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Study on Atorvastatin Calcium and Its Marketed Product

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Abstract. When combined with a healthy diet, atorvastatin may reduce "bad" cholesterol and fats (such LDL and triglycerides) while increasing "good" cholesterol levels (HDL). It is a statin, one of a class of medications used to lower cholesterol. Exercising, decreasing excess weight, and giving up smoking may all improve the effectiveness of this medicine. In the pharmaceutical treatment of hyperlipidaemia, low-density lipoprotein (LDL-C) is the major lipid component being addressed. Among statins, Atorvastatin looks to be the most effective in lowering triglyceride levels. In addition, it raises HDL-C levels by around 5-15 percent. The underlying mechanism has not been determined. To lower cholesterol, low-density lipoprotein cholesterol, and triglycerides in people with hypercholesterolemia, atorvastatin is superior to other HMG-CoA reductase inhibitors. To verify its superiority over existing statins used for hyperlipidaemia therapy, however, post-marketing monitoring for this newly introduced drug is required.

Keywords: Atorvastatin calcium, Triglyceride, Hyperlipidaemia, Hypercholesterolaemia

INTRODUCTION:

With the help of a healthy diet, atorvastatin may be used to raise "good" cholesterol (HDL) levels while lowering "bad" cholesterol and fats (including LDL and triglycerides) in the blood [1]. In the medical world, this drug is classified with the "statins." The liver's cholesterol production is lowered, which is the mechanism of action[2]. The risk of cardiovascular disease and stroke may be mitigated by increasing good cholesterol while decreasing bad cholesterol and triglycerides. In addition to eating a healthy diet (such as a low-cholesterol/low-fat diet), other lifestyle adjustments may improve the effectiveness of this medication. Consult your physician for additional details[3].

1. Chemistry and pharmacology

Synthetic atorvastatin calcium is the stereoisomer of a pentasubstituted pyrrole. Atrastatin, unlike the prodrugs lovastatin and simvastatin that came before it, is an active compound after it has been metabolised. Statins work by competitively inhibiting the enzyme HMG-CoA reductase in the liver, which converts HMG-CoA into mevalonic acid, a precursor to cholesterol[4]. In animal studies, statins were shown to reduce cholesterol availability, leading to increased LDL-receptor expression in the liver. These LDL receptors encourage the absorption and subsequent removal of low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and intermediate-density lipoprotein (IDL), therefore maintaining lipid homeostasis[5].

Hyperlipidaemia is often treated with drugs that lower LDL-C levels. Excessive triglyceride levels may also cause atherosclerosis. It seems that atorvastatin reduces triglyceride levels more so than other statins. Atorvastatin's ability to reduce triglycerides is thought to occur through two different mechanisms. The primary method for lowering triglyceride levels has improved. Atorvastatin raises LDL-receptor expression, which promotes the uptake of VLDL and LDL particles[6]. The VLDL particles (which contain both apoB and apo E) may be more able to bind to these LDL receptors than the LDL particles (which only carry apoB). The second way in which atorvastatin works is by reducing triglyceride production. The decline is due to less cholesterol being manufactured[7]. To form, VLDL particles need cholesterol. Lower triglyceride levels are a direct outcome of decreased secretion and VLDL particle formation. Reducing triglyceride levels to normal might take as little as four weeks or as long as more than six months. In addition, atorvastatin increases high-density lipoprotein cholesterol

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(HDL-C) levels by around 5 to 15%. However, the precise mechanism remains unknown[8].

There have been a number of atorvastatin comparison studies published in the previous four years. In a clinical study, it was shown that atorvastatin boosted HDL-C by 12% regardless of dosage and reduced LDL-C by 90% compared to placebo in the first two weeks of treatment[9]. After 52 weeks of therapy, atorvastatin produces bigger changes in all lipid fractions outside HDL-C than lovastatin does. Atorvastatin reduces triglyceride, TC, LDL-C, and apoB levels more than simvastatin does after 16 and 52 weeks of therapy. According to the same studies, simvastatin increases HDL-C and apoA-I more than atorvastatin does. Consequently, the metabolic effects on plasma lipids and lipoproteins of these two statins are dissimilar[10]. A lower dose of atorvastatin was significantly more effective than pravastatin in reducing TC, LDL-C, and triglycerides in patients who had had heart transplantation. It was determined that the safety and tolerability profiles of these two medicines were comparable. Simvastatin (10 mg), lovastatin (20 mg & 40 mg), pravastatin (20 mg), and fluvastatin (40 mg) all significantly decreased LDL-C in the curves trial, which also compared atorvastatin to four other statins (20 mg & 40 mg)[11]. Atorvastatin's 20 mg dose substantially lowered LDL-C, but simvastatin's 20 mg and 40 mg doses did not (40 mg)[12].

Nitrous oxide production was shown to be elevated when using atorvastatin. It was shown to decrease vascular smooth muscle cell proliferation and atherosclerotic lesion size in an in-vitro model. Based on these findings, it is plausible that atorvastatin might aid dyslipidemic patients by facilitating platelet deaggregation and vasodilation[13].

2. Pharmacokinetics

Taken orally, atorvastatin is rapidly absorbed, with peak plasma levels occurring within 2.5 hours. Atorvastatin's absorption is dose-dependent and non-linear. Because of extensive first-pass metabolism, atorvastatin's bioavailability is only around 12% and is seldom affected by food. About 70% of the circulating HMG-CoA reductase inhibitory activity is a result of its widespread metabolism by cytochrome P4503A4 to active metabolites. About 98% of it is linked to proteins in the blood. Atorvastatin and its metabolites are mostly excreted in the bile after undergoing hepatic and/or extrahepatic metabolism; however, there does not seem to be any enterohepatic recirculation of the drug. While the elimination half-life in plasma is only around 14 hours on average, the half-life of the HMG-CoA reductase inhibitory action is more like 24 hours due to the presence of active metabolites[14].

3. Adverse effects

Atorvastatin has a good safety profile, with most side effects being minor and short-lived. Constipation, flatulence, dyspepsia, and stomach discomfort are common side effects. Also noted are headaches, rashes, and trouble sleeping. Abnormal liver function results have been reported in people on atorvastatin and other HMG-CoA reductase inhibitors. Up to 0.7% of individuals using atorvastatin have had persistent increases (>3 times upper limit of normal value) in blood transaminases. As a result, it is advised to check liver function before to starting treatment, after 6 and 12 weeks of medication, and whenever a dosage increase is made. Patients receiving prolonged treatment should have their liver function checked on a semiannual basis. Patients with elevated transaminase levels need close observation until the anomalies normalize [15].

Myoglobinuric rhabdomyolysis has been described with other medications in this family, but not with atorvastatin. A few people using atorvastatin have reported experiencing mild muscle pain. If myopathy is diagnosed or is suspected, or if CPK levels become abnormally high while using atorvastatin, the drug should be stopped. HMG-CoA reductase inhibitors like atorvastatin are not recommended for use during pregnancy or during breastfeeding, despite the fact that it has not been shown to cause teratogenicity in animal trials[16].

4. Drug interactions

A combination of atorvastatin plus erythromycin, azole antifungals (such as ketoconazole or fluconazole), cyclosporine, gemfibrozil, or niacin may increase serum concentrations of atorvastatin and the risk of myopathy. In addition, the usage of atorvastatin with digoxin may lead to elevated blood concentrations of the latter. The pharmacokinetics of pravastatin were unaffected by grapefruit juice, whereas the bioavailability of atorvastatin, lovastatin, and simvastatin were all shown to be increased. The reduction in CYP3A4-mediated first-pass metabolism of atorvastatin in the gut is likely to blame [17].

5. Dosage of atorvastatin

The most common dosages of atorvastatin are 10 and 20 milligrammes, and they come in white, film-coated tablets. Atovastatin calcium dose ranges from 10 to 80 mg daily, with 10 mg being the recommended starting point. Depending on the patient's risk status, the dose might be increased by 100% every four weeks in order to achieve the desired degree of lipid reduction[18].

6. How to use Atorvastatin calcium

Before starting on atorvastatin and at each refill, ask your doctor or pharmacist for the product's Patient Information Leaflet. Consult your physician or pharmacist if you have any concerns[19].

Unless otherwise ordered by your doctor, this drug should be taken orally once day, either with or without meals[20].

Dosage considerations include your current health status, how well you're responding to therapy, your age, and any other drugs you're taking. Tell your doctor and pharmacist what you're taking (including prescription drugs, nonprescription drugs, and herbal products)[21].

Unless your doctor tells you differently, you should not consume grapefruit or grapefruit juice while taking this medicine. The blood concentration of this drug may rise if you consume grapefruit with it. Please see your healthcare provider or pharmacist for more information[22].

It's recommended to take atorvastatin at least 1 hour before or 4 hours after taking bile acid-binding resins like cholestyramine or colestipol, which are also used to decrease cholesterol. Atorvastatin absorption may be reduced due to interactions with certain products[23].

Make sure to take this medicine on a consistent basis so you can get the full benefits. Take it regularly and at the same time each day. Do not stop using this drug even if you feel OK. When it comes to elevated cholesterol or triglycerides, most patients report no symptoms[24].

It's crucial that you keep up with your doctor's recommendations for a healthy diet and regular exercise. Full effectiveness from this medication may not be seen for up to 4 weeks[25].

Table 1: Marketed preparation of Atorvastatin calcium

S. no.	Brand name	Composition	Marketed by
1	Satvastin 20	Atorvastatin calcium 20mg	Saturn formulation Pvt Ltd
2	Toralip10 AC	Atorvastatin 10 mg + Aspirin 75mg + Clopidrogel 75 mg	Archicare Limited
3	Storvas 10	Atorvastatin calcium 10mg	Ranbaxy
4	Tinorvas 10	Atorvastatin calcium 10mg	Vitabiotech Healthcare Private Limited
5	Lipnor 10	Atorvastatin calcium 10mg	Pharma Solution
6	Nutova 10	Atorvastatin calcium 10mg	Biophar Lifesciences Private Limited
7	Atofin 10	Atorvastatin calcium 10mg	Pacific Pharmaceuticals
8	Ramitorva	Aspirin-75mg + Atorvastatin-10mg + Ramipril-5mg	Zydus cardiva
9	Peditor AS	Atorvastatin 10 mg + Aspirin 75 mg	Pedicon Pharmaceuticals
10	Ecosprin-AV	Atorvastatin 10 mg + Aspirin 75 mg	Care Exim

CONCLUSION

In those who have hypercholesterolemia, the effectiveness of atorvastatin in lowering total cholesterol, low-density lipoprotein cholesterol, and triglycerides is greater to that of other HMG-CoA reductase inhibitors. However, in order to determine whether or not this recently introduced medication is more effective than the statins that are currently being used for the treatment of hyperlipidemia, post-marketing monitoring is required to be carried out on the product.

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REFERENCES:

[1]. Nouh F, Omar M, Younis M. Risk factors and management of hyperlipidemia. Asian Journal of Cardiology Research. 2019;2(1):1-0.

[2]. Nwodo NJ, Nnadi CO, Ibezim A, Mbah CJ. Plants with hypolipidaemic effects from Nigeria flora. Antioxidant-Antidiabetic Agents and Human Health. 2014 Feb 5:242-55.

[3]. Diamond DM, Bikman BT, Mason P. Statin therapy is not warranted for a person with high LDL-cholesterol on a low-carbohydrate diet. Current Opinion in Endocrinology & Diabetes and Obesity. 2022 Oct 1;29(5):497-511.

[4]. Arrastia I, Arrieta A, Cossío FP. Application of 1, 3- Dipolar Reactions between Azomethine Ylides and Alkenes to the Synthesis of Catalysts and Biologically Active Compounds. European Journal of Organic Chemistry. 2018 Nov 25;2018(43):5889-904.

[5]. Roy D, Sarkar S, Laha RM, Pramanik N, Maiti DK. Ni (0)–Cu (I): a powerful combo catalyst for simultaneous coupling and cleavage of the C–N bond with cyclization to valuable amide-based pyrroles and 4-pyridones. RSC advances. 2015 Aug 28;5(90):73346-51.

[6]. Su L, Mittal R, Ramgobin D, Jain R, Jain R. Current management guidelines on hyperlipidemia: the silent killer. Journal of lipids. 2021 Oct;2021.

[7]. Hirano T. Pathophysiology of diabetic dyslipidemia. Journal of atherosclerosis and thrombosis. 2018 Sep 1;25(9):771-82.

[8]. Felmlee DJ, Hafirassou ML, Lefevre M, Baumert TF, Schuster C. Hepatitis C virus, cholesterol and lipoproteins—impact for the viral life cycle and pathogenesis of liver disease. Viruses. 2013 May;5(5):1292-324.

[9]. Kunutsor SK, Seidu S, Khunti K. Statins and primary prevention of venous thromboembolism: a systematic review and meta-analysis. The Lancet Haematology. 2017 Feb 1;4(2):e83-93.

[10]. Armitage J, Baigent C, Barnes E, Betteridge DJ, Blackwell L, Blazing M, Bowman L, Braunwald E, Byington R, Cannon C, Clearfield M. Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials. The Lancet. 2019 Feb 2;393(10170):407-15.

[11]. Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, Tonstad S, Wiegman A, Drogari E, Ramaswami U. Statins for children with familial hypercholesterolemia. Cochrane Database of Systematic Reviews. 2017(7).

[12]. Gupta A, Mackay J, Whitehouse A, Godec T, Collier T, Pocock S, Poulter N, Sever P. Long-term mortality after blood pressure-lowering and lipid-lowering treatment in patients with hypertension in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Legacy study: 16-year follow-up results of a randomised factorial trial. The Lancet. 2018 Sep 29;392(10153):1127-37.

[13]. Tousoulis D, Kampoli AM, Tentolouris Nikolaos Papageorgiou C, Stefanadis C. The role of nitric oxide on endothelial function. Current vascular pharmacology. 2012 Jan 1;10(1):4-18.

[14]. Liu X. Transporter-mediated drug-drug interactions and their significance. Drug Transporters in Drug Disposition, Effects and Toxicity. 2019:241-91.

[15]. Omolaoye TS, Halabi MO, Mubarak M, Cyril AC, Duvuru R, Radhakrishnan R, Du Plessis SS. Statins and Male Fertility: Is There a Cause for Concern?. Toxics. 2022 Oct 20;10(10):627.

[16]. Mollazadeh H, Tavana E, Fanni G, Bo S, Banach M, Pirro M, Von Haehling S, Jamialahmadi T, Sahebkar A. Effects of statins on mitochondrial pathways. Journal of Cachexia, Sarcopenia and Muscle. 2021 Apr;12(2):237-51.

[17]. Moßhammer D, Schaeffeler E, Schwab M, Mörike K. Mechanisms and assessment of statin- related muscular adverse effects. British journal of clinical pharmacology. 2014 Sep;78(3):454-66.

[18]. Awad K, Mikhailidis DP, Toth PP, Jones SR, Moriarty P, Lip GY, Muntner P, Catapano AL, Pencina MJ, Rosenson RS, Rysz J. Efficacy and safety of alternate-day versus daily dosing of statins: a systematic review and meta-analysis. Cardiovascular Drugs and Therapy. 2017 Aug;31:419-31.

[19]. Ali N, Begum R, Faisal MS, Khan A, Nabi M, Shehzadi G, Ullah S, Ali W. Current statins show calcium channel blocking activity through voltage gated channels. BMC Pharmacology and Toxicology. 2016 Dec;17:1-7.

[20]. Hourihane JO, Beyer K, Abbas A, Fernández-Rivas M, Turner PJ, Blumchen K, Nilsson C, Ibáñez MD, Deschildre A, Muraro A, Sharma V. Efficacy and safety of oral immunotherapy with AR101 in European children with a peanut allergy (ARTEMIS): a multicentre, double-blind, randomised, placebo-controlled phase 3 trial. The Lancet Child & Adolescent Health. 2020 Oct 1;4(10):728-39.

[21]. Frank D, Mateu-Gelabert P, Perlman DC, Walters SM, Curran L, Guarino H. ―It's like ‗liquid handcuffs‖: The effects of take-home dosing policies on Methadone Maintenance Treatment (MMT) patients' lives. Harm Reduction Journal. 2021 Dec;18(1):1-0.

[22]. Chorin E, Hochstadt A, Granot Y, Khoury S, Schwartz AL, Margolis G, Barashi R, Viskin D, Ghantous E, Schnapper M, Mekori T. Grapefruit juice prolongs the QT interval of healthy volunteers and patients with long QT syndrome. Heart Rhythm. 2019 Aug 1;16(8):1141-8.

[23]. Zema MJ. Colesevelam hydrochloride: evidence for its use in the treatment of hypercholesterolemia and type 2 diabetes mellitus with insights into mechanism of action. Core evidence. 2012;7:61.

[24]. Weston PS, Smith CA. The use of mini-CEX in UK foundation training six years following its introduction: lessons still to be learned and the benefit of formal teaching regarding its utility. Medical Teacher. 2014 Feb 1;36(2):155-63.

[25]. You A. Dietary guidelines for Americans. US Department of Health and Human Services and US Department of Agriculture. 2015;7.