Is short stature a problem? The psychological view

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Abstract

The use of GH in short normal children remains a controversial issue as physicians and parents alike are under continuing pressure to identify and to treat such children. Before asking who might respond to growth-promoting therapy, we should first ask who needs it. Rational intervention assumes some abnormality, physical or psychological, that can be corrected. Where short stature is the result of GH deficiency, the case for intervention is clear and uncontroversial. Where there is no clear deficiency, treatment can be regarded neither as replacement therapy, nor as corrective, but simply cosmetic. However, there might be a case for therapy if there were clear evidence of an association between short stature and psychosocial dysfunction. The common perception that short stature is an inevitable handicap has been founded on unreliable evidence, largely clinic-based studies, where children experiencing the greatest difficulties are likely to be found. Such reports, unless challenged, can only lead to an increasing demand for treatment, both from and for those who were previously unconcerned. The Wessex Growth Study recruited an unselected cohort of short normal children, not from the clinic, but from the community at large, and has challenged the widely held belief that short stature is an inevitable disadvantage. The progress of these children, followed over some 13 years, has given little cause for concern. Indeed, this study, and others subsequently, has demonstrated the normality of the psychosocial functioning of the short normal child.

European Journal of Endocrinology 155 S39–S45

Introduction

In 2003, the Food and Drug Administration (FDA) signed the seal of approval for growth hormone (GH) to be given to children with idiopathic short stature (ISS), i.e. stature on or below the 1.2 percentile, even where there is no discernible medical problem (1). It was a landmark decision, and not without controversy (2, 3). As Allen and Fost remarked, 'the cause of the short stature has ceased to be morally relevant in deciding, who is entitled to treatment' (4). It seems likely that a similar application will be made in the European Union (5). All that is now required is evidence of a disability arising from short stature (SS).

Prior to the advent of biosynthetic GH in 1985, limited supplies of GH were strictly rationed and only those children with classic GH deficiency (GHD) were eligible for treatment. Thereafter, limitless supplies have led to an increasing number of approved indications, such as Turner's syndrome, Prader-Willi's syndrome,

chronic renal insufficiency and 'small-for-gestational age' (2, 6). A condition known as GH 'insufficiency' was also a target, prompted by the observation that the distribution of GH secretion appears to be continuous, tall children secreting more GH than short (7). The fact that biochemical tests for GHD are unreliable only strengthened the argument and led, inevitably, to this somewhat grey area of 'insufficiency' at the lower end of the continuum.

An apparently poor rate of growth also became a criterion for therapy (8). Short-term growth data, however, largely because of measurement error, cannot reliably distinguish between normal and abnormal growth (9, 10). Crucially, there is no correlation between successive annual height velocities, so that height velocity, even over 12 months, neither predicts the future nor reports the past. In the long-term, of course, short children will grow more slowly than tall, but this does not make their rate of growth abnormal. 'Normal' height velocity is conditional on stature (11). Indeed, were all children to grow at a uniform rate, there would be no variation in adult stature.

What has arisen over recent years is, in essence, a situation where short stature has become medicalised, allowing even the short normal child to become a

This paper was presented at the 4th Ferring Pharmaceuticals International Paediatric Endocrinology Symposium, Paris (2006). Ferring Pharmaceuticals has supported the publication of these proceedings.

potential target for growth-promoting therapy. To begin with, GH was largely given in the context of clinical trials, but the recent FDA ruling will have opened the floodgates. The exact proportions of children currently receiving treatment are unknown, but even before 2003, one report suggested some 40% of children on GH appeared not to be GHD (12), and at one time in the US, ISS alone accounted for around one in three of all children on GH (13).

One argument used in support of GH therapy for the short normal child is based on the notion that medicine is about the relief of suffering, the treatment of people, not diseases (14). Why should we offer GH only to the child who is GH deficient and withhold it from another, who is GH replete but equally short, when the goals, such as an improvement in psychosocial functioning, might be the same? (15). Although there may be metabolic benefits of GH therapy in some pathological conditions, in most cases, the rationale behind the treatment is an increase in height velocity in the short-term and taller adult height. This is based on a widespread belief that SS constitutes a psychosocial disadvantage and that is where the disability lies, but where should we look for the evidence?

Stature and social stereotypes

Social stereotypes associated with unusual stature at either end of the range of height include the so-called 'gentle giant' at one extreme and the derogatory 'short-man syndrome' or 'Napoleon complex' at the other. The literature suggests that social stereotypes of height may be established at an early age. Even very young children ascribe positive attributes to tall and negative attributes to short silhouettes (16). Experimental studies with young adults in hypothetical social situations have shown 'status' to equate with 'stature', whereby tall men are attributed qualities expected of successful people (17). The results of other studies indicate that those in high-esteem jobs are generally believed to be taller than those in low-status jobs (18, 19). A physically imposing presence apparently confers an advantage in modern day politics, at least in the US, where taller presidential candidates have typically won elections (20). In the absence of additional information, first impressions may well be biased by popular stereotypes, but it has been shown that the influence of height is diminished where contextual factors, such as education and other individual characteristics are incorporated. Although there have been some reports linking height and income, they are inconsistent and the relationship is attenuated when controlled for potentially confounding variables, such as level of education, marital status and race (2, 21, 22).

Short stature in the paediatric clinic

Most commonly, SS appears as an isolated physical characteristic in an otherwise healthy child, i.e. 'idiopathic SS'. Nevertheless, the belief that such children are disadvantaged by their height is widespread (23–26). In one survey, 56% of physicians said that height impaired emotional well-being in children below the third percentile (27). There are several likely explanations for this belief.

Until recently, almost all studies designed to assess the psychological adaptation of children with SS were based on clinically referred patients with a whole variety of medical diagnoses. The underlying pathology specific to each condition, one such example would be Turner's syndrome, is likely to hamper normal psychosocial and educational adjustment. Moreover, many of the earlier studies were conducted at a time when GH therapy was strictly rationed, and thus will have included only those most severely affected by their SS.

Problems of social adaptation reported to the paediatrician have included stigmatization, juvenilisation, immaturity and unassertiveness (28). Some have suggested that short children are conditioned to behave in a socially immature manner and that the stereotypical anxious, introverted short child could well be the result of 'experiences associated with the small stature' (29, 30). The child or adolescent, who is treated according to height age rather than chronological age is likely to withdraw from the peer group, or may prefer to socialise with younger children or even adults. Some short children might perhaps try to overcompensate for SS by being over assertive and belligerent or to seek peer approval as the group mascot or clown (31). Alternatively, it has been suggested that some adults overly protect the short child from his/her peer group (32–34). Parental overprotection has in fact been shown to be a strong predictor of victimization by peers in the general school population (35).

Most reports on short children's school performance have also been based on clinic-referred samples (36). These studies commonly report academic underachievement in spite of average intelligence, but are likely to reflect specific neurocognitive deficits associated with specific syndromes, rather than the psychosocial consequences of SS (28, 37). Importantly, it has been shown that within clinic-referred populations the problems of academic achievement are not related to height, nor are they remedied by GH therapy (37, 38).

SS is commonly associated with delayed puberty and Gordon *et al.* were the first to propose that the psychological benefits of accelerating height velocity might outweigh any reduction in final adult height (39). There is no evidence, however, to support this. Although delayed puberty may serve as an additional problem in adolescents with SS, the data are inconclusive (40–44). Most studies seem to confirm few long-term psychological sequelae of early growth delay (45–47).

Many clinic-based studies have been subject to a variety of methodological flaws, not only mixed diagnostic groups, mixed age groups and small sample sizes, but also they have often lacked an appropriate control or comparison group (48). Volunteer controls are likely to yield an above average group in terms of psychological functioning (49). Details of short stature recruitment into studies sponsored by the pharmaceutical industry are often lacking, making it impossible to assess how representative they are. A recent review of all referrals for SS to the growth clinic over a 12-month period found twice as many boys as girls, even though boys are no more prone to SS (50). This gender bias would seem to reflect a social or cultural difficulty, at least in the US, in accepting short stature in males.

The findings from more recent clinic-based studies, with improved methodology, have questioned many of the established beliefs regarding the psychosocial consequences of SS (51). In 1994, Sandberg reported on 522 consecutive referrals for SS to the paediatric clinic, using both parent and self-report measures. The majority of youths with short stature experienced teasing or juvenilisation, but only minor difficulties of behavioural adaptation were identified (52). A Dutch study reported similar findings for a group of untreated young adults with idiopathic SS. The authors of this study concluded that although three quarters of the participants reported a negative experience attributed to their SS, this had not resulted in a reduced quality of life (QOL) (53). Skuse and colleagues detected no significant differences in terms of peer acceptance, self-perception or social competence between physically healthy clinic-referred short children and their classmates (54). Further analysis of this study revealed that intelligence was a better predictor than height for most aspects of psychosocial adjustment (55).

Short stature in the community

Most of the children with idiopathic SS' or 'short normal stature' will never appear in the paediatric clinic and it would be a mistake to conclude that the psychosocial or educational experience of those who have been medically evaluated will be typical of those in the general population. On the contrary, they are likely to be those who are (or who are perceived to be) experiencing the greatest educational or behavioural difficulties. So, where to look for the evidence?

The Wessex Growth Study (WGS), a prospective cohort study, was unique in having recruited an unselected population of short, but otherwise healthy children (56). Children with known organic disease were excluded, the age range lay within a tight band, a wide range of socioeconomic classes was represented and the study incorporated case matched controls of average stature. Psychometric testing was largely based on well validated and standardised tests. In this community-based study,

few differences were found between the short children and their controls. As others have shown (46), the shorter children, when asked, said they would have preferred to be taller. Although mean IQ between the short and control groups in the WGS was significantly different, height, on its own, explained only 2% of the variance in IQ, emphasizing the need always to look beyond *P* values and consider effect size (57).

The WGS was the first study to look at both victims and bullies in the context of physical stature (58). It confirmed that bullying was widespread, regardless of stature, but noted a significant difference between short children and their controls. It is possible that short pupils may simply perceive that they are more bullied, mistaking the normal rough and tumble of the playground for bullying. However, these data could also be explained by the fact that significantly fewer of the controls admitted to being bullied, in spite of the fact that their parents complained that they were. More short pupils did, nevertheless, report a degree of social isolation, perhaps the result, but equally likely the cause of their being bullied. None of the above, however, had a measurable effect over the years on school performance or self-esteem (48, 59). As Illich has claimed, one aspect of good health is to be 'successful in coping with reality' (60).

In summary, the WGS has shown no evidence of maladaptation or psychosocial dysfunction, before, during or after puberty, in these youngsters who were, by current standards, very short indeed (61, 62). What the study clearly showed was that socioeconomic factors, rather than stature, best predict psychosocial and academic outcome. In one recent study of a large cohort of Swedish conscripts, poorer health, more psychological problems and a lower mean intellectual performance in those with a height more than 2 s.d. below the mean were reported. Crucially, however, no correction was made for social background (63).

Other studies have followed confirming the inherent bias in clinic-based samples. Busschbach *et al.* compared adults with idiopathic SS, who had presented as children to a paediatric clinic, with equally short adults sampled from the population (64). The former clearly had poorer coping skills, and claimed that the social disadvantages of SS dominated their social interactions. The latter showed no impairment in their QOL. Kranzler *et al.* directly compared three groups: referred and non-referred children with SS and case controls of average stature (65). The referred SS group exhibited significantly more behaviour problems than the non-referred SS group, who were indistinguishable from controls. The authors concluded that the discrepancy between earlier and more recent research could be explained by participant selection bias. Finkelstein and colleagues examined the leisure behaviour of three groups of adolescents: those with short stature, delayed puberty and diabetes mellitus. Their activities and experiences were no different and, indeed, were similar to

non-clinical comparison groups (66). Finally, an original and definitive large-scale community-based study has recently been reported. Using peer informants, Sandberg *et al.* were able to assess psychosocial adaptation across the range of heights in middle- and high-school students. No statistically significant relationships were found between height and measures of friendship, popularity or most aspects of reputation among peers, despite substantial statistical power. The authors concluded that extremes of stature in the general population, short or tall, have minimal impact on peer perceptions of social behaviour or acceptance among classmates. Even the very shortest children made friends and earned the respect of their peers as well as any other (67).

Does GH make a difference?

Papers continue to appear in the literature purporting to demonstrate the benefits of growth hormone (GH) therapy. The evidence, however, rarely extends beyond an apparent gain in final height (68). The corollary of the assumption that SS is disadvantageous is that the addition of a few centimetres must help psychosocial functioning. In a recent survey in the US, 32% of physicians believed that GH makes a difference and that an increase in height will improve the QOL in non-GHD SS (27). Blethen assures that 'other benefits of GH therapy include improvement in psychosocial functioning' (69), yet there is no rigorously controlled study to show a benefit from so doing.

In one widely quoted study, the benefits of GH could have been explained by regression towards the mean (70). As Sandberg has remarked, changes observed in the treated group were not compared with changes seen over the same period in a sample with similarly elevated baseline scores (71). Theunissen recently looked at QOL and self-esteem in children diagnosed with ISS and found them largely comparable to population norms (72). Moreover, despite an increase in height in those randomly treated, there was no clear improvement in measures of psychosocial adaptation compared with untreated controls. The paediatrician reported an improvement, the parents no change, and the children either no change or a deterioration. In a retrospective study of two groups of adults with ISS, no differences were seen in educational level or QOL between those who had received GH in childhood and those who had not. Unexpectedly, the untreated group was more likely to report having a romantic partner (73).

In the only randomised, double blind, placebo controlled study of the psychosocial effects of GH in ISS, the psychosocial adaptation and self esteem of the GH-treated youngsters were comparable to that of the placebo group at baseline (74). Interestingly, relatively taller children showed more emotional problems at baseline than the very shortest, replicating an earlier

finding by this group (52). During the first 2 years of treatment, no significant differences in psychosocial adaptation between the two treatment arms were detectable. At no point did measures of self-esteem differ, but in the fourth year, parents reported significantly more behaviour problems in the placebo-treated group. Nevertheless, no systematic relationship was observed between change in height and change in psychosocial adjustment.

Finally, where there is no GHD, the outcome of GH treatment is generally not very dramatic in terms of centimetres gained and in ISS is largely unpredictable (68, 75, 76). Nevertheless, it has been claimed that parents, and their children, usually regard the immediate psychological benefits of a short-term increase in growth rate as justifying the treatment, even if the long-term improvement is minimal (77), but there is little evidence to support this notion from the few longitudinal trials to include a psychometric assessment (78–80). In summary, most commentators agree that GH treatment of ISS or short normal stature cannot be justified (5, 81, 82).

Ethical issues

The ethical problems associated with attempting to enhance the stature of a short, but otherwise healthy child have been well rehearsed (83). Not least is that by increasing the height of all those below an arbitrary percentile, we inevitably leave a new group below that cut-off. As Freemark has pointed out, this may be the only circumstance in which treatment of one group of children creates illness in another previously healthy group (3). Routine growth screening may be of value if it facilitates the detection of previously undetected pathology, but most short children thus identified will have no obvious pathology (84). Care must be taken to reassure them that they are indeed healthy and normal. Importantly, it had been demonstrated that perceived height is a better predictor of psychosocial adaptation than measured height (85).

Pressure to treat may come from sources that are not in the child's best interests. Whenever investigators are funded to discover new indications for a drug, commercial pressures inevitably come into play (86). Indeed, the cynical view would be that shortness only became a disease when a treatment became available (83). As Gill reminds us, terms such as 'short normal stature', 'normal variant short stature' and 'familial short stature' have been around for a while. ISS, on the other hand, is a relatively recent concoction and implies that these children are suffering from some, as yet, undiagnosed endocrine disorder (5). He notes that the term does not appear in the index of any of the large standard paediatric text books, in the UK or the US.

Demands for treatment may also be motivated, less by concern for the children, than by aspirations of their

parents. Some, including those with children well within the normal range for height, may seek GH therapy because they perceive tallness to be desirable and wish to give their own offspring a perceived advantage in life by enhancing what are essentially normal physical characteristics (87). The danger here is that any attempt by parents to modify their child's appearance may signal tacit disapproval and lead them to feel unacceptable as they are (88). Children as well as parents can also overestimate the potential for final height, leading to disappointment and perceived treatment 'failure' (85, 89).

A further consideration is the long-term safety of recombinant human GH, which has yet to be established, especially when given in supra-physiological doses effects (90, 91). Although few adverse events have been documented to date, the increase in incidence of type-2 diabetes recently reported in children is one concern (92). Young children do not understand the risks and benefits of therapy and cannot give valid, informed consent or even assent (93).

There is a serious economic consideration as well, with estimates from €50 000 to €75 000 for a course of treatment to more than \$35 000/inch (\$14 000/cm) (5, 76). There is a clear argument for not spending limited resources on expensive, so-called 'cosmetic endocrinology', when there may be cheaper (albeit largely untried) options (5, 75, 94). Moreover, if treatment becomes an option available only to those who can afford to pay, social injustice inevitably follows by selectively allocating morbidity to poor children (93).

Central to the ethical argument is the notion that most of the short children are indeed normal and, as such, do not require growth-promoting drugs. However, the term 'normal' is no longer simply descriptive, showing us what is, in the sense of usual or typical. It has become prescriptive, telling us how things ought to be (83). As Illich has warned, 'Society has become a clinic, and all citizens have become patients whose blood pressure is constantly being watched and regulated to fall within normal limits' (60).

Conclusion

The continuing widespread use of GH risks perpetuating a climate of opinion where SS is unacceptable, both to parents and society, and is likely to lead to a spiralling demand for what is increasingly becoming a lifestyle drug. There remains a wealth of literature, in both the medical and the popular press, warning physicians and parents alike of the difficulties that the short individual might expect to encounter and a real danger of these publications themselves creating anxiety in those who were previously unconcerned.

There is no compelling evidence to show an association between short stature and cognitive and psychosocial maladaptation or dysfunction. Any

problems, academic, behavioural or psychological, that a short child might meet in life are not necessarily attributable to short stature. There is an urgent need to redress the balance with this more positive message. Parents and children alike should be reassured by these findings.

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Received 28 April 2006

Accepted 20 July 2006