Testosterone replacement therapy

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Guideline for use of testosterone replacement therapy for induction of and progression through puberty in hypogonadotrophic hypogonadism (HH), androgen deficiency secondary to testicular disease and in constitutional delay of growth and puberty (CDGP).

Background:

The aim of testosterone replacement therapy is to mimic the normal cadence of puberty and match requirements at different stages of pubertal development in patients with in HH, androgen deficiency secondary to testicular disease and in CDGP. Testosterone replacement therapy is used to induce development of secondary sexual characteristics and promote linear growth, normal accrual of muscle mass and bone mineral density while avoiding mistimed epiphyseal plate closure. In boys with CDGP, testosterone replacement therapy may also be commenced to alleviate the distress boys often suffer because of their lack of growth and pubertal progression, which can affect their school performance and social relationships. In androgen deficiency secondary to hypogonadism (hypogonadotrophic or hypergonadotrophic), testosterone replacement therapy is usually started at between 12 to 14 years of age and life-long treatment is required. Low dose, intermittent testosterone should be used in CDGP to avoid suppression of endogenous axis.

Licenced testosterone preparations (in BNFc):

IM testosterone:

- A long-acting testosterone ester (testosterone enantate, testosterone proprionate (Virormone®, Nordic) or mixture of esters (Sustanon 250®, Organon) at 50–75 mg/month is used initially and escalated gradually every 6 months to 100–150 mg/month before changing to 250mg 3 weekly after 3–4 years.
- A long-acting testosterone ester (testosterone enantate, testosterone proprionate (Virormone®, Nordic) or mixture of esters (Sustanon 250®, Organon) at 25 mg/month for 3 months in infants with micropenis or DSD.
- IM testosterone undeconate (Nebido®, Bayer) at 1g every 10-14 weeks can be used in men over 18 years (not licensed for children). This should not be used for induction of puberty or progression through early stages of puberty (and CDGP) as it is not appropriate for dose titration.

Oral testosterone:

- Testosterone undecanoate (Restandol® Testocaps, Organon) starting at 40 mg once daily, and gradually titrated up every 6 months to a maximum dose of 80 mg tds after 2–3 years.
- Oral testosterone has a short half-life and must be taken with food for satisfactory absorption, and has a tendency to be 5a-reduced to DHT in the gut.

Testosterone cream:

- Testosterone 5% cream can be used for treatment of microphallus in gonadotrophin deficiency to stimulate phallic growth.
- Dose: apply cream three times daily for 3 weeks.

Other options (in BNF):

The following preparations are unlicensed for use in children.

Transdermal gel:

- 1% testosterone strength (Testogel®, Bayer or Testim®, Ferring):
  - Adult dose: 50–100 mg of testosterone in 5–10 g gel sachets.
  - For children: the starting dose should be around one-third of a 50mg/5g satchet ie. 10-20mg daily for the first year, and gradually increasing by one-third of a satchet daily every year to a final dose of 50 mg daily in the third year (Han and Bouloux, 2010).
- Metered-dose 2% testosterone gel (Tostran®, ProStrakan) 10mg/metered application:
  - Adult dose: apply 60–80mg of testosterone (3–4 g of gel) daily.
  - For children: 10-20mg (1-2 metered applications) daily (extrapolated from adult dose, no evidence in literature).
- Metered dose 2% testosterone gel allows much easier titration compared with 1% testosterone sachet preparations.
- Advice for application:
  - Apply thin layer of gel on clean, dry, healthy skin such as shoulders, arms or abdomen. Allow to dry before dressing.
  - Be careful to avoid potential cross-contamination - wash hands with soap and water after applying gel.
  - Preferably apply at bedtime, avoid shower or bath for at least 6 hours.
  - Gels should not to be applied on genital area as high alcohol content may cause local irritation.

Transdermal patch:

- Andropatch® (Glaxo-SmithKline): 2.5-5mg/24hrs
- Intrinsa® (Warner Chilcott): 300mcg/24hrs.
- Evidence for use in children: A study by Mayo et al. (2004) assessed the pharmacokinetics and effects on pubertal status, short-term growth and bone turnover of transdermal testosterone application. They found that use of a 5mg/24hrs patch (Virormone®, Nordic) applied overnight for 8-12hrs may be a potentially acceptable method to induce puberty and stimulate short-term growth and bone turnover. The study was a prospective randomized, crossover study over 26weeks, involving 8 boys aged 12.4 to 14.9 years.
- Patches should be applied to dry skin on the back or buttocks and have been associated with localised skin irritation.

Testosterone implant:

- Testosterone, Organon implant can be used in children over 16 years (BNF)
- Dose: 100–600 mg; 600 mg usually maintains plasma-testosterone concentration within the normal adult range for 4–5 months.

None of the transdermal preparations (gels, patches or implants) have been licensed for induction of puberty in the UK and experience of their use is limited in adolescent practice. By contrast, in adults, transdermal systems provide testosterone pharmacokinetics that most closely mimic natural diurnal variation in testosterone concentrations and are convenient when changing from the IM route at late puberty to adult replacement therapy.

References

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