

Growth hormone

Do we have a national perspective of indications for its use?

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ABSTRACT

Objective: Presentation of indications for growth hormone use in children, from the view of physicians practising in Saudi Arabia.

Methods: A questionnaire containing a list of common possible indications of growth hormone use was collected from 52 physicians practising in Saudi Arabia who were attending a didactic endocrinology course.

Results: All (100%) physicians considered growth hormone deficiency to be an indication. Sixty four and 29% considered Turner's syndrome and chronic renal failure to be indications. Other indications included Russell-Silver syndrome in 23%, X-linked hypophosphatemic rickets in 10%, Achondroplasts in

10%, Sickle cell anemia in 10% and Barter's syndrome in 2%. Genetic and constitutional short stature were considered in 17 and 19%. Only 65% did not advocate the use of growth hormone for short non-growth hormone-deficient children.

Conclusion: Indications of growth therapy are not clearly defined in Saudi Arabia. It is indicated to define this by a clear, national decided criteria which should take into consideration the internationally approved indications, availability and cost of this hormone.

Keywords: Growth hormone, use, national.

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Since 1985, synthetic growth hormone has become more available through deoxyribonucleic acid molecular engineering technology.^{1,2} With this increased availability, although expensive, more physicians have access to its use even in the absence of clear guidelines towards its indications. Abuse or overuse is, therefore, a continuing concern.³ The practicing physicians were trained in different programs and represent heterogenous schools of medicine. It has therefore become natural to have different views of management particularly in a controversial and unsettled issue like growth hormone usage.

Methods. A questionnaire was distributed to 104 physicians attending a one-week course in

Endocrinology organized by the Postgraduate Center of the College of Medicine, King Saud University, Riyadh, Saudi Arabia. They practice in various levels of function and have different years of experience, qualifications and backgrounds. The questionnaire was distributed and collected before lectures about issues on growth disorders and growth hormone were given. The questionnaire included items on speciality, rank of function, years of experience, degree obtained, and whether there are other practicing physicians in their area who may also be dealing with growth disorders and growth hormone dispensing. Questions were then addressed as to whether physicians prescribe growth hormone for the listed indications. The issue of growth hormone use for short non-growth hormone deficient children was addressed.

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Results. Fifty-two physicians completed the questionnaire of whom 37 (70%) were males. The majority were pediatricians 25 (48%), 19 (39.5%) were internists and 8 (15%) were of other specialities or of undisclosed speciality. The experience of these physicians since the date of their latest qualification was less than 2 years in 5 (10%), 2-5 years in 16 (31%), 5-10 years in 9 (17%) and more than 10 years in 9 (17%). Twenty-three (44%) stated that they are able to use growth hormone in their practice. Indications for growth hormone use in the view of the 52 physicians is shown in Table 1. Only thirty-four (65%) did not advocate the use of growth hormone for short non-growth hormone deficient children.

Discussion. In this study, we present the indications of growth hormone therapy in the opinion of 52 practicing physicians attending a didactic endocrinology course. Growth hormone is not always available in every center. However, when it is available, there are no clear regulations on how and to whom it should be dispensed. The indications are left in the hands of the practicing physicians. One hundred percent of the physicians in this series considered appropriately that growth hormone deficiency is the main indication for growth hormone prescription. The case was not as clear for the less recognized indications i.e. Turner syndrome and chronic renal failure. The fact that children with these disorders, are usually managed by pediatricians, more pediatricians (100% for the former and 40% for the latter) considered them as

indications for its use compared to internists (10.5% and 10.5%). These 2 indications were the second and third next to growth hormone deficiency especially in the opinion of pediatricians which is appropriate. Growth hormone deficiency, Turner syndrome and chronic renal failure are accepted indications.^{4*} In Turner syndrome, ultimate adult height improved from 142.5 cm to 151 cm when growth hormone was used.⁷

Growth hormone has also been used in many other conditions where it improved linear growth over a short-term basis but studies failed to show long term benefits. These conditions include Russell-Silver syndrome, X-linked hypophosphatemia rickets, Achondroplasia, Sickle cell anemia and Barter's syndrome.^{9,13} This therefore, may have influenced the practicing physician's views in taking it as a recommended proven value. Twenty-three percent of responders advocate use of growth hormone in Silver-Russell syndrome despite lack of evidence of long-term benefit. There are single reports of the use of growth hormone in Silver-Russell syndrome which is not sufficient in the view of the authors to put this as the next common indications. X-linked hypophosphatemic rickets is a condition characterized by short stature, rickets and hypophosphatemia. Stature usually improves with phosphate replacement. Growth hormone however, has been advocated for this condition without proof of long term benefit.⁹ Achondroplasia is another condition which attracts the attention of growth hormone users with controversial benefits only on a short term basis.^{10,11} Barter's syndrome is a

Table 1 - Indication of growth hormone prescription in the view of the 52 physicians and breakdown of the number and percentage as per their speciality (others include physicians of other specialities or who did not disclose their speciality).

Indications	Number and percentage of total physicians	Number of pediatricians (%)	Number of internists (%)	Others (%)
Growth hormone deficiency	52 (100)	25 (48)	19 (36.5)	8 (15)
Turner syndrome	33 (64)	25 (76)	2 (6.0)	6 (18)
Chronic renal failure	15 (29)	10 (67)	2 (13.0)	3 (20)
Russell Silver syndrome	12 (23)	5 (42)	3 (25.0)	4 (33)
Constitutional short stature	10 (19)	5 (50)	4 (40.0)	1 (10)
Genetic short stature	9 (17)	1 (11)	7 (78.0)	2 (22)
X-linked hypophosphatemic rickets	5 (10)	3 (60)	1 (20.0)	1 (20)
Achondroplasia	5 (10)	3 (60)	1 (20.0)	1 (20)
Sickle cell anemia	5 (10)	2 (40)	1 (20.0)	2 (40)
Barter's syndrome	1 (2)	1 (100)	0 (0.0)	0 (0)

condition which leads to short stature. Isolated reports of growth hormone benefit have been postulated. This, however, does not dictate its use.¹² There may be local studies of growth hormone status in sickle cell anemia but its long term benefits are awaited.¹³ Despite the smaller percentage of participants considering these to be indications of growth hormone use compared to the previously discussed indications, the number are worrisome especially among pediatricians.

The ultimate adult stature in constitutionally short children is normal. Growth hormone should therefore bring no benefit towards the normal ultimate adult height. The hypothesis that short term benefit may improve the self image of these children awaiting scientific well controlled studies. Genetic short stature is certainly not an indication to use growth hormone. Unfortunately, 19% and 17% of the responders advocated growth hormone for these entities.

Participants are not considered a representative sample of all practicing pediatric endocrinologists. They are, however, practicing physicians who deal with growth disorders in their clinics and 44% of them have access to dispense growth hormone for their patients.

We feel that the growth hormone indications should be restricted to proven growth hormone deficiency, Turner's syndrome and chronic renal failure. Use of growth hormone for other conditions should be limited to experimental well-controlled studies which should clearly show long-term advantage. Using growth hormone for short non-growth hormone is not an indication. However many participants in this study advocated its use for this indication. If growth hormone supply is feasible and accessible to physician and parents, more numbers of short children may unnecessarily be treated with growth hormone. The data presented is worrisome as many responders advocated growth hormone use for children with genetic and constitutional short stature. Furthermore, only 65% did not advocate its usage for short non growth hormone deficient children. This study falls short of including usage of growth hormone in the adult population. If this was included, more unclear indications would have been added. This deserves further studies which emphasize the importance of controlling growth hormone prescription for the internationally accepted indications namely growth

hormone deficiency, Turner's syndrome and chronic renal failure.

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