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RESEARCH ARTICLE

AN OBSERVATIONAL STUDY OF EFFECT ON LIPID PROFILE BY SHORT TERM USE OF LOW DOSE STEROID THERAPY IN COMMON ORTHOPAEDIC CONDITIONS

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Abstract

Introduction: Corticosteroids, potent anti-inflammatory drugs used for decades, provide symptomatic relief but carry risks like infection and chronic conditions. Despite complications, they're prescribed for orthopedic issues. Glucocorticoids influence lipid levels, with conflicting effects. Steroids are termed a 'double-edged sword.' This study aims to assess lipid profile effects of short-term, low-dose steroid therapy in Orthopedics and Rheumatology, evaluating glucocorticoid therapy impact and investigating other effects on musculoskeletal patients.

Materials and Methods: This prospective, non-randomized observational study was conducted, focusing on patients with orthopedic and rheumatological issues. Over 150 patients were included, selected through convenient sampling. Inclusion criteria involved patients aged 18-65 without dyslipidemia or cardiovascular conditions, while exclusion criteria included those with specific medical conditions or high BMI. Patients provided written informed consent before undergoing blood tests for lipid profile and blood sugar levels, with vital signs measured. They received Medrol 4 mg thrice daily for ten days, after which outcomes including lipid levels, blood sugar, and blood pressure were assessed.

Results: At baseline, 88.67% had desirable cholesterol levels and 11.33% had borderline levels. At follow-up, 20.67% had borderline levels and 79.33% had desirable levels, a statistically significant difference. Mean cholesterol levels decreased from 169.16 ± 19.70 mg/dl to 161.11 ± 27.60 mg/dl, also significant. For triglycerides, 92.67% had normal levels at baseline, decreasing to 65.33% at follow-up, with mean levels increasing from 131.33 ± 6.97 mg/dl to 139.12 ± 23.88 mg/dl. HDL levels showed improvement, with 84.67% having desirable levels at baseline compared to 43.33% at follow-up, with mean levels increasing from 41.09 ± 5.13 mg/dl to 50.71 ± 4.21 mg/dl. LDL levels decreased from 132.43 ± 16.86 mg/dl to 122.59 ± 16.93

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mg/dl, with significant changes in distribution. **Conclusions:**Short-term steroid use for orthopedic conditions affects lipid profiles: Total cholesterol, LDL, and TG rise significantly, countered by increased HDL, offering protection. Long-term effects on lipid profiles and cardiovascular risk require further study. Risk of avascular necrosis due to subtle lipid profile changes also warrants investigation.

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Introduction:-

Corticosteroids are powerful anti-inflammatory drugs that have been used to treat a variety of diseases for over seven decades[1] . A strong driver of corticosteroid use is the potent symptomatic relief they give to many patients. Yet long term use of corticosteroids is generally avoided, given the risks of serious acute complications such as infection, venous thromboembolism, avascular necrosis, and fracture, as well as chronic diseases such as diabetes mellitus, hypertension, osteoporosis, and other features of iatrogenic Cushing's syndrome[2] . Though the various complication of steroid therapy, they have been prescribed in various common orthopaedic conditions e.g. bursitis, tendinitis, osteoarthritis, myositis, carpal tunnel syndrome, adhesive capsulitis (frozen shoulder), spondyloarthropathy and rheumatoid arthritis also in polymyalgia rheumatica, fibromyalgia, polymyositis[3,4] . Glucocorticoid excess is also related to increase in serum lipid level, especially total cholesterol and low density lipoprotein cholesterol, several reports have indicated that level of high density lipoprotein cholesterol (HDL) and apolipoprotein A-1 are high in glucocorticoid treated patients. However, the implicated causal link between Glucocorticoid use and these lipid profiles is potentially confounded by the variables that are themselves associated with corticosteroid use and possess known adverse effect on lipid profile such as disease status (e.g. uraemia), physical activity levels, diet and concomitant medication. Results of subsequent prospective studies have indicated that prednisone use actually improved lipid profile, increase in HDL, decrease total cholesterol: HDL cholesterol ratio and insignificant change in TG[5,6]. On the other hand, numerous studies have pointed out the atherogenic effects of steroids leading to severe consequences. Some of the consequences reported are increased oxidative stress and inflammation of intima, endothelial dysfunction, alteration of serum LDL, HDL and lipoprotein a [7–10]. Based on the above inferences, one word description of effect of steroids on the patients is that it is a 'double edged sword'. In routine practice of orthopaedics low dose steroids are frequently used for common conditions. Keeping in the view of effects and side effects of the medications prescribed, we conducted a study to evaluate the lipid profile among our out patients who were on short term low dose steroids for their medical conditions in orthopaedics and rheumatology cases.

Aims and Objectives:-

To evaluate the effect on lipid profile by short term use of low dose steroid therapy in Orthopaedics and Rheumatology cases.

To evaluate the effect of glucocorticoids therapy on patient's lipid profile and to evaluate the other effect of glucocorticoid on patients with musculoskeletal complaints

Materials and Methods:-

A prospective, non-randomized and observational study. Sample size calculation revealed that 150 samples with inclusion criteria visiting to Orthopaedic and Rheumatology Department and treated with short term low dose steroid therapy.

Inclusion Criteria

1. Patients with Musculoskeletal complaints.
2. Patientswithoutdyslipidaemia(serumcholesterol<220mg%,Triglycerides<140mg%, LDL <130 mg%, HDL <55 mg %).
3. Age18-65yearsoldmale/female.
4. Patientsgivingwritteninformedconsent.
5. Patientswithoutcardiovascularcondition(e.g.ischemic heart disease).

Exclusion Criteria

1. Patients not giving consent.
2. Patients with avascular necrosis of femur head.
3. Patients BMI >35 kg/m^2.
4. Patients without.
5. Patients without hypothyroidism.
6. Immunocompromised patients in Orthopaedics.
7. Patients with diabetic mellitus and hypertension

Methodology:-

The study was explained to the prospective patients in detail including the aim, procedure, risks/benefits, etc. After obtaining verbal consent, a voluntary written informed consent was obtained from the patient and/or his/her legally acceptable representative. All the study related procedure was conducted after obtaining voluntary written informed consent. All the patients underwent blood sample for lipid profile (Serum total cholesterol, triglyceride, HDL and LDL cholesterol) and blood sugar level investigations. Patient's vitals were also measured. This sample was taken in the early morning hours (7-8 AM) and after a recommended 8 hours of fasting period.

All these patients were given Tablet Methyl-Prednisolone 4 mg to be taken three times a day, per orally. These patients were followed-up after 10 days and repeat lipid profile, blood sugar level investigations and measurement of vitals were carried out. Outcome measures including Serum Total Cholesterol, Triglyceride, HDL-Cholesterol, LDL-Cholesterol, Random blood sugar level, Systolic blood pressure (SBP), Diastolic blood pressure (DBP) andmean arterial pressure (MAP) were assessed.

Results:-

We included 150 study subjects in the present study.The mean age of the study subjects was 42.64 ± 9.85 years with majority of them being in the age group of 41 to 50 years of age. (Table 1) Majority of them were males (70%) in the present study. (Table 2)

At baseline, about 88.67% were having desirable cholesterol levels and 11.33% ad borderline cholesterol levels. At follow up, 20.67% had borderline levels and 79.33% had desirable levels. (Table 3)

The mean cholesterol levels at baseline and follow up were 169.16 ± 19.70 mg/dl and 161.11 ± 27.60 mg/dl respectively and this difference was statistically significant. (Table 4)

At baseline, the total triglyceride levels were normal in 92.67% and 7.33% had borderline TG levels. But, at follow up 65.33% of them were normal, 33.33% were having borderline TG levels and 1.33% had high risk levels of TG in the present study. This was statistically significant difference. (Table 5)

The mean triglyceride levels at baseline and follow up were 131.33 ± 6.97 mg/dl and 139.12 ± 23.88 mg/dl respectively and this difference was statistically significant. (Table 6)

At baseline 84.67% had desirable HDL levels, 8% had borderline levels and 7.33% had high risk levels. At follow up, 43.33% had desirable levels, 56.67% had borderline levels and none had high risk levels. (Table 7)

The mean HDL levels at baseline and follow up were 41.09 ± 5.13 mg/dl and 50.71 ± 4.21 mg/dl respectively and this difference was statistically significant. (Table 8)

At baseline 42% the patients had normal LDL and 58% had borderline LDL. But, at follow up 62% had normal LDL and 38% had borderline LDL levels and none had high risk LDL levels. This difference was statistically significant. (Table 9)

The mean LDL levels at baseline and follow up were 132.43 ± 16.86 mg/dl and 122.59 ± 16.93 mg/dl respectively and this difference was statistically significant. (Table 10)

Conclusions:-

The short dose of steroid used in our setup for common orthopaedic conditions has effect of the lipid profile. There is significant but short interval increase in the total cholesterol, LDL and TG levels. But there is significant increase in the HDL levels also which serves as a protective effect on the individuals. Further follow up studies have to be conducted to have a clearer picture of the effects of these drugs over the lipid profile and of course the cardiovascular risk of the patients. Future studies on the risk of avascular necrosis due to subtle changes in the lipid profile with use of short use steroids have to be conducted.

Discussion:-

It has been more than four decades that steroids alter the plasma lipid levels in the various conditions which are prescribed throughout the clinical practice[11]. Very few studies have hypothesized effects of short-term low dose steroids used inorthopaedicconditions. So, we conducted astudytounderstandtheeffectoftabletMethylPrednisolone4mgtakenthriceadayonthe lipidprofileofthepatients.

Totaltriglyceridelevels:

At baseline, the total triglyceride levels were normal in 92.67% and 7.33% had borderline TG levels. But, at follow up 65.33% of them were normal, 33.33% were having borderline TGlevels and 1.33% had high risk levels of TG in the present study.Themeantriglyceridelevelsatbaselineandfollowupwere131.33±6.97 mg/dl and 139.12 ± 23.88 mg/dl respectively. Van Raalte DH et al[12] (2011) At the dose of 7,5mg of prednisolone the median levels of TG'swere 0.76mmol/l pre-treatment Vs.the median level of 0.74mmol/l after 2 weeks of treatment. Further, with dose of 30mg, the median TG was 0.59 mmol/l pre-treatment as compared to 0.68 mmol/l post treatment. There was a significant difference in the pre-treatment and post treatment values of the TG levels in their study. Although we used Medrol, still we found there was significant increase in the TG levels in the present study.Ettinger et al[10] (1987)studied the effect of low dose short term corticosteroid on plasma lipid and lipoprotein cholesterol was measured in 23 subjects who received Prednisone for active rheumatic disease. After 1 month, plasma cholesterol increased from 195 to 219mg/dl and HDL c from 52 to 70. Garcia Gomez C et al[13] (2008) evaluated the association of low dose glucocorticoid therapy with plasma lipid levels was evaluated in female RA patients. Serum levels triglyceride was not increased in patients on glucocorticoid therapy.

HDLlevels:

At baseline 84.67% had desirable HDL levels, 8% had borderline levels and 7.33% had highrisk levels. At follow up, 43.33% had desirable levels, 56.67% had borderline levels and none had high risk levels. The mean HDL levels at baseline and follow up were 41.09 ± 5.13 mg/dl and 50.71 ± 4.21 mg/dl respectively.Garcia Gomez C et al[13] (2008) evaluated the association of low dose glucocorticoid therapy with plasma lipid levels was evaluated in female RA patients. These patients had 14.7% higher serum high-density lipoprotein cholesterol (HDL-c) levels than untreated patients ($P = 0.043$), mainly at the expense of HDL2 subfraction, which was 24.4% higher ($P < 0.039$), whereas HDL3-c was only 7.4% higher ($P = 0.219$).Ettinger et al[10] (1987)studied the effect of low dose short term corticosteroid on plasma lipid and lipoprotein cholesterol was measured in 23 subjects who received Prednisone for active rheumatic disease. Mean plasma triglyceride (TG) didnotshowsignificantchanges. TaskinenMRetal [14] (1988)studiedtheshort-termeffects of prednisolone on the lipid profile. Serum high density lipoprotein (HDL) cholesterolincreased significantly after 2 days of prednisone administration; the maximal increase was27%($P<0.01$after5days).TheriseofHDLcholesterolwasaccountedforbythatofHDL2cholesterol.

LDLlevels:

At baseline 42% the patients had normal LDL and 58% had borderline LDL. But, at follow up 62% had normal LDL and 38% had borderline LDL levels and none had high risk LDL levels. The mean LDL levels at baseline and follow up were 132.43 ± 16.86 mg/dl and 122.59 ± 16.93 mg/dl respectively.Garcia Gomez C et al[13] (2008) evaluated the association of low dose glucocorticoid therapy with plasma lipid levels was evaluated in female RA patients. Serum levels low-density lipoprotein cholesterol (LDL –c) were not increased in patients on glucocorticoid therapy.Taskinen MR et al[14] (1988) studied the short-term effects of prednisolone on the lipid profile. Prednisone induced no significant changes in very low density or low density (LDL) lipoproteins. Ettinger et al[10] (1987)studied the effect of low dose short term corticosteroid on plasma lipid and lipoprotein cholesterol was measured in 23 subjects who received Prednisone for active rheumatic disease. Mean low density lipoprotein cholesterol (LDL c) did not show significant changes.

Some orthopaedic conditions like rheumatoid arthritis need frequent screening of hypertension, lipid profile and cardiovascular risk.In some studies, glucocorticoidsatevenlow or moderate dose have been associated with hypertension, but this may be a reflection of channeling bias due to RA disease severity[15]. Glucocorticoids can cause sodium retention. In patients receiving less than 10 mg/day, age and elevated pre-treatment blood pressure likely better explain significant hypertension than the use of glucocorticoids. Although several observational studies suggest that glucocorticoids at doses of greater than 10 mg/day adversely affect serum lipid profiles, a national sample from the United States was unable to confirm this association[4]. Moderate- to low-dose glucocorticoids had no significant adverse effect on lipoprotein levels if other risk factors were controlled.Some studies even have suggested that glucocorticoids reverse an unfavourable lipid profile[16,17]. Low-dose glucocorticoid therapy in RA patients generally was associated with an increase in HDL, without increasing LDL or triglyceride— changes which may be favourable[13].

Total cholesterol levels Present study:
At baseline, about 88.67% were having desirable cholesterol levels and 11.33% ad borderline cholesterol levels. At follow up, 20.67% had borderline levels and 79.33% had desirable levels. This difference was statistically significant. The mean cholesterol levels at baseline and follow up were 169.16 ± 19.70 mg/dl and 161.11 ± 27.60 mg/dl respectively. Garcia Gomez C et al[13](2008)evaluated the association of low dose glucocorticoid therapy with plasma lipid levels was evaluated in female RA patients. Serum levels of total cholesterolwerenotincreasedinpatientsonglucocorticoidtherapy.

Table1:-Distributionofthestudysubjectsbasedonagegroup

AgeGroup	Frequency	Percentage
21to30	19	12.67
31to40	41	27.33
41to50	47	31.33
51to60	43	28.67
Total	150	100.00
Mean	42.64	
SD	9.85	

Table2:- Distributionofthestudysubjectsbasedongender.

Gender	Frequency	Percentage
Female	45	30.00
Male	105	70.00
Total	150	100.00

Table 3:- Distribution of the subjects based on the total cholesterol levels at baseline and follow up.

Totalcholesterollevels(mg/dl)	Baseline		Followup		Pvalue
	Number	%	Number	%	
<200(Desirable)	133	88.67	119	79.33	0.0145
200to239(Borderline)	17	11.33	31	20.67	
>240(Highrisk)	0	0	0	0	
Total	150	100.00	150	100.00	

Table 4:- Distribution of the subjects based on the total cholesterol levels at baseline and follow up.

Total cholesterol levels (mg/dl)	Baseline		Followup		Pvalue
	Mean	SD	Mean	SD	
	169.16	19.70	161.11	27.60	0.0031

Table 5:- Distribution of the subjects based on the total triglyceride at baseline and follow up.

Totaltriglyceridelevels (mg/dl)	Baseline		Followup		Pvalue
	Number	%	Number	%	
<150(Desirable)	139	92.67	98	65.33	0.0133
150to199(Borderline)	11	7.33	50	33.33	
>200(Highrisk)	0	0	2	1.33	

Total	150	100.00	150	100.00	

Table 6:- Distribution of the subjects based on the total triglyceride at baseline and follow up.

Total triglyceride levels (mg/dl)	**Baseline**		**Followup**		**Pvalue**
	Mean	**SD**	**Mean**	**SD**	
	131.33	6.97	139.12	23.88	0.0632

Table 7:- Distribution of the subjects based on the high density lipid at baseline and follow up.

Highdensitylipidlevels (mg/dl)	**Baseline**		**Followup**		**Pvalue**
	Number	**%**	**Number**	**%**	
>50(Desirable)	127	84.67	65	43.33	<0.001
35to50(Borderline)	12	8.00	85	56.67	
<35(Highrisk)	11	7.33	0	0	
Total	150	100.00	150	100.00	

Table8:-DistributionofthesubjectsbasedontheHDLlevelsatbaselineandfollowup.

HDLlevels(mg/dl)	**Baseline**		**Followup**		**Pvalue**
	Mean	**SD**	**Mean**	**SD**	
	41.09	5.13	50.71	4.21	<0.001

Table9:- DistributionofthesubjectsbasedontheLDLatbaselineandfollowup.

LDLlevels(mg/dl)	**Baseline**		**Followup**		**Pvalue**
	Number	**%**	**Number**	**%**	
<130(Desirable)	63	42.00	93	62.00	0.0331
130to159(Borderline)	87	58.00	57	38.00	
<160(Highrisk)	0	0	0	0	
Total	150	100.00	150	100.00	

Table10:-DistributionofthesubjectsbasedontheLDLlevelsatbaselineandfollowup.

LDLlevels(mg/dl)	**Baseline**		**Followup**		**Pvalue**
	Mean	**SD**	**Mean**	**SD**	
	132.43	16.86	122.59	16.93	0.0331

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