15	Cardiovascular risk	Higher likelihood of atherosclerosis, heart disease, and stroke

4. Pioglitazone: Drug Profile

Pioglitazone is an oral antidiabetic drug, which is a thiazolidinedione TZD family medication and is mainly administered to enhance the insulin sensitivity. Contrary to the insulin secretagogues, which stimulate insulin secretion of endogenous sources, pioglitazone is a molecular mechanism of reversing insulin resistance as the underlying defect leading to metabolic syndrome and type 2 diabetes mellitus [18]. Due to its pleiotropic metabolic activity, pioglitazone has become significant in the glycemic control as well as in the overall management of cardiometabolic risk factors [19].

4.1 Chemical and Pharmacological Classification

Pioglitazone is a synthetic derivative of thiazolidinedione, which is supposed to be a five-membered heterocyclic ring that is crucial in the biological effect of the drug chemically. Pharmacologically, it is an insulin sensitizer, acting as a selective agonist of peroxisome proliferator-activated receptor-gamma (PPAR- gamma), a nuclear hormone receptor which acts by controlling the transcription of glucose and lipid metabolism-related genes. PPAR-7 is expressed mostly in adipose tissue, but also in skeletal muscle, liver, and vascular endothelium, which also explain the extensive metabolic effects of pioglitazone [20].

4.2 Mechanism of Action (PPAR-γ Activation)

Pioglitazone is an activator of PPAR-7 which causes a change of gene expression resulting into increased insulin sensitivity of peripheral tissues. This stimulation enhances adipocyte differentiation, expression of glucose transporters and enhances glucose uptake in skeletal muscle and adipose tissue and decreases hepatic gluconeogenesis [21]. Moreover, pioglitazone positively regulates the adipokine secretion through a rise in adiponectin and a fall in pro-inflammatory factors, which include tumor necrosis factor-alpha and interleukin-6. All these interventions lead to better insulin sensitivity, less inflammation, and a positive lipid metabolism and endothelial performance [22].

4.3 Pharmacokinetics

Absorption:
Pioglitazone is rapidly and well absorbed following oral administration, exhibiting high oral bioavailability. Food intake has minimal effect on the extent of absorption [23].

Distribution:
The drug is extensively bound to plasma proteins, mainly albumin, and is widely distributed to insulin-sensitive tissues, facilitating its systemic metabolic effects [24].

Metabolism:
Pioglitazone undergoes extensive hepatic metabolism primarily through cytochrome P450 enzymes, generating active metabolites that contribute significantly to its prolonged therapeutic action [25].

Elimination:
Pioglitazone and its metabolites are eliminated via both biliary and renal routes. Its relatively long elimination half-life supports convenient once-daily dosing in clinical practice [26].

Table 2: Pharmacological Profile of Pioglitazone [27]

Sr. No.	Parameter	Description
1	Generic name	Pioglitazone
2	Drug class	Thiazolidinedione (TZD)

Sr. No.	Parameter	Description
3	Pharmacological category	Insulin sensitizer
4	Primary mechanism	PPAR-γ agonist
5	Site of action	Adipose tissue, skeletal muscle, liver
6	Therapeutic indication	Type 2 diabetes mellitus, metabolic syndrome
7	Effect on insulin sensitivity	Significantly increases peripheral insulin sensitivity
8	Effect on glucose metabolism	Enhances glucose uptake and reduces hepatic gluconeogenesis
9	Effect on lipid profile	Decreases triglycerides, increases HDL cholesterol
10	Anti-inflammatory action	Reduces TNF-α, IL-6 and other inflammatory markers
11	Cardiovascular effects	Improves endothelial function and reduces atherogenic risk
12	Route of administration	Oral
13	Dosing frequency	Once daily
14	Major adverse effects	Weight gain, edema, fluid retention
15	Clinical relevance	Addresses underlying insulin resistance in metabolic syndrome

5. Mechanism of Insulin Sensitization by Pioglitazone

Pioglitazone shows its insulin-sensitizing effects via a complex and tissue-specific process that is mainly achieved by the activation of the peroxisome proliferator-activated receptor- gamma (PPAR -g) a ligand-binding nuclear transcription factor that is key in controlling glucose and lipid metabolism. Pioglitazone approach through direct changes in the expression of genes directly impacts the underlying metabolic impairments that cause insulin resistance in metabolic syndrome [28].

Pioglitazone increases the insulin sensitivity by increasing the adipocyte differentiation and improving adipose tissue functions in adipose tissue. PPAR- g activation helps to redistribute lipids that may be in ectopic locations like skeletal muscles and liver to adipose tissue, which decreases lipotoxicity and enhances insulin signaling [29]. It also causes the decreased circulating fatty acids which have been known to contribute to insulin resistance. Pioglitazone enhances insulin-mediated glucose uptake in skeletal muscle via glucose transporter expression and enhancing the insulin receptor signaling pathways. It inhibits hepatic gluconeogenesis excessively in the liver and enhances insulin-mediated glucose production, which leads to a better fasting glucose and postprandial glucose levels [30].

One of the most important effects of insulin-sensitizing effect of pioglitazone is the regulation of adipokine secretion. Pioglitazone treatment raises the level of adiponectin, an insulin-sensitizing, anti-inflammatory, and anti-atherogenic adipokine, significantly. At the same time, it suppresses the synthesis of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which suppresses chronic low-grade inflammation related to metabolic syndrome [31].

Besides, it has been shown that pioglitazone positively affects glucose and lipid metabolism, decreasing plasma triglycerides, increasing high-density lipoprotein cholesterol, and oxidative stress. The net effect of the inflammatory markers and endothelial functioning are further beneficial to insulin sensitivity and decreased cardiovascular risk. The use of pioglitazone as a disease-modifying agent in the treatment of metabolic syndrome is through these integrated mechanisms [32].

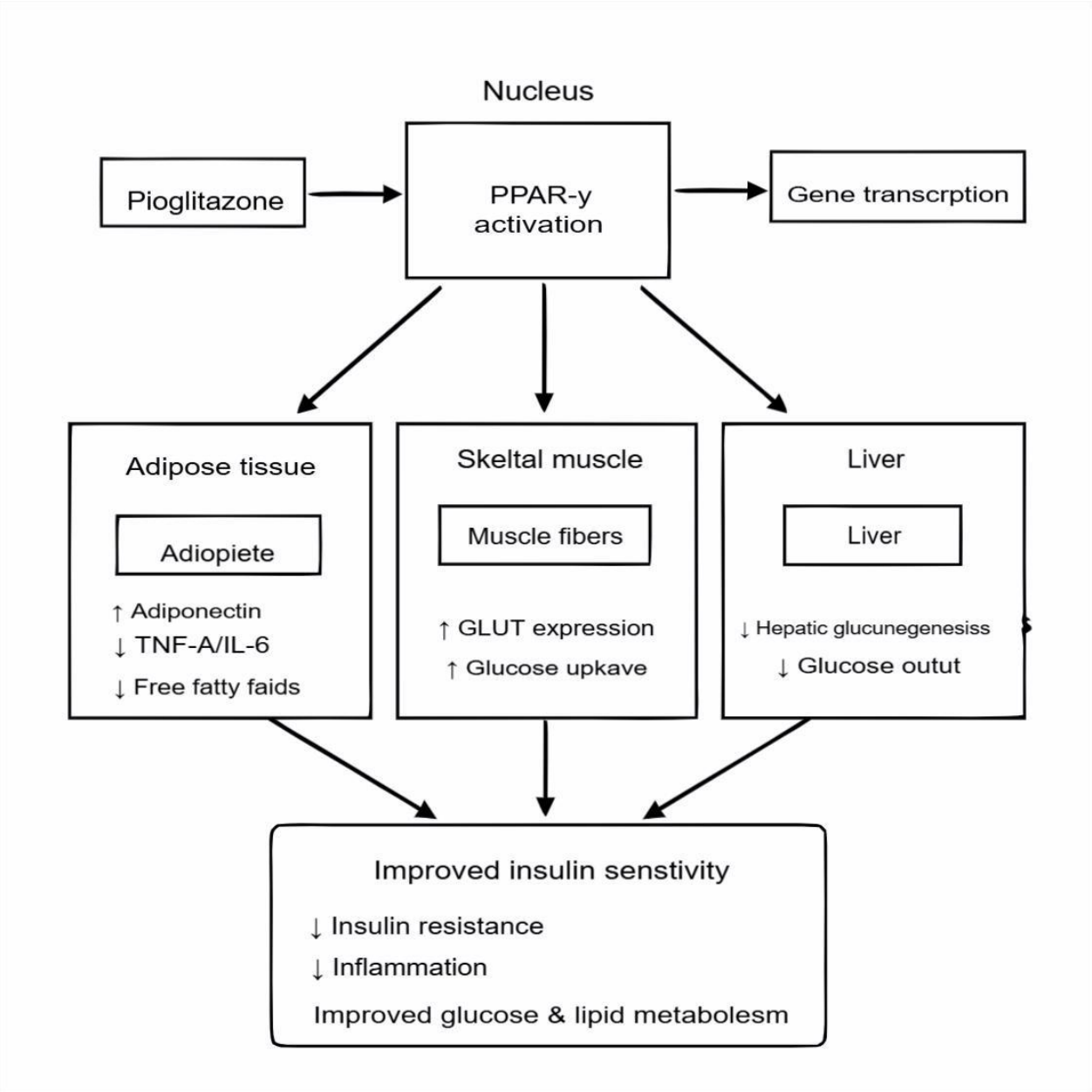

Figure 1: Mechanism of action of pioglitazone via PPAR-γ activation in insulin-sensitive tissues [33]

6. Role of Pioglitazone in Metabolic Syndrome Components

Pioglitazone is important in the overall management of metabolic syndrome as it combines several metabolic defects treatment through insulin sensitization and pleiotropic effects. Its outcomes are not just limited to glycemic regulation, but also improvements in lipid metabolism, inflammation and vascular, thus, solving the multifactorial nature of metabolic syndrome [34].

6.1 Glycemic Control

Pioglitazone is an improvement that lowers glycemic regulation through the amplification of the insulin sensitivity of the peripheral tissues and the reduction of the glucose production in the hepatic production. It increases the insulin-dependent uptake of glucose in the skeletal muscle and adipose tissue and suppresses the gluconeogenesis in the liver through the stimulation of PPAR- 0. These interventions cause significant reductions in the degree of fasting plasma glucose and glycated hemoglobin (HbA1c) without raising the risk of developing hypoglycemia on monotherapy. The increased 3-cell activity and reduced insulin dose also help to support a normal glycemic control [35].

6.2 Lipid Profile Improvement

In addition to possessing a glucose-lowering effect, the pioglitazone has positive effects in lipid metabolism. It reduces the triglyceride levels in circulation and increases the high-density lipoprotein cholesterol which is advantageous to the lipid profile as a whole. Pioglitazone also interferes with the quality of the low-density lipoprotein particles by lowering the percentage of small dense LDL particles which are highly atherogenic. Such lipid modifying actions help to get rid of cardiovascular risk factors that accompany metabolic syndrome [36].

6.3 Anti-inflammatory and Anti-atherogenic Effects

The metabolic syndrome is characterized by chronic low-grade inflammation. Pioglitazone suppresses the systemic inflammation through lowering pro-inflammatory cytokines like tumor necrosis factor-alpha, interleukin-6 and elevating the level of adiponectin. These anti-inflammatory effects are converted into anti-atherogenic effects, such as a decrease in the activation of macrophages, the stability of the plaque, and the inhibition of the atherosclerotic progression [37].

6.4 Impact on Blood Pressure and Endothelial Function

Pioglitazone has small yet clinically significant impacts on blood pressure, which is mainly mediated by the enhancement of insulin sensitivity and decreased vascular inflammation. It improves endothelial activity by augmenting the bioavailability of nitric oxide and lowering oxidative stress resulting in elevated vascular compliance. The net effect of these is an increase in cardiovascular outcomes in patients with metabolic syndrome [38].

7. Clinical Evidence Supporting Pioglitazone Use

Extensive clinical evidence supports the therapeutic role of pioglitazone in improving insulin resistance and multiple metabolic abnormalities associated with metabolic syndrome. Its efficacy has been evaluated through several large-scale clinical trials and long-term outcome studies, highlighting both metabolic and cardiovascular benefits [39].

Major Clinical Trials

Several randomized controlled trials have proved the efficacy of pioglitazone to patients with insulin resistance, metabolic syndrome and type 2 diabetes mellitus. The studies by Landmark have demonstrated that pioglitazone was found to have significant improvement on insulin sensitivity and glycemic parameters as a monotherapy or combination with other antidiabetic agents. These studies have always shown long-term metabolic advantage to long-term treatment which is evidence of disease-modifying, not short-term glycemic control [40].

Effects on HbA1c, Insulin Resistance Indices, and Lipid Parameters

Clinical evidence indicates that the use of pioglitazone leads to substantial decreases in the level of glycated hemoglobin (HbA1c), which indicates that the drug levels to better glycemic control. There is a consistent improvement in insulin resistance indices including the homeostatic model assessment of insulin resistance (HOMA-IR) which is a sign of increased peripheral insulin sensitivity. Besides the glycemic effect, lipid parameters are also positively changed by pioglitazone by decreasing triglycerides, increasing high-density lipoprotein cholesterol, and changing low-density lipoprotein particles to a less atherogenic type. All these together leads to enhanced cardiometabolic health [41].

Long-Term Cardiovascular Outcomes

The clinical outcome studies conducted over long-term periods indicate that the use of pioglitazone can lower the odds of major adverse cardiovascular events in patient groups. It is protective on the heart because of improvements in endothelial functionality, decreased inflammation, and positive lipid regulation. Although appropriate selection of patients is crucial because of the safety factors, there is evidence of the potential of the agent pioglitazone to enhance long-term cardiovascular outcomes in patients with metabolic syndrome and severe insulin resistance [42].

Table 3: Clinical Effects of Pioglitazone in Metabolic Syndrome [43]

Sr. No.	Clinical Parameter	Observed Effect
1	Insulin sensitivity	Significant improvement in peripheral insulin responsiveness
2	Fasting plasma glucose	Reduction in fasting glucose levels
3	HbA1c	Decrease indicating improved long-term glycemic control
4	Insulin resistance index (HOMA-IR)	Marked reduction
5	Triglycerides	Decreased plasma triglyceride levels
6	HDL cholesterol	Increase in cardioprotective HDL levels

Sr. No.	Clinical Parameter	Observed Effect
7	LDL particle size	Shift toward less atherogenic LDL particles
8	Adiponectin levels	Significant increase
9	Inflammatory markers	Reduction in TNF-α, IL-6, and CRP
10	Endothelial function	Improvement in vascular reactivity
11	Blood pressure	Modest reduction in systolic and diastolic pressure
12	Cardiovascular risk	Overall reduction in atherogenic and metabolic risk

8. Safety Profile and Adverse Effects

Although pioglitazone is promising in terms of metabolic and cardiovascular benefits to the treatment of metabolic syndrome, its clinical application is surrounded with various safety issues which require close patient selection and observation.

Weight gain is one of the most frequent side effects of the treatment with pioglitazone that are most likely explained by the augmentation of adipose tissue differentiation and fluid retention. PPAR-g activation facilitates fat deposition in subcutaneous depots, whereas reabsorption of sodium in the kidney helps to increase fluid volume. This gain in weight is usually small, which might be unacceptable in an obesity-dominant metabolic syndrome patient [44].

The peripheral edema and aggravation or triggering heart failure can be computed by the fluid retention linked with the usage of pioglitazone, especially in the patients with the existing heart malfunction. Consequently, it is recommended that pioglitazone should not be used in people with severe heart failure and it should be administered with care through the insulin treatment in patients with impaired heart functions [45].

Long-term use of pioglitazone has also been reported to have an increased risk of bone fractures especially in postmenopausal women. Such effect is thought to be caused by an abnormal bone metabolism such as reduced osteoblast activity and increased bone resorption which causes bone mineral density to be reduced [46].

Hepatic safety is also a factor of concern since the pioglitazone is highly metabolized in the hepatic region. Even though severe hepatotoxicity is not common, regular monitoring of liver element tests is advised particularly when using the medication in long-term conditions or in those with existing liver illness [47].

In general, the risk-benefit analysis of pioglitazone in metabolic syndrome needs to be tailored. Metabolic advantages could exceed the possible harm in patients with the high level of insulin resistance and the low risk of cardiovascular diseases, and individualized decisions regarding the therapeutic choices are to be considered [48].

9. Combination Therapy and Future Perspectives

Metabolic syndrome is complex and multifactorial requiring a multidimensional approach in therapy and in most cases combination therapy is necessary to effectively address insulin resistance, hyperglycemia, dyslipidemia, and cardiovascular risk factors. Pioglitazone presents an insulin-sensitizing, pleiotropic metabolic action that is beneficial to combination regimens with a goal of comprehensive metabolic management [49].

Pioglitazone-metformin combination is a common practice that is therapeutically logical because both drugs complement each other, enhancing insulin sensitivity. Whereas metformin lowers the amount of glucose produced in the liver and optimizes peripheral glucose uptake, pioglitazone increases the insulin action at the transcriptional level and produces complementary effect on glycemic and metabolic control [50]. On the same note, co-administration of pioglitazone with glucagon-like peptide-1 (GLP-1) receptor agonists has synergistic benefits of enhancing insulin sensitivity and reducing weight and decreasing appetite, which is a counterpoint to the adverse effects of weight gain of using pioglitazone. The inclusion of sodium- glucose cotransporter-2 (SGLT-2) inhibitors also increases the metabolic outcomes via the promotion of urinary excretion of glucose, cardiovascular outcomes, and fluid retention [51].

Individualized treatment is coming out as an established pillar in the management of metabolic syndrome. Therapeutic choice should rely on patient-specific variables including levels of insulin resistance, cardiovascular risk, obesity profile, and comorbid conditions. Pioglitazone, in this case, can be especially helpful in those patients with significant insulin resistance and minimal risk of heart failure [52].

The future observations are that there will be the creation of better formulations with better safety profiles and the consideration of new selective PPAR modulators that will have insulin sensitizing effects with minimal adverse effects. Such developments can widen therapeutic effects of the pioglitazone-based interventions in the management of metabolic syndrome [53].

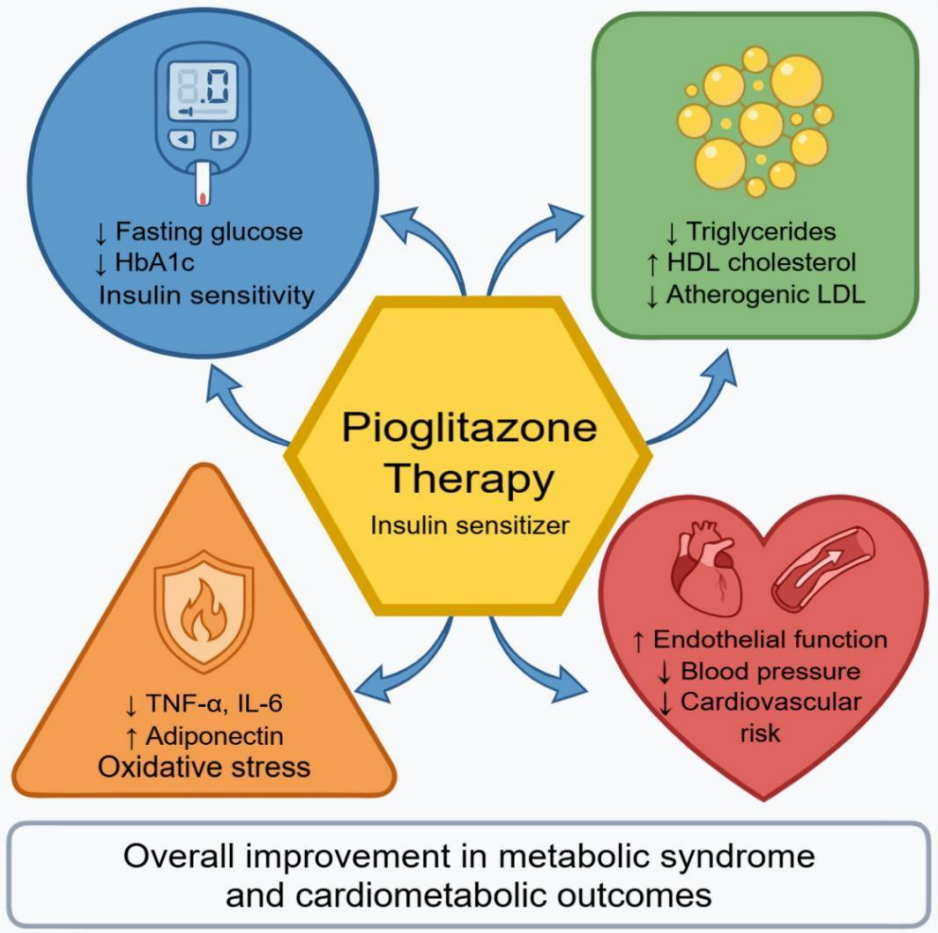

Figure 2: Role of pioglitazone in improving metabolic syndrome components [54]

10. Conclusion

Pioglitazone represents a well-established insulin-sensitizing agent with significant therapeutic potential in the management of metabolic syndrome. By targeting insulin resistance—the central pathological mechanism of metabolic syndrome—pioglitazone provides multifaceted metabolic benefits that extend beyond glycemic control. Its ability to enhance insulin sensitivity, improve glucose utilization, favorably modify lipid profiles, and reduce chronic inflammation underscores its role as a disease-modifying therapy.

The clinical relevance of pioglitazone in metabolic syndrome lies in its capacity to simultaneously address multiple components of the disorder, including hyperglycemia, dyslipidemia, inflammatory burden, and endothelial dysfunction. These combined effects contribute to improved cardiometabolic outcomes and position pioglitazone as a valuable therapeutic option, particularly in patients with pronounced insulin resistance and high metabolic risk.

However, the use of pioglitazone requires cautious patient selection due to associated adverse effects such as weight gain, fluid retention, increased risk of heart failure, and bone fractures. Careful assessment of individual patient characteristics, comorbid conditions, and cardiovascular risk is essential to maximize therapeutic benefits while minimizing potential harms. Regular monitoring and judicious dose optimization further enhance its safe clinical application.

Future research should focus on long-term outcome studies to better define cardiovascular benefits and risks across diverse patient populations. Additionally, the development of novel PPAR modulators with improved safety profiles, optimized combination therapies, and personalized treatment strategies holds promise for expanding the clinical utility of pioglitazone. Such advancements may enable more effective and safer management of metabolic syndrome in the evolving landscape of cardiometabolic care.

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Conflict of Interest: Nil

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