Original Research

Role of Atorvastatin in suppressing tumor growth of Uterine Fibroids

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ABSTRACT

Aim: The purpose of this study is effect and role of Atorvastatin in suppressing Tumor growth of Uterine Fibroids , Endometrium Thickness and Clinical symptoms of patient .

Methods

Initially, We conducted a retrospective study of 100patients with uterine fibroids . Then, we evaluated the effect of atorvastatin on proliferation and apoptosis both in immortalized uterine fibroids cells and primary uterine fibroids cells. Furthermore, the molecular mechanism by which atorvastatin suppressed uterine fibroids cell growth was explored.

Results: Our results showed that atorvastatin use for 1 years significantly suppressed growth of uterine fibroids. Uterine fibroid demonstrated significant reduction in size as well as significant changes following the atorvastatin treatment after 6 months in a dose dependent manner, while endometrial thickness demonstrated insignificant differences as measured by transvaginal ultrasound (TVS). Atorvastatin inhibited the proliferation of immortalized and primary uterine fibroids cells in a dose and time-dependent manner and stimulated apoptosis of uterine fibroids

Conclusions: The current study demonstrated that atorvastatin exerts anti-tumoral effects on uterine fibroids and has promising effects in cases with uterine fibroids as it was associated with a reduction of fibroid size Our results provide the first clinical and preclinical data on the use of atorvastatin as a promising nonsurgical treatment option for uterine fibroids.According to the present study there is also in reduction in clinical symptoms of patient as well as effective on reduction of endometrium thickness

Keywords: Gynaecological, Malignancy, non-Hodgkin's lymphoma

INTRODUCTION

The incidence of uterine fibroid tumors increases as women grow older, and they may occur in more than 30 percent of women 40 to 60 years of age. Risk factors include nulliparity, obesity, family history, black race, and hypertension. Many tumors are asymptomatic and may be diagnosed incidentally.[1,2]Although a causal relationship has not been established, fibroid tumors are associated with menorrhagia, pelvic pain, pelvic or urinary obstructive symptoms, infertility, and pregnancy loss. Transvaginal ultrasonography, magnetic resonance imaging, sonohysterography, and hysteroscopy are available to evaluate the size and position of tumors.[3] Ultrasonography should be used initially because it is the least invasive and most cost-effective investigation. Treatment options include hysterectomy, myomectomy, uterine artery embolization, myolysis, and medical therapy. Treatment must be individualized based on such considerations as the presence and severity of symptoms, the patient's desire for definitive treatment, the desire to preserve childbearing capacity, the importance of uterine preservation, infertility related to uterine cavity distortions, and previous pregnancy complications related to fibroid tumors.[3, 4]

Women often consult family physicians because of symptoms related to fibroid tumors or after the lesions have been diagnosed incidentally during physical or radiologic examinations. This article reviews the epidemiology and etiology of uterine fibroid tumors, common clinical presentations, diagnostic strategies, and treatment options . [5]

Several approaches are available for the treatment of uterine fibroids. These include pharmacologic options, such as hormonal therapies and gonadotropin-releasing hormone agonists; surgical approaches, such as hysterectomy, myomectomy, myolysis, laparoscopic uterine artery occlusion, magnetic resonance imaging-guided focused ultrasound surgery, and uterine artery embolization.[6,7] New treatment options for uterine fibroids would be minimally invasive, have long-term data demonstrating efficacy and safety, have minimal or no incidence of fibroid recurrence, be easy to perform, preserve fertility, and be cost effective. New treatment approaches are under investigation, with the goals of being effective, safe, and less invasive[8,9]Therefore, it is of great clinical value to develop new treatment strategy for uterine fibroids. Statins are a drug family primarily used for hyperlipidemia. By inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, statins prevent the conversion of HMG-CoA to mevalonate, and thus lead to dramatic reductions in both cholesterol and its isoprenoid precursors; farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP) .[9,10]Therefore, in the present study, we proceeded to investigate therapeutic effects of atorvastatin on uterine fibroids. The aim of the current study was to evaluate the effect of atorvastatin on decreasing fibroid related symptoms and fibroid size, endometrial thickness. [1,10]

PATIENTS AND METHODS

Prospective randomized controlled trial was conducted over a period of 1 year between 2022and 2023 on 100patients admitted to emergency unit and gynaecology department .

Inclusion criteria: Age range 40–50 years old,diagnosed as symptomatized uterine fibroid, and completing her family.

Exclusion criteria: Hypersensitivity to atorvastatin, taking any medication that affects uterine fibroid within last 6 months, using any hormonal contraception, and association with any medical disorder, e.g. liver disease, renal disease, and thyroid disorder or muscle weakness.

Sample Size calculation:

- The calculated sample size of the study was 50 participants for each group at 6% level of significance and 60% power.
- Entire cases were included following steps
- Full History taking- Personal history, menstrual history, obstetric history, past history, family history.
- Presenting symptoms- which included menorrhagia and dysmenorrhea.
- Physical examination- which included general and abdominal examinations.
- Transabdominal US (TAS): determined type and size of uterine fibroid.
- TVS: determined type and size of uterine fibroid
- Size of uterine fibroid both before and after atorvastatin treatment.
- The length (d1), width (d2) and depth (d3) of each tumor were measured, and the volumes were calculated by the following formula: volume (cm3) = 0.52× d1 × d2 × d3 5.
- Laboratory investigation - CBC, Cholesterol level, Liver function test, Kidney function test, Thyroid profile. Thereafter: A total of 100 patients were prospectively recruited and received the parcel of medicine as described below :
  - Group A: receiving atorvastatin 20 mg for 6 months.
  - Group B: receiving atorvastatin 40 mg for 6 months.

Follow up: Patients were re-examined after 3 months and 6 months for evaluation and we examine the clinical evaluation of symptoms,US : TAS and TVS for follow up of fibroid size , symptoms regarding pain and bleeding before and after administration of drug and last cholesterol level . Initial evaluation was done Before administration of drug And Follow up evaluation is done after 3 months of administration of drugAnd final evaluationafter completing administration of drug. The protocols were compared regarding the overall response rate i.e., fibroid size and fibroid related symptom.

The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test. Continuous variables were presented as mean ± SD (standard deviation) for normally distributed data and median (min-max) for non-normal data. Quantitative data were compared by ANOVA test when normally distributed or by KruskalWallis test when abnormally distributed, and when the difference was significant; post hoc test was used for multiple comparison. The results was considered significant when $p \leq 0.05$.

RESULTS

Table: 1 shows Distribution of patient according to study group

GROUP	N
GROUP I - (RECEVING ATROVASTATIN 20 MG FOR 6 MONTHS)	50
GROUP II - (RECEVING ATROVASTATIN 40 MG FOR 6 MONTHS)	50

Present Study was Conducted including 100 patient with Uterine Fibroid between the age group of 40 – 50 year old , divided in to two major group . group I was receiving atorvastatin 20 mg for 6 months and group II is receiving atorvastatin 40 mg for 6 months .

Table (2): Size of uterine fibroidand Endometrial thickness after receiving Atorvastatin at presentation and after 3 month and 6 month as measured by TVS in the studied group

TVS	GROUP I (n=50)	GROUP II (n=50)	P value	P 1
Size at presentation	4.62± 1.22	4.60± 1.02	P=0.825	-
Size after 3 months	4.12± 1.22	4.12± 1.02	P=0.77	-
Size after 6 months	4.05±0.62	3.45±0.36	P<0.001	P<0.001
Endometrial thickness	6.72±2.42	6.31±2.80	P=0.779	-

Data are expressed as mean and standard deviation or as percentage and frequency. P1: Group A vs group B

DISCUSSION

The present study included 100 patient randomized into 2 groups: (group I: receiving atorvastatin 20 mg for 6 month), (group B: receiving atorvastatin 40 mg for 6 month) . The present study found that the uterine fibroid size by TVS At the time of presentation and also after 3 months of treatment, there was no statistically significant difference between two groups. statistically, there is significant difference after 6 months and the size decreased by 15.8% in group A and 26.8% in group B and there was statistically significant difference between group A and group B in reduction of size with increased dose of atorvastatin. Additionally, there was no statistically significant difference between two groups as regard endometrial thickness.

CONCLUSIONS

The current study demonstrated that atorvastatin exerts anti-tumoral effects on uterine fibroids and has promising effects in cases with uterine fibroids as it was associated with a reduction of fibroid size Our results provide the first clinical and preclinical data on the use of atorvastatin as a promising nonsurgical treatment option for uterine fibroids. According to the present study there is also in reduction in clinical symptoms of patient as well as effective on reduction of endometrium thickness .

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