Information About Hormonal Treatment for Trans Women©

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Introduction

As part of your treatment for gender dysphoria we will be prescribing you hormonal treatment (oestrogen). The aim of this treatment is to allow your body to develop the physical appearances of a genetic female by using oestrogen. At the same time we will decrease your production of male hormones (testosterone), which will decrease your male physical appearance using either oestrogen alone or more often using oestrogen with a GNRH analogue drug which will stop the testicles working. The hormonal treatment is very effective, you can expect the changes in your body to be noticeable but it may be necessary undergo cosmetic procedures (e.g. electrolysis, breast augmentation) for fuller feminisation.

Although a very safe treatment there are some side effects with the oestrogen (female hormone) that you should be aware of and these will be explained. The good news is that transgendered people treated with oestrogen have the same life expectancy as the general population telling us that this is a very safe treatment even if it is taken over many years. The changes in the body produced by hormone treatment are somewhat reversible if you stop treatment but some physical changes are permanent such as breast development and so it is important to be sure that hormone treatment is the right option for you before it is started.

At the West London Mental Health NHS Trust (Charing Cross) clinic you will be seen and assessed by 2 psychiatrists or psychologists before hormonal treatment is recommended to make sure that hormonal treatment is the best way to manage your gender identity disorder. We also ask that you change gender role before hormonal therapy is started in all but the most exceptional of cases, so that in cases where a person chooses to remain in their male role there are no permanent changes in their body that may need an operation to correct and they have not been exposed to the side effects of hormone treatment.

Initiation of Hormone Therapy

The way that we organise hormone treatment is based on the internationally agreed guidelines. This is known as Triadic Therapy, which consists of three critical elements; Real Life Experience; Hormonal Therapy of the Desired Gender and finally Genital Reconstruction Surgery. We follow this strategy to protect you. As you advance through a sequence of treatment that has progressively more irreversible effects on your body with more and more significant physical alterations should you choose to revert to your birth gender.

Hormonal Treatments

Our Standard Regimen

The standard hormonal regimen used at our clinic is the initiation of oestrogen valerate 2mg increasing to a maximum of 10mg per day. This is a natural oestrogen which means we can measure it in your blood and change the dose until we get to the level seen in a young genetic female. Dose increases are made after 3 months of therapy. We know from treating genetic females that have not had a natural puberty that if too much oestrogen is given too quickly then breast development is not normal and you may end up with small cone shaped breasts not a natural female contour. Natural puberty occurs over 2 years and we aim to mimic this in our treatment.

Using excessive amounts of oestrogen does not improve breast development, indeed there is an enzyme present in the body that converts excess oestrogen back into testosterone and so this may be counterproductive.

A GNRH analogue such as Goserelin (Zoladex) 10.8mg/3months or Decapeptyl 11.25mg/3 months is added to your treatment if your testosterone is too high when you are on 4 mg of oestradiol valerate to suppress testosterone production. This medicine works by over activating the gland under the brain which controls the testicles. When this gland is over

stimulated it goes to sleep and so the production of testosterone will stop. Because of the way this medicine works for the first 2 weeks following the first injection you may notice an increase in erections and sexual thoughts. To prevent this cyproterone acetate 50-100mg per day is given for the first 2 weeks; it is not needed with subsequent injections. Genetic females produce testosterone and the aim of treatment is to get your testosterone level to that of a genetic female (<3nmol/l).

In patients over 45 years old oestrogen on its own may be enough to control your testosterone production. In those over 45 then oestrogen valerate 2mg is commenced and titrated 3 monthly. If plasma testosterone is not suppressed on 4mg o.d. then a GNRH analogue may be added.

In individuals that cannot tolerate oestrogen valerate therapy ethinyl oestradiol 50-150μg per day or conjugated equine oestrogens 2.3-7.5mg per day are alternative treatments. The usual reasons for discontinuation of oestrogen valerate are nausea and headache.

Six weeks prior to genital reconstruction surgery your oestrogen therapy will be stopped to reduce the incidence of perioperative deep venous thrombosis (DVT) and this will continue for 2 weeks postoperatively.

After Surgery

If you were on a GNRH analogue (Zoladex Triptorelin or Decapeptyl) before surgery it should be stopped and you should continue with the same dose of oestrogen that you had before your operation. If you were not on a GNRH analogue before surgery you will need a lower dose, typically 1/3 – 1/2 of the dose you were taking before surgery.

The aim of treatment is to prevent osteoporosis (brittle bones), increase general well being and have a healthy heart. Standard hormone replacement dose can be used although in many case higher levels such as twice the normal amount are administered which reflects the generally larger body size of a trans woman. The replacement dose is worked out using

blood tests with the aim of achieving a plasma oestrogen level in the upper follicular phase (350-600 pmol/l). Goserelin (Zoladex) is stopped after your operation.

Alternative therapies include oestrogen patches at either 50 or 100μg twice per week, ethinyl oestradiol 50μg daily or conjugated equine oestrogens 2.5mg o.d.

Oestrogen valerate has the advantage of allowing plasma oestradiol levels to guide therapy aiming for a plasma oestradiol of 400-600pmol/l.

Effects of hormone replacement

Facial Hair

The beneficial effects of oestrogen in transwomen are induction of female characteristics. You will find that your skin texture becomes finer and there is a reduction in the growth of your facial hair. This effect is maximal after 4 months of treatment. Oestrogen therapy itself only rarely reduces facial hair growth adequately to provide a female facial appearance once a person has adult beard development. You will need local treatment such as electrolysis, waxing, shaving, sugaring or laser therapy to reduce the appearance of facial hair and help your female presentation.

Male pattern hair loss also slows and may stop as your testosterone levels fall however regrowth of hair once it is lost does not occur.

Breast Growth

During normal puberty breast growth needs oestrogen and takes 18 months to 2 years. Your oestrogen therapy mimics this process. Breast development will begin about 2-3 months after the start of treatment and the maximum effect of oestrogen on breast development is not seen until 2 years of oestrogen therapy. Doses of oestrogen in the order of 100μg ethinyl oestradiol or oestrogen valerate 6mg are adequate for this to occur. Using higher doses of oestrogen does not have any additional benefit in inducing breast

development. In general the maximum breast development a patient can expect to achieve is a cup size less than your mother.

Breast development is dependant on the deposition of fat into the breast and if you are thin gaining some weight can increase your breast growth.

Despite hormonal treatment 60% of transwomen progress to breast augmentation surgery.

Body fat distribution

The proportion of fat in your body will increase. This is seen mainly around the hips and buttocks to give a more rounded form to the body. There is an average 4kg (9lb) weight gain.

This is accompanied by a decrease in muscle bulk and upper body muscle strength. The increase in subcutaneous fat will decrease muscle definition promoting a more female body outline

Genital Effects

Oestrogen treatment will decrease your sex drive and erections. The testicles will become smaller and softer.

Sperm production will decrease and eventually stop. If you would like to have children in the future with a female partner or surrogate then you will need to store your sperm before you start oestrogen. This will have to be arranged at a local infertility clinic. There may be a charge for this as sperm storage is not always available on the NHS.

Other Hormonal Treatments

Antiandrogens and Testosterone Blockers

Cyproterone acetate is a potent androgen receptor blocking drug. It is derived from progesterone and is metabolised in the liver. Its use is associated with liver problems and requires regular monitoring of the liver function. More importantly there is a significant risk of depression associated with the use of cyproterone in up to 30% of users. The same problems occur with the use of finasteride as both depression and liver function disturbance

have been described with the use of this drug. Antiandrogens have been necessary in the past as many patients failed to stop their production of testosterone with oestrogen treatment. Now we have the availability of GnRH analogues (Zoladex or Decapeptyl). These drugs work by over stimulating the testicles which then go to sleep and testosterone production is reduced. There has been a large experience in using these drugs both in the treatment of prostate cancer and infertility and they have an excellent side effect profile. Therefore in the vast majority of people antiandrogens are not needed as we can stop testosterone production rather than try to fight against it as we did in the past.

Progesterone

Progesterone is used by some centres and is widely purported by Trans websites to improve breast development. In the only study published comparing oestrogen with oestrogen and progesterone there was no benefit of progesterone on breast growth over oestrogen alone. More worryingly we know that in scientific trials of hormone replacement with both oestrogen and progesterone in women there is an increased occurrence of heart attacks and strokes. There was also a trend towards increasing levels of breast cancer. These risks were not seen if oestrogen only was used, suggesting that progesterone is not good for both heart and breast health.

Negative Effects of Oestrogen Therapy

Oestrogen therapy is safe and effective, but several side effects of this treatment have been described in the transfemale population the most important of these are thromboembolic complications (deep venous thrombosis), breast cancer risk, liver function abnormalities and hyperprolactinaemia (increased prolactin level in the blood).

Thromboembolic disease (DVT)

The incidence of DVT in transsexual patients is approximately 2.6% (2.5 per hundred people), which is twenty times that of people not on oestrogen treatment. Most of these

happen during the first 2 years of treatment. There is however an ongoing risk of 0.4% per year (4 people per thousand per year) which continues.

The risk of DVT is affected by several factors. The type of oestrogen may be important. It has been shown that ethinyl oestradiol alters the levels the chemicals in the blood that make the blood clot. These changes were not seen when either oestrogen patches or oral oestrogen valerate (progynova) were used. In that study there was not an increase in the occurrence of DVT. In our clinic we have moved away from using ethinyl oestradiol to oestrogen valerate, we have not yet demonstrated any change in the incidence of DVT in our patients, however we believe it will be safer in the long term to use this form of oestrogen.

In transsexual women on ethinyl oestradiol we know the risk of DVT and this form of oestrogen treatment has been used for over 40 years. We know that overall transsexual people have the same lifespan as the non-hormone treated population and so long term use of ethinyl oestradiol is also safe.

Smoking in women taking the oral contraceptive pill increases the risk of stroke and deep venous thrombosis (DVT). The dose of oestrogen in the pill is less than half that used in oestrogen treatment in transsexual people and so we do not prescribe oestrogen for people who smoke to minimise the risk of deep venous thrombosis.

Breast Cancer

The incidence of breast cancer with standard HRT in genetic females are 3.2/1000 aged 50-59 and 4/1000 aged 60-69 (beral lancet 2002). This is based on large population based studies. We know from big trials the inclusion of progesterone in the HRT administered increases this risk. There are no similar studies available in the transwomen. There have only been 4 case reports of breast tumours occurring in treated transsexual patients

suggesting that the risk of breast cancer secondary to feminising hormone therapy is very low.

In view of the fact that progesterone does not improve breast development in transwomen and there is evidence that they may increase breast cancer risk their use we believe it should not be used in the treatment of transwomen.

Hyperprolactinaemia (Raised prolactin in the blood)

Prolactin is the hormone that is made during pregnancy to make the breast produce milk. It is made in a small gland called the pituitary gland, which sits below the brain near the back of the eyes. Oestrogen, which is high in pregnancy, causes the pituitary to grow and release the prolactin. After pregnancy the oestrogen level decreases and the gland goes back to normal. Your oestrogen treatment, especially if you are on very high levels of oestrogen, can cause a similar growth in this gland. Over a long period of time this growth may become a lump in this gland. If it does happen these lumps are almost always benign (not cancerous) but will need treatment as they can press on the nerves coming from your eyes and affect your vision. High prolactin levels occur in about 10-14% of patients but there have only been 2 cases of prolactinomas (lumps in the pituitary gland) in transwomen and none have needed withdrawal of oestrogen treatment.

If your prolactin level rises it can be treated by reducing your oestrogen dose and the using Zoladex to reduce your testosterone. Interestingly one of the patients who developed a pituitary lump had been self-administered oestrogen in addition to her prescribed oestrogen therapy showing how risky self-medication can be.

Abnormal Liver Function.

The liver is the organ in the body that removes toxins from the blood stream. It also destroys many chemicals such as hormones after they have finished working. As this organ is so important we measure the levels of the chemicals it makes (liver function tests) in your blood to make sure it remains healthy while you are on oestrogen treatment. The risk

of abnormal liver function tests is approximately 3% in transwomen. In half of these the abnormalities persist for more than three months. However the increases are mild and as long as blood levels are watched closely will cause no harm. It is only very rarely that the liver function tests become very abnormal and then we have to stop oestrogen treatment.

In women on the oral contraceptive pill gall stones are more common but this has not been seen in trans people.

Other Side Effects

Oestrogen therapy is associated with other minor side effects that appear in the literature as isolated case reports. These are often minor and include dry hair and brittle nails, believed to be due to a decrease in oil production from the skin

Safety Monitoring

The safety monitoring for this ongoing treatment is outlined in the table. This monitoring is designed to detect the major side effects of hormonal therapy at an early stage so that the treatment can be altered and prevent ongoing unwanted effects of the treatment.

The side effects of oestrogen do appear to be related to the length of time that you take them. It is known that prolonged HRT use beyond 5 years after the menopause (about age 55) is associated with an increased risk of breast cancer. This fact applies to genetic females and although this is the best evidence available on the long term effects of oestrogen therapy we do know that the lifespan for transsexual people is normal suggesting that long term oestrogen therapy beyond 55 is not harmful.

Transwomen		
Initial Visit		**Every 12 Months Post-Operatively**
	LH	Weight	Decrease oestrogens to high HRT dose
	FSH	Blood Pressure	Serum Prolactin
	Testosterone	Lipid profile	LFTs
	Oestradiol	Glucose	Blood Pressure
	SHBG		Weight
	Prolactin		***Over 40:***
	Dihydrotestosterone		Consider Transdermal Oestrogen
	PSA		***Over 50:***
Every 3-6 Months			Discuss stopping HRT
	Testosterone levels until stable		Mammography every 5 years
	Oestradiol blood level (if on oestrogen valerate)		PSA
	LFT		DEXA scan
	Breast examination		
	Blood Pressure		
	Weight		
EVERY 6-12months Pre-Operatively			
	Serum Prolactin		
	Over 50:		
	PSA		

Summary

Hormonal treatment is essential in the treatment of transwomen. It can produce permanent changes in the way your body looks and so it should only be given when your psychiatrist or psychologist feels it is the best treatment for you. Rushing into hormone treatment does not improve the result of feminisation and indeed can make the treatment less effective. Hormone treatment is safe but there are side effects, especially the risk of blood clots and these must be minimised by stopping smoking and maintaining a normal body weight.

Hormonal treatment is intrinsic to the management of gender dysphoria. It should be undertaken only in the context of an active multidisciplinary approach involving both the mental health professional and the endocrinologist. The principal of treatment follows international guidelines and should not be initiated without approval from a mental health practioner with a special interest in gender dysphoria.

For transwomen the hormone regimen usually consists of oestrogen as oestrogen valerate in combination with testosterone suppression, usually as goserelin. This combination allows measurement of plasma oestrogen and testosterone levels to guide therapy. Alternative approaches include the use of the synthetic oestrogen ethinyl oestradiol and anti-androgens such as cyproterone acetate, spironolactone and finasteride.

The major side effect of oestrogen therapy is the development of blood clots usually as deep venous thrombosis with a rate of 2-3%. Other important risks are breast cancer, liver enzyme derangement and hyperprolactinaemia (increased blood prolactin levels).

Treatment is very successful with good feminisation in the majority of cases. Many patients, however, do require breast augmentation. Breast development occurs over 2 years of hormone therapy and treatment - beyond this will not produce further breast development.

There is no evidence that progestins improve breast development in transwomen. They may increase the risk of heart disease and stroke and promote breast cancer development. For these reasons their use is difficult to justify.

Following genital reconstruction surgery oestrogen doses can be reduced to levels used for high dose standard HRT but more usually higher doses are required. If oestrogen valerate is used plasma monitoring can be used to get the oestradiol level to the upper follicular range.

Hormone treatment in people with gender dysphoria does not alter their life span confirming that these treatments are safe as well as effective. They also do not increase the incidence of any conditions that one might predict would be more common in hormonally treated patients such as breast cancer in transwomen with the exception of thromboembolism in oestrogen treated patients.