Correction of steroidopenia as a new method of hypercholesterolemia treatment

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ORIGINAL ARTICLE

Abstract

OBJECTIVE: In 2002 we proposed a new hypothesis of the etiology and pathogenesis of hypercholesterolemia. There is paucity of information in the literature regarding the association of steroidopenia and hypercholesterolemia. Our goal is to determine if the treatment of steroidopenia with hormonorestorative therapy (HT) to youthful levels will normalize total cholesterol (TC) levels.

MATERIAL AND METHODS: We retrospectively analyzed 43 hypercholesterolemic patients treated with HT. Laboratory workup included lipid profile, serum pregnenolone, dehydroepiandrosterone sulfate (DHEA-S), progesterone, total estrogen, cortisol, total testosterone, and vitamin D-3 levels at presentation with follow up ranging from 3 to 9 months. HT therapy included a combination of several agents such as pregnenolone, dehydroepiandrosterone (DHEA), triestrogen, progesterone, testosterone, hydrocortisone, and vitamin D-3.

RESULTS: HT lowered mean TC from 228.8 mg/dL to 183.7 mg/dL (19.7%) ($p<0.05$) in all patients. In 12 men of mean age 58, HT statistically significantly lowered TC from 227.9 mg/dL to 177.1 mg/dL (22.3%) ($p<0.05$). Apparently it did so mostly by lowering LDL and triglycerides (TRG) while HDL did not appreciably change. In 31 women, mean age 57, TC declined from 229.2 mg/dL to 186.3 mg/dL (19%) ($p<0.05$). HDL, LDL, and TRG are also decreased to a statistically significant degree. These results were associated with statistically significant elevations in pregnenolone, DHEA Sulfate, testosterone, progesterone but not total estrogen, cortisol or vitamin D-3 changes in both men and women.

CONCLUSIONS: We conclude that correction of steroidopenia with the use of hormonorestorative therapy is an effective strategy for normalizing and maintaining cholesterol homeostasis.

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INTRODUCTION

Hypercholesterolemia is a very widely debated and frequently discussed subject in medical literature. There are multiple methods to treat this affliction ranging from diet and exercise to pharmacological intervention with various medications (Bhatnagar *et al.* 2008; Schuff-Werner & Kohlschein, 2002; Manzoli *et al.* 2001). However, the problem remains because the etiology and pathogenesis of hypercholesterolemia remains unclear.

There is no information in the medical literature regarding the relationship between low levels of steroid hormones and the development of high cholesterol except for a few studies (Dzugan & Smith, 2002 a,b; Dzugan, 2004; Dzugan *et al.* 2004; Dzugan, 2007; Dzugan *et al.* 2009). In 2002 a ground-breaking study of hormonodeficit hypothesis of hypercholesterolemia was described that showed the association between steroidopenia and hypercholesterolemia (Dzugan & Smith, 2002 a,b). This novel study proposed that hypercholesterolemia develops as a compensatory response caused by declining levels of steroid hormones.

The goal of this study is to test a hypothesis concerning the association of steroidopenia and hypercholesterolemia by evaluating the impact of the restoration of multiple steroidal hormone deficiencies to youthful levels in hypercholesterolemia treatment.

MATERIAL AND METHODS

This study is a retrospective chart review of 43 patients treated for hypercholesterolemia with HT after they failed the conventional treatment of high cholesterol or had side-effects of cholesterol lowering drugs. There were 12 male and 31 female patients. The mean overall age was 58.4 years, mean female age was 57.0 years, and mean male age was 62.3 years. HT was utilized in all of the patients. In 1996 we employed the term hormonorestorative therapy into our practice for the regimen that was used for our patients. HT is defined as a multi-hormonal therapy with the use of chemically identical formulas to human hormones (anthropo-identical) and is administered in physiologic ratios with dose schedules intended to simulate the natural human production cycle at optimal levels.

Hormonorestoration includes a combination of several agents such as pregnenolone, DHEA, triestrogen, progesterone, testosterone, hydrocortisone, and vitamin D-3.

Lipid profile, serum pregnenolone, DHEAS, progesterone, total estrogen, cortisol, total testosterone, and vitamin D-3 levels were checked at presentation and at 3 months intervals. The follow up period was from 3 to 9 months.

One of the most significant age-related events is an alteration in amplitude and pulsatile pattern of hormone release (Smith *et al.* 2005). Hormone restoration should provide a serum hormone profile similar to that found in normal physiology. For restoration of estrogen, progesterone, and testosterone we utilize topical gels because they contain highly lipophilic molecules with low molecular weight, are very well absorbed through the skin, may use adipose tissue as a reservoir, and facilitate individualized dose of prescription. The typical formulation for Triest gel (E3:E2:E1 – 90:7:3) was 1.25–2.5 mg/mL, progesterone 5–10% – 50–100 mg/mL, and testosterone 5–10% – 50–100 mg/mL. In cases of insufficient absorption with gel we utilized drops of Triest (E3:E2:E1 – 80:10:10) at 5 mg/ml, progesterone at 50 mg/mL, and testosterone at 50 mg/mL. Pregnenolone, DHEA, and hydrocortisone were used in oral form (capsules or tablets). The pregnenolone dose ranged from 15 mg to 300 mg, DHEA from 15 mg to 200 mg, and hydrocortisone from 2.5 mg to 10 mg. Vitamin D-3 was used in the doses that ranged from 1000 IU to 5000 IU.

The following factors were included in our decision making in the dosing of our patients during the HT:
1. the recommended dosages for different patients during HT varied significantly and were determined by clinical data and serum hormonal levels during serial testing
2. dosages were individually selected during HT to produce physiologic serum levels typical for healthy individuals between the age of 20 and 30 years for both genders
3. we administered hormones in doses sufficient to restore the optimal level that was defined as the level of hormones in the upper one third of normal range from the testing laboratory.

We employed the following rules in the use of our hormones:
- anthropo-identical structure of hormones
- individually modified doses
- cyclical manner
- larger doses in the morning
- treatment control by serum hormonal level
- mono- or bi-hormonal therapy is usually inadequate
- multi-hormonal therapy is optimal.

RESULTS

All of the patients responded favorably to HT (Figure 1). There were no adverse effects. The student T Test was chosen to evaluate the results. The mean TC dropped from 228.8 mg/dL to 183.7 mg/dL (19.7%). Seven patients still had cholesterol levels ranging from 202 mg/dL to 211 mg/dL but all of these patients had a beneficial drop in TC. These patients still required additional treatment and optimization of their steroid levels. The mean TC in women declined from 229.2 mg/dL to 186.3 mg/dL (18.7%). The mean TC in men decreased from 227.9 mg/dL to 177.1 mg/dL (22.3%). Total cholesterol declined an average of 51 points in men and 43 points in women and 45 points in all patients. This

decline in total cholesterol was found to be statistically significant ($p<0.05$) in men despite the small sample size and significant ($p<0.05$) in female as well as the entire population of patients.

The mean HDL dropped from 65.0 mg/dL to 53.8 mg/dL. The mean HDL in women declined from 73.3 mg/dL to 59.5 mg/dL ($p<0.05$). The mean HDL in men declined from 43.6 mg/dL to 38.8 mg/dL, but was not statistically significant. The mean LDL dropped from 137.4 mg/dL to 110.2 mg/dL ($p<0.05$). The mean LDL in women decreased from 132.8 mg/dL to 109.3 mg/dL ($p<0.05$). The mean LDL in men decreased from 149.3 mg/dL to 112.5 mg/dL ($p<0.05$). It must be remembered that total cholesterol is a calculation of HDL plus LDL plus triglycerides divided by 5. Therefore, it was expected that LDL levels were found to decline in males, females, and in all patients at highly statistical ($p<0.05$) levels consistent with the change in total cholesterol. HDL on the other hand, being a carrier bringing substances back to the liver was found to not have changed in men at a statistically significant ($p=0.09$) level but did decline in women ($p<0.05$) and was statistically significantly ($p<0.05$) declined in all patients. The mean triglycerides dropped from 132.7 mg/dL to 100.3 mg/dL (24%). The mean triglycerides in women declined from 115.0 mg/dL to 86.7 mg/dL ($p<0.05$). The mean triglycerides in men declined from 178.7 mg/dL to 135.6 mg/dL ($p<0.05$). Triglyceride levels were found to be statistically significantly declined in men and women in all patients.

Figures 2 and 3 portray the most significant steroid hormone level change in males and females after HT. The mean pregnenolone was elevated from 53.9 ng/dL to 172.1 ng/dL. The mean pregnenolone in women increased 61.2 ng/dL to 193.5 ng/dL. The mean pregnenolone in men increased from 35.0 ng/dL to 112.0 ng/dL. Pregnenolone levels were found to be significantly elevated ($p<0.05$) in men and women in all patients. Mean DHEA-S was elevated from 92.8 µg/dL to 457.0 µg/dL. Mean DHEA-S in women increased from 88.3 µg/dL to 408.5 µg/dL. Mean DHEA-S in men increased from 104.4 µg/dL to 597.3 µg/dL. DHEA-S levels were also found to be elevated in a statistically significant ($p<0.05$) manner for men and women and all patients. In men, testosterone level was elevated on the program from 424.0 ng/dL up to 625.1 ng/dL on average and this was statistically significant ($p<0.05$). The mean testosterone in women increased from 37.6 ng/dL to 63.2 ng/dL ($p<0.05$). Total estrogen decreased in men from 124.0 pg/mL to 112.5 pg/mL, but did not change statistically significant. In women significant changes in total estrogen also were not observed. The mean progesterone level increased in women from 3.2 ng/mL to 7.5 ng/mL. Progesterone levels increased in women in a statistically significant ($p<0.05$) manner. The same result was observed for men – progesterone was elevated from 0.4 ng/mL to 2.5 ng/mL. The mean cortisol level in all patients increased from 13.8 µg/dL
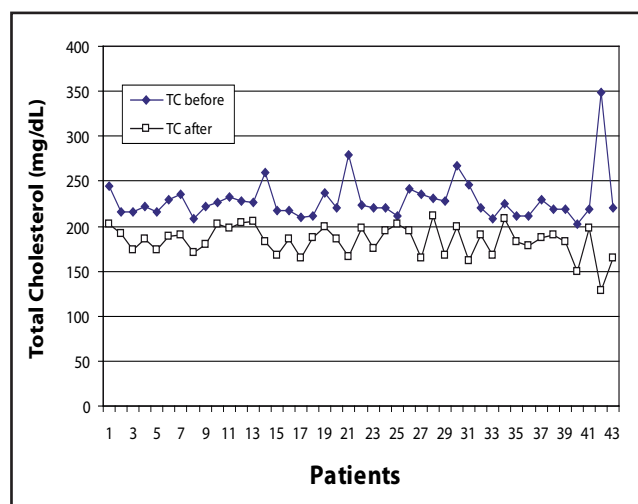

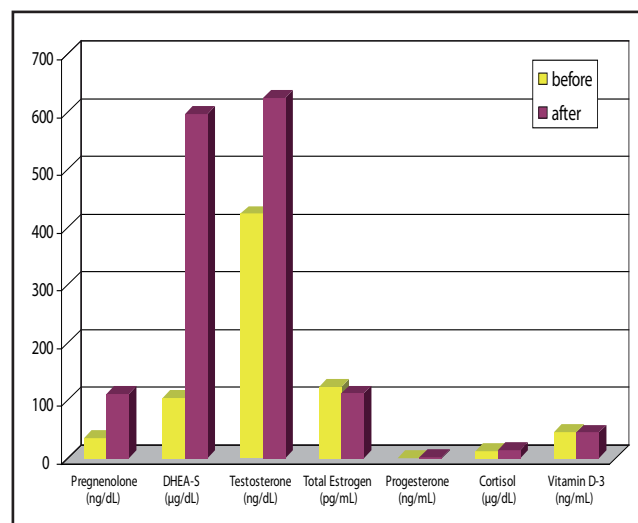**Fig. 1.** Total Cholesterol Before and After Hormonorestorative Therapy.

Fig. 2. Steroid hormone levels in males before and after Hormonorestorative Therapy.
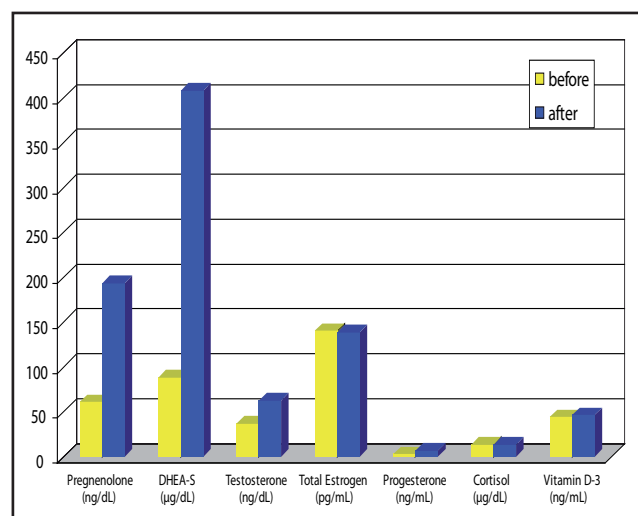

Fig. 3. Steroid hormone levels in females before and after Hormonorestorative Therapy.

to 14.1 µg/dL. Cortisol levels were not elevated in men or women to a statistically significant degree. The mean vitamin D-3 level for all patients increased from 44.8 ng/mL to 46.3 ng/mL. Vitamin D-3 levels were also not elevated in a statistically significant manner in men and women.

DISCUSSION

In men, HT lowered total cholesterol. Apparently it did so mostly by lowering LDL and triglycerides. However, HDL did not appreciably change. Based on this analysis, the decline of cholesterol and LDL levels was related to the elevation in pregnenolone, DHEA Sulfate, testosterone, and progesterone. No significant change had occurred in vitamin D-3 levels, cortisol or total estrogen as explained in the results.

In women, total cholesterol declined after HT as did HDL, LDL and triglycerides to a statistically significant degree. This is associated with statistically significant elevations in pregnenolone, DHEA Sulfate, testosterone, progesterone but not total estrogen, cortisol or vitamin D-3 changes.

We believe that decreasing the level of HDL during HT is a good sign of our intervention if HDL was not very low initially, because if we normalize the level of TC, what reason is there for extra production of HDL? If there is nothing to transport back to the liver, why produce the extra carrier? HDL, by this logic, should decrease! The absence of significant changes in the levels of total estrogen in females can be explained by the fact that total estrogen was measured as a sum of estrone and estradiol only. Even though the laboratory values of the total estrogen did not change, clinically all of the patients experienced resolution of menopausal symptoms. The mean vitamin D-3 level was not elevated in a statistically significant manner because more than eighty percent of the patients were taking certain doses of vitamin D-3 supplement prior to the initiation of our HT, and this can explain small changes in the levels of vitamin D-3 in our study.

Cholesterol is the precursor or the building block for the basic steroid hormones such as pregnenolone, DHEA, progesterone, cortisol, aldosterone, estrogen, testosterone, and others (Figure 4). As the human body ages there is a natural decline in the level of these steroid hormones. We proposed that, since cholesterol is responsible for the production of the steroid hormones, the human physiology is designed to increase the production of cholesterol to balance or attempt to reverse declining hormones. As a result, the cholesterol level rises in a way negative feedback loops work to compensate for the low steroid hormones. Unfortunately, in the aging body the enzymatic system is less efficient and, therefore, these hormones never quite reach the "normal" youthful level. This is how we arrive at the picture of hypercholesterolemia and steroidopenia. Cholesterol elevation should, therefore, be seen as a marker for steroid hormone deficiency.

The administration of steroid hormones restores their optimal levels in the body and, thus, alleviates the need to over-produce of cholesterol. As the feedback loop is complete and steroid hormone levels are normalized, then cholesterol level normalizes as well, since the body is now in equilibrium.

This study reconfirms our hypothesis that steroidopenia and hypercholesterolemia are closely interrelated strongly suggesting that one drives the other. The con-
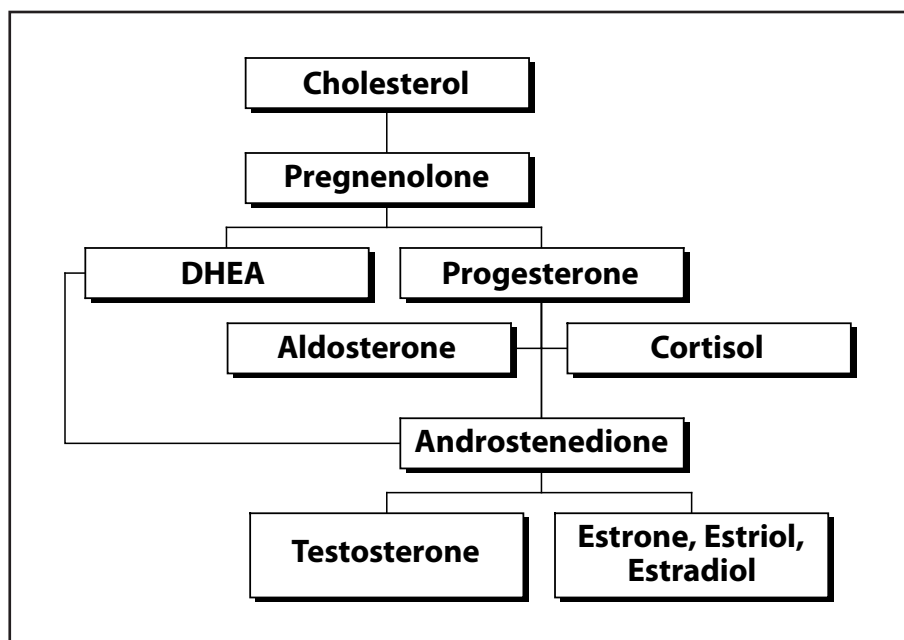

Fig. 4. Simplified version of cholesterol metabolism.

sequence and ramification of these results argue that the optimization of physiology or physiologic medicine should precede pharmacologic intervention. Physiologic medicine treats the symptoms of deficiency and imbalance. Pharmacologic medicine of cholesterol elevation interferes with normal physiologic mechanisms and is associated with numerous side effects. The mindset of our methodology is based on the optimization of human physiology with gentle assistance, whereas the root of the conventional treatment of hypercholesterolemia is based on "fighting" the body with drugs.

CONCLUSION

Our study confirms that there is indeed a valid connection between steroidopenia and hypercholesterolemia. We believe that correction of steroidopenia with anthropo-identical hormones could serve as an inexpensive and effective method of treatment of hypercholesterolemia in healthcare.

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