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Original Research Article

Efficacy of 500 IU HP-hCG in the Management of Testosterone Deficient Secondary Male Hypogonadism

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ABSTRACT

Background : Hypogonadism is a condition marked by low testosterone levels, impacting men across different ages and affecting not just sexual health but overall well-being. While testosterone supplementation has become a common treatment, it can adversely affect testicular function and fertility, leaving many men seeking available alternative options including Gonadotropins. Despite its promise, scant literature exists on use of hCG as a monotherapy for patients with hypogonadic hypogonadism. The purpose of this study was to assess the efficacy and safety of its use in such a population.

Objectives : To assess the efficacy of low dose Highly Purified Human Chorionic Gonadotropin in promoting parameters of sexual function through normalization of Serum Testosteone in Hypogonadal patients.

Methods : In this study, the relationship between normalization of testosterone and the improvement in sexual parameters like libido and erectile function as recorded subjectively through International Index of Erectile Function (IIEF) score was studied. Both serum total testosterone levels and IIEF scores were recorded at baseline and after 6 weeks with 500 IU highly purified hCG, given twice weekly.

Results : 16 men were given treatment for 6 weeks. Among these 16 secondary hypogonadal , after 6 weeks, the serum testosterone levels have recorded a 79% increase from the baseline (mean serum Testosterone concentrations increasing to 371.4 ng/dL, as against base line Testosterone concentrations of 207.3 ng/dL). Very interestingly, according to the International Index of Erectile function score, these 16 patients have shown an improvement to 39 as against 24 in the baseline. That is, a 61% of improvement as assessed by IIEF score is observed.

Conclusion : In hypogonadal men, 500 IU HP-hCG is effective in elevating endogenous testosterone from baseline which is quite reflective in the improvement of Testosterone dependent libido, erectile function and the improvement in semen parameters, just after 6 weeks.500 IU HP-hCG, subcutaneously, can be an alternative to the conventional TRT, with a better patient compliance.

INTRODUCTION

Several forms of Male Sexual Dysfunction have been successfully treated through the use of Phosphodiesterase type 5 (PDE5) inhibitors by combining with or without testosterone. Endocrine causes, being responsible for a significant number of all sexual dysfunctions in men[1]. Published experience clearly emphasizes about the importance of threshold testosterone levels to be present in a man, for even PDE5 inhibitors to act. While the role of testosterone in promoting libido is quite well understood, its role in promoting erectile function cannot be neglected, as voluntary erection depend upon normal androgen levels in a man[2]. Studies suggest that 10-20% of Erectile Dysfunction cases may involve hormonal abnormalities[3,4]. Hypogonadism, more popularly known as Testosterone Deficiency Syndrome is quite frequently interpreted to be of primary in nature, that is, the testicular failure in response to the deprivation of leyding cells in the testicular environment. By and large, the testes has a functional capacity to respond to stimulus till 60 years of age. When testes has the functional capacity, in cases of reported hypogonadism, screening is required, whether the hypogonadism is of primary or secondary in nature. Except for cases of established testicular failure due to genetic defects like Kleinfelter syndrome, patients with diabetes, hypothyroidism and obesity, present hypogonadism of secondary in nature raise questions about the integrity of

Hypothalamo Pituitary axis. In such scenario, our endeavor in this study is to understand the improvement of testosterone dependent sexual function by physiological boosting in cases of disrupted HPT axis.

MATERIAL & METHODS

Inclusion criteria :

In this study, we included 20 conjugated males suffering from various components of Erectile Dysfunction(E.D.) with low serum testosterone who attended our center in last 6 months. 2 cases were exclusively obese, 1 case being enrolled with obesity & hypothyroidism and 1 case with diabetes and obesity.

Exclusion criteria :

All young hypogonadic males were clinically Normosmic idiopathic hypogonadotropic hypogonadism.We excluded those cases who presented with primary testicular failure, genetic and anatomic disorders, also those who were above 40 years (suspected andropause), having psychiatric disorders, chronic alcoholic and on various addictive regimes.

Out of the enrolled 20 patients, 16 patients have completed 6 weeks protocol and 4 dropouts have been noted. We completed a questionnaire which included complete history of E.D. associated illness, clinical examination, including Sexual Maturity Rating(S.M.R.) and patient's serum testosterone,semen analysis, I.I.E.F. score and other relevant investigations. Data were collected at baseline before study and after 6 weeks of injections of 500 I.U. Highly purified hCG (Pubergen NANO), given subcutaneously with twice a week regimen (which is minimum in dose and duration). We report here the documentation of 16 cases, enrolled & completed 6 weeks study. During the course psychosexual counseling has been done.

Results :

In the present work, an association between lowest possible dose of highly purified hCG, which raised patient's serum testosterone level with increase of 79% from baseline (mean increase was 371.4 ng/dL, as against baseline testosterone concentration of 207.3 ng/dL) is observed. Among all 16 patients, 11 responded very well on all assessment tools with respect to baseline. Those who were having only obesity i.e. Case

No. 1 and 9 responded very well and shown increase in net elevation of testosterone 339.86 ng/dL and 229.78 ng/dL respectively. But those two cases who were having obesity with other endocrine disorders i.e. case no. 5 hypothyroidism with obesity and case no. 16 type II D.M. with obesity responded poorly and increase in testosterone level was only 29.00 and 15.13 ng/dL and only case no. 13 showed no increase in testosterone level from baseline. Possibility he might be a case of basic defect in testis and need further evaluation.

Serum Testosterone Levels (ng/dl) – Baseline

S.NO.	AGE	L.I. OF E.R.	S.M.R.	S.A.	S.TESTOSTERONE (BASELINE)
1	29	POOR	S-4	AZOO	226
2	29	POOR	S-4	S-F	151.76
3	26	POOR	S-4	S-F	231.52
4	28	POOR	S-4	S-F	226.51
5	28	POOR	S-4	AZOO	207.34
6	25	POOR	S-3	S-F	241.58
7	31	POOR	S-3	S-F	237.15
8	27	POOR	S-4	S-F	200.45
9	28	POOR	S-4	S-F	234.68
10	23	POOR	S-3	S-F	230.68
11	32	POOR	S-4	S-F	184.8
12	33	POOR	S-4	S-F	195.75
13	26	POOR	S-4	AZOO	167.25
14	30	POOR	S-4	S-F	218.72
15	31	POOR	S-5	S-F	135.67
16	30	POOR	S-3	S-F	225.9

Serum Testosterone Levels (ng/dl) – After 6 weeks

S.NO.	AGE	S.TESTOSTERONE (BEFORE)	S.TESTOSTERONE (AFTER)	S.TESTOSTERONE (DIFFERENCE)
1	29	226	565.86	339.56
2	29	151.76	208.14	56.36
3	26	231.82	334.6	102.75
4	28	226.51	305.41	78.9
5	28	207.34	236.4	29.06
6	25	241.58	618.44	376.86

7	31	237.15	310.29	73.64
8	27	200.45	258.29	57.84
9	28	234.68	464.46	229.78
10	23	230.68	450.43	219.75
11	32	184.8	709.11	524.31
12	33	195.75	518.96	323.21
13	26	167.25	158.96	-9
14	38	218.75	311.34	92.62
15	31	135.67	249.6	113.93
16	30	225.9	241.03	15.13

Very interestingly, according to the I.I.E.F. scale, these 16 patients have shown as improvement to 39 as against 24 in baseline. That is, a 61% improvement as assessed I.I.E.F. score is observed. What is interesting is though Case no. 5 & 16 reported with a marginal increase in testostenone levels, the improvement in Erectile function as assessed by IIEF scoring is encouraging. However, since both these cases, are with concomitant endocrine causes such as hypothyroidism & type 2 diabetes mellitus,it is quite possible that psychosexual counseling might have also had its contribution for the improvement of IIEF parameters and that these patients may require longer treatment with an increase in frequency to normalize testosterone levels.

HEF SCORE – BASELINE

S.No.	Ecectile Function (1-30)	Intercourne satisfaction (0-15)	Orgasmic function (0-10)	Sexual desire (2-10)	Over all satisfaction (2-10)	Total Score
1	12	6	4	5	5	32
2	11	3	3	4	3	24
3	9	2	3	3	2	19
4	10	2	3	3	2	20
5	8	6	4	4	3	25
6	11	3	6	4	3	30
7	8	3	4	4	3	25
8	11	3	4	4	3	25

9	8	2	2	2	3	17
10	6	0	0	2	2	10
11	11	3	3	4	3	24
12	10	2	3	3	2	20
13	20	6	4	4	5	39
14	10	2	3	3	2	20
15	11	6	6	4	3	30
16	5	6	4	4	3	25

HEF SCORE – AFTER 6 WEEKS

S.No.	Ecectile Function (1-30)	Intercourne satisfaction (0-15)	Orgasmic function (0-160)	Sexual desire (2-10)	Over all satisfaction (2-10)	Total Score
1	14	9	5	6	6	41
2	18	17	5	6	6	42
3	14	8	6	6	4	38
4	14	9	6	5	4	38
5	12	8	6	6	7	44
6	14	7	7	6	6	40
7	17	9	6	6	6	41
8	17	7	6	6	5	41
9	14	8	6	6	4	38
10	8	0	0	5	4	17
11	14	7	6	5	4	38
12	17	8	6	6	5	41
13	14	8	6	6	4	38
14	14	9	6	6	6	41
15	17	7	6	6	5	41
16	14	9	6	5	4	38

HEF SCORE – COMPARISON OF BASELINE & AFTER 6 WEEKS

S. No.	Total score BEFORE THERAPY (5-75)	Total Score AFTER THERAPY (5-75)	INCREASE IN SCORE
1	32	41	9
2	24	42	18
3	19	38	19
4	20	38	18
5	25	44	19
6	30	40	10

7	25	44	19
8	25	41	16
9	17	38	21
10	10	17	7
11	24	38	14
12	20	41	19
13	39	38	-1
14	20	41	21
15	30	41	11
16	25	38	13

DISCUSSION

Poor Sexual ability due to poor libido in a man has one root cause, that is sub-physiological serum testosterone. When uncorrected, higher mental functions are affected negatively which influences low and irregular pulsatile release of gonadotropin releasing hormone (GnRH), which in turn is unable to stimulate pituitary gonadotropins with adequate bio potency[5]. In such cases, there may be a discrepancy of LH pulse or amplitude or both, which leads to further testosterone output. So, in such patients with ED, monitoring of testosterone levels and nomalisation of testosterone levels, if found inadequate is very much relevant. We were left with two options, namely, to supplement exogenous testosterone periodically or to stimulate physiologically, the healthy leydig cells to have endogeneous testosterone. The basic aim of the study was to break the vicious cycle by normalizing testosterone levels and improve sexual function. Preliminary studies in young healthy men using Positron Emission Tomography (PET) suggest that some of the paralimbic zones activated due to visually evoked sexual arousal correlated with an increase in plasma testosterone levels[6]. However, the strongest evidence of a possible role of testosterone in erectile function comes from castrated men. As reported by McCullagh & Renshaw, sexual potency was diminished in all castrated men, with complete loss of erection in some patients[7]. Theoretically, it is sound that hCG can be used to normalize testosterone levels, with twice a week regimen, while in practice it is reserved to treat infertility for long. Fundamentally, it sounds louder that 95% of testosterone has its origin from testes in a man and that a man whose testicular function is intact, that is in all established cases of secondary hypogonadism, can actually respond to

LH/hCG stimulus for a proper physiological testosterone ouput. Conventional dose of hCG, when used for a longer period of time has a property of down regulating the LH/hCG receptor, consequentially end-organ resistance is quite possible[8]. Segaloff & Ascoli, 1993 emphasizes that time course of LH/hCG receptor activity is a function of duration of stimulation[9].For longer stimulations with high dose, during first few minutes, the receptor exhibits hCG induced changes, followed by a slow decrease in no. of receptors and decrease in receptor gene transcription[10].Minegishi et al., 1993 hypothesized that the receptor gene expression is related to agonist exposure and that it is increased at a low level of hCG, while it is depressed at a high level of hCG[10]. As hCG has the ability to stimulate testosterone levels, a more optimal result is possible with low does hCG. Also, according to Knobil& Neill, 1988 only a small fraction of approximately 20,000 cellular receptors need to be occupied for a maximum testosterone synthesis[11]. 700 million leydig cells are present in the pair of testes of a man at 20 years of age and by every decade, the decline in no. of leydig cells is by 80 million leydig cells[12]. If so, stimulation with low doses of hCG can actually help in providing stable physiological testosterone, and thus testosterone dependent sexual function, as it is understood with the recent literature that testosterone has a role in promoting erectile function apart from libido[13,14]. According to A G Smals et al., 1980 testosterone response to hCG stimulus in cases of gonadotropin deficiency seems to be delayed compared to the biphasic response in eugonadotropic individuals[15]. This may probably, be one of the reasons, why poor responders in the study might require longer treatment. The fact that 500 IU hCG is enough to stimulate endogenous testosterone[16], and that 5000 IU is a diagnostic dose, prompted us to evaluate the efficacy of 500 IU highly purified hCG in normalizing testosterone levels and also testosterone dependent sexual function. During the course of study, we have done psychosexual counseling for the patients to motivate them towards participating in sexual intercourse with spouse. Based on our observations, we conclude that in hypogonadal men, whose testicular function is intact, 500 IU HP-hCG is effective in elevating endogenous testosterone from baseline which is quite reflective in the improvement of Testosterone dependent libido and erectile function. 500 IU HP-hCG subcutaneously, can be an alternative to the conventional Testosterone Repacement Therapy(TRT), with a better patient compliance.

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