Steroid therapy and metabolic syndrome in patients with sarcoidosis

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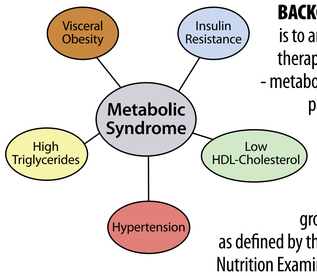
Abstract



BACKGROUND: The aim of this study is to analyze the influence of steroid therapy on metabolic impairments - metabolic syndrome in sarcoidosis patients. 88 biopsy positive sarcoidosis patients. (69 female/19male) were enrolled in this study. **METHODS:** 39 patients from the analyzed group had metabolic syndrome as defined by the Third National Health and Nutrition Examination Survey (ADPIII) [1].129 patients were on high doses of steroid therapy (20mg/daily), 32patients were on morbostatic doses (5-10mg daily) and 27 patients were without steroid therapy. **RESULTS:** Statistically significant difference was found in lipid metabolism between patients with metabolic syndrome and sarcoidosis patients without metabolic syndrome. (F=2629.336;df1=4;df2=80; p<0.01). Multivariant analyses revealed significant link between metabolic syndrome and dose of steroid therapy (F=4.911;df1=4;df2=82;p<0.01).Patients on low doses of steroid therapy with metabolic syndrome had significantly higher TRG /HDL ratio compared with the same therapy regime patients without metabolic syndrome (F=2.672;df=4;p<0.05). However, in patients on high doses of steroid therapy with metabolic syndrome TRG/HDL ratio (1.22±0.807) compared with patients without metabolic syndrome(1.13±1.063) did not show significant difference. Statistically significant interaction was found between the doses of steroid therapy and glucose fasting. (F=52.743;df=6;df2=82;p<0.01).Patients without metabolic syndrome, on low doses of steroid therapy had significantly lower(5.20±0.88) glucose fasting, than patients with metabolic syndrome(7.92±4.30) on same dose of steroid therapy. No significant difference in glucose fasting between patients on high doses of steroid therapy and metabolic syndrome and patients without metabolic syndrome was found. **CONCLUSION:** The surprising fact from this analyses is that high doses steroid therapy did not influence metabolism to the degree we expected towards the developing of metabolic syndrome. The possible explanation is that high doses are more efficient in strengthening physical activity and therefore seemed even safer towards metabolic syndrome which is usually generated by insulin resistance under conditions of low physical activity. During physical activity corticosteroids re direct the glucose metabolism towards the loss of lipids. JAMA,2002;287(3):356-9

Introduction

Metabolic syndrome (Syndrome X)

- **Central obesity**
- **High blood pressure**
- **High triglycerides**
- **Low HDL-cholesterol**
- **Insulin resistance**

Sarcoidosis is granulomatous multisystem disease of unknown etiology. Granuloma formations frequently require steroid therapy.

The aim of this study is to analyze the influence of steroid therapy on metabolic derangements i.e. metabolic syndrome.

People with metabolic syndrome are at increased risk for developing diabetes mellitus and cardiovascular disease as well as increased mortality from cardiovascular disease and all causes. The recently released Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (ATP III) draws attention to the importance of the metabolic syndrome and provides a working definition of this syndrome for the first time. [1]

Methods

As detailed in the ATP III report, participants having 3 or more of the following criteria were defined as having the metabolic syndrome:

1. Abdominal obesity: waist circumference >102 cm in men and >88 cm in women.

2. Hypertriglyceridemia: ≥150mg/dL (1.69 mmol/L);

3. Low high-density lipoprotein (HDL) cholesterol: < 40 mg/dL (1.04 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women;

4. High blood pressure: ≥ 130/85mm Hg;

5. High fasting glucose: ≥ 110 mg/dL (≥ 6.1 mmol/L).

We counted participants who reported currently using antihypertensive or antidiabetic medication (insulin or oral agents) as participants with high blood pressure or diabetes, respectively.

Patients

88 biopsy positive sarcoidosis patients were enrolled in this study. 69 female /19 male. 39 patients had metabolic syndrome as defined formerly.

- 27 patients were without steroid therapy.
- 32 patients received low doses steroid therapy (5-10mg prednisone daily or alternatively)
- 29 patients were treated with high doses of prednisone, 20-30mg daily.

Table 1. Patients characteristics (Descriptive)

Variable	Gender	Mean	SD	N
Height	female	163.4058	6.34619	69
	male	180.8421	7.79076	19
	Total	167.1705	9.80291	88
Weight	female	75.3043	13.95613	69
	male	96.1579	17.91729	19
	Total	79.8068	17.12084	88
BMI (kg/m2)	female	34.8961	13.29290	69
	male	50.9668	19.04429	19
	Total	38.3659	16.04291	88
Waist (cm)	female	94.8986	12.77077	69
	male	105.0526	12.26320	19
	Total	97.0909	13.27571	88
Total triglycerides (mmol/L)	female	1.7243	.96701	69
	male	2.0379	.85716	19
	Total	1.7920	.94854	88
HDL cholesterol (mmol/L)	female	1.5938	.64890	69
	male	1.3563	.43856	19
	Total	1.5425	.61527	88
Trg/HDL ratio	female	1.4182	1.24126	69
	male	1.6334	.76624	19
	Total	1.4647	1.15484	88
Fasting glucose (mmol/L)	female	7.0870	4.25844	69
	male	5.3421	1.32469	19
	Total	6.7102	3.88051	88
Systolic pressure (mmHg)	female	130.4348	16.86318	69
	male	133.6842	13.42077	19
	Total	131.1364	16.16594	88
Diastolic pressure (mmHg)	female	79.9275	10.30751	69
	male	86.0526	12.42521	19
	Total	81.2500	11.01853	88
% fat	female	48.5420	15.96778	69
	male	54.4749	23.06166	19
	Total	49.8230	17.75811	88

Results

Figure 1. TRG/HDL Ratio - metabolic syndrome and steroid dose

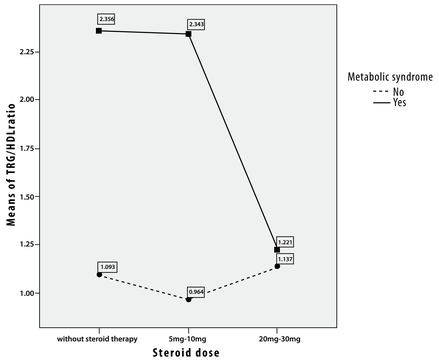


Figure 1. In patients on high doses of steroid therapy with metabolic syndrome TRG/HDL Ratio (1.22±0.807) compared with patients without metabolic syndrome(1.13±1.063) did not show significant difference.

Table 2. Descriptive statistics (variables: lipid metabolism, metabolic syndrome and steroid dose)

Variables	Metabolic syndrome	Steroid dose	Mean	SD	N
TRG/HDL Ratio	No	without steroid therapy	1.0931	.80105	15
		5mg-10mg	.9644	.60828	18
		20mg-30mg	1.1372	1.06349	16
		Total	1.0602	.82304	49
	Yes	without steroid therapy	2.3555	1.46603	12
		5mg-10mg	2.3427	1.32829	14
		20mg-30mg	1.2212	.80795	13
		Total	1.9728	1.31218	39
% fat	No	without steroid therapy	44.5211	9.53522	15
		5mg-10mg	47.9652	18.64280	18
		20mg-30mg	46.5775	22.08942	16
		Total	46.4578	17.43908	49
	Yes	without steroid therapy	50.6817	7.51792	12
		5mg-10mg	58.6730	16.70172	14
		20mg-30mg	52.1837	23.90414	13
		Total	54.0510	17.46090	39
BMI (kg/m2)	No	without steroid therapy	33.7153	10.35628	15
		5mg-10mg	36.5789	16.59523	18
		20mg-30mg	34.3656	17.70023	16
		Total	34.9796	15.10993	49
	Yes	without steroid therapy	37.2625	4.81782	12
		5mg-10mg	46.6971	17.15623	14
		20mg-30mg	43.1762	21.41266	13
		Total	42.6205	16.35534	39
Waist (cm)	No	without steroid therapy	90.6000	9.63476	15
		5mg-10mg	92.8333	11.79357	18
		20mg-30mg	92.1875	15.53585	16
		Total	91.9388	12.35484	49
	Yes	without steroid therapy	103.2500	8.48662	12
		5mg-10mg	105.9286	12.30050	14
		20mg-30mg	101.3077	13.43741	13
		Total	103.5641	11.55261	39

Other variables related to lipid metabolism % fat (F=0.463;df=4;p>0.05), BMI (F=0.658;df=4; p>0.05) and waist (F=0.315;df=4; p>0.05) did not show significant difference in patients with metabolic syndrome and patients without metabolic syndrome. (Table 2).

Statistically significant difference was found in lipid metabolism between sarcoidosis patients with metabolic syndrome and patients without metabolic syndrome. (F=2629.336;df1=4;df2=80; p<0.01).

Statistically significant correlations were found in all variables related with lipid metabolism

- **TRG / HDL Ratio (F=97.703;df=2;p<0.01),**
- **% fat (F=347.980;df=2;p<0.01),**
- **BMI (F=258.548;df=2;p<0.01)**
- **waist (F=2778.013;df=2;p<0.01).**

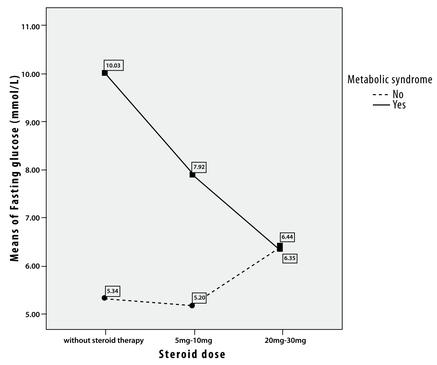
Multivariate analyses revealed significant association between metabolic syndrome and the dose of steroid therapy (F=4.911;df1=4;df2=82;p<0.01).

Patients on low doses of steroid therapy with metabolic syndrome had significantly higher TRG/HDL Ratio compared with patients on the same therapy regime without metabolic syndrome (F=2.672;df=4;p<0.05).

Impaired fasting glucose (IFG) and metabolic syndrome

Statistically significant interaction was found between the doses of steroid therapy on glucose fasting. (F=52.743;df=6;df2=82;p<0.01).
Patients without metabolic syndrome, on low doses of steroid therapy had significantly lower (5.20±0.88) glucose fasting, than patients with metabolic syndrome (7.92±4.30) on same dose of steroid therapy.

Figure 2. IFG (mmol/l) :metabolic syndrome and steroid dose



No significant difference in glucose fasting between patients on high doses of steroid therapy and metabolic syndrome and patients without metabolic syndrome was found. (Figure 2).

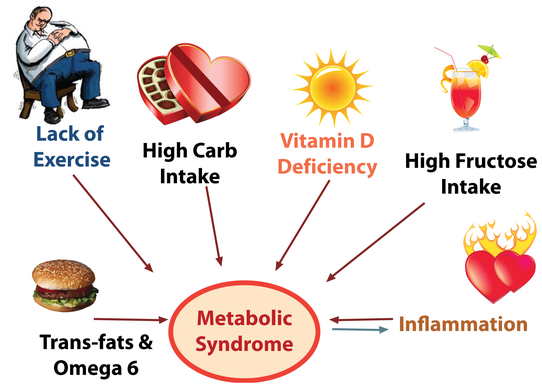
Conclusion

Not the doses of prednisone therapy , but the therapy duration (long lasting steroid therapy with low doses) significantly correlates with the possibility of developing metabolic syndrome in sarcoidosis patients requiring long term treatment.

Statistical analyses

ANOVA (two ways) was used to analyze the coexistence (if any) of metabolic syndrome (glucose fasting) and the dose of steroid therapy, and for the analyses of the dose of steroid therapy (low/high) and the effect on lipid metabolism (TRG/HDL Ratio, % fat, BMI, waist circumference) MANOVA two ways was used.

Discussion



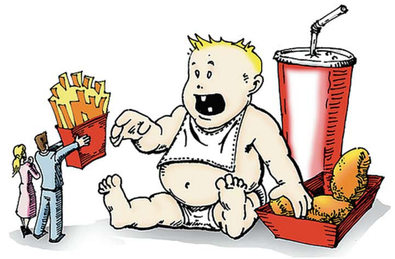
This small sample study revealed the existing interaction between metabolic syndrome and metabolic derangements of lipids and carbohydrates (glucose).

✓ The surprising fact is that patients on high doses of steroid therapy with metabolic syndrome did not differ from the patient group without metabolic syndrome analyzing the TRG/HDL Ratio and fasting glucose.

✓ On the contrary patients on low doses of steroid therapy with metabolic syndrome had significantly higher TRG/HDL Ratio and significantly higher fasting glucose impairment. (IFG)

Our results show that high doses steroid therapy has no influence on the impaired metabolism of lipids and carbohydrates in this analyzed group of patients.

The possible explanation is that patients on high doses steroid therapy are physically active group of patients (no joint or muscle pains, stuffiness), comparing to patients on low doses steroid therapy (the majority of them patients with chronic sarcoidosis). The fact is that physical activity (exercise) enables better glucose metabolism and greater exploitation of fatty acids in their muscles. High doses steroid therapy (short time) seems to be good choice considering physical activity; high doses steroid therapy seems to be safe considering metabolic syndrome impairments too.



Literature:

1. FORD E, GILES W, DIETZ W. PREVALENCE OF THE METABOLIC SYNDROME AMONG US ADULTS. FINDINGS FROM THE THIRD NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY JAMA, 2002; VOL 287 (3):356-359