Growth modulation in the management of growing spine deformities

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Abstract The Hueter–Volkmann law explains the physiological response of the growth plate under mechanical loading. This law mainly explains the pathological mechanism for growing long-bone deformities. Vertebral endplates also show a similar response under mechanical loading. Experimental studies have provided information about spinal growth modulation and, now, it is possible to explain the mechanism of the curvature progression. Convex growth arrest is shown to successfully treat deformities of the growing spine and unnecessary growth arrest of the whole spine is prevented. Both anterior and posterior parts of the convexity should be addressed to achieve a satisfactory improvement in the deformity, albeit epiphysiodesis effect cannot be stipulated at all times. Anterior vertebral body stapling without fusion yielded better results with new shape memory alloys and techniques. This method can be used with minimally invasive techniques and has the potential advantage of producing reversible physeal arrest. Instrumented posterior hemiepiphysiodesis seems to be as effective as classical combined anterior and posterior arthrodesis, where it is less invasive and morbid. Convex hemiepiphysiodesis with concave-side distraction through growing rod techniques provide a better control of the curve immediately after surgery. This method has the advantages of posterior instrumented hemiepiphysiodesis, but necessitates additional surgeries. Concave-side rib shortening and/

or convex-side lengthening is an experimental method with an indirect effect on spinal growth. To conclude, whatever the cause of the spinal deformity, growth modulation can be used to manage the growing spine deformities with no or shorter segment fusions.

Keywords Scoliosis · Growth modulation · Growing spine

Introduction

The treatment of the growing spine deformities are challenging. One who wants to treat the growing spine must appreciate the principles of normal growth and biomechanics. Spinal column growth occurs in all three dimensions. Ninety-five percent of the adult spinal canal size is achieved by the age of 5 years. The vertebral body grows similarly to a long bone: ossification starts posterior, then radiates cranial and caudally, and finally fully ossifies after the age of 25 years [1].

Scoliosis is a three-dimensional deformity of the spine with lateral flexion, lordosis or kyphosis, and a rotational component. Idiopathic scoliosis, specifically, is enigmatic, as it develops as the normal spinal alignment deteriorates over time due to an unknown mechanism that, ultimately, produces a curve. The concave side of the apical vertebrae becomes shorter than the convex side to produce wedging [2–4]. The Hueter–Volkmann law, which is primarily applicable to the long bones, indicates that the concave side of the deformity undergoes non-physiological loading, and this produces a suppression of the growth at the physis [5]. Treatment modalities based on the Hueter–Volkmann law have been successfully used for many years in the management of long-bone deformities. The concept for the

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Fig. 1 Experimental study showing the effect of passive tethering across rabbit proximal tibial physis. Radiographs of a rabbit at the beginning of the experiment (a), at the end of 3 weeks (b), and at the end of 6 weeks (c) following implant removal. Passive tethering across the growth plate produces significant deformity, then it is fully reversed following cessation of the tethering effect. (From reference [6] with permission)

management of long-bone deformities rely on passive tethering. Convex-side tethering is produced via implants not by producing a compression but, rather, passively obscuring the vertical growth at the convexity [5, 6] (Fig. 1). Smith et al. adapted this passive tethering to the spine via anterior stapling, but the results were not satisfactory mainly due to inappropriate implant designs. This work was laid aside for many years [7]. Recent studies, however, have elucidated the vertebral growth mechanisms and pioneered more secure implant designs, which have made the growth modulation concept popular once again [8–11].

Basic principles of growth modulation

Scoliotic deformities, independent of etiology, show more of a progression during the skeletal growth period [12, 13]. Mechanical modulation of the endochondral growth yields angular deformity that may end up with an enhanced loading of the endochondral growth, thus, creating a vicious cycle. Hueter, Volkmann, and Delpech defined the principles for this process and the law of Hueter–Volkmann explains the pathomechanism of weight-bearing bone deformities in childhood. Although this law seems to apply to the appendicular bone deformities, it may also be applied to the growing spine deformities. The concave side of the curve undergoes non-physiological compressive forces, which suppress vertebral growth at the concave side. We do not know the exact initiator of the vertebral load imbalance which leads to asymmetrical distribution along the endplate and causing growth asymmetry [5].

Experimental research on spinal growth modulation

Growth modulation is used to produce spinal deformities in animal models and in the treatment of these deformities.

Modulation of the vertebral growth can be performed directly through interfering with neuro-central cartilage (NCC) or vertebral endplates and indirectly through rib cage procedures.

Neuro-central cartilage-related growth modulation

NCC growth asymmetry leading to pedicle length asymmetry was thought to be the initiator of the imbalance in vertebral column load distribution. Pig models showed that NCC epiphysiodesis affects pedicle growth and yields smaller pedicles and canal area. It is known that the cross-sectional area of the pin crossing the physis is important for the occurrence of physeal arrest and these studies showed that NCC arrest occurs when the pin cross-sectional area occupies 20% of the physis [14–16] (Fig. 2). The NCC growth asymmetry yields an axial deformity which may trigger a three-dimensional deformity. It was shown that pedicle screw-induced NCC epiphysiodesis in porcine vertebrae yields scoliosis with convexity on the instrumented side [17]. Pathogenesis studies gave a rise to the idea that a shift or rotation of the eight thoracic vertebrae, which may be due to a shorter pedicle, would be responsible for the asymmetry [18]. However, biomechanical spine model studies found no correlation with the short pedicle and spinal deformity [19].

Endplate-related growth modulation

Vertebral endplates are responsible for the longitudinal growth of the spine. As vertebrae grow in length, anterior and posterior elements show a difference in growth pattern, which leads to the physiological curvatures in the sagittal plane [1]. Adams put forward the theory that this physiological growth pattern difference may be disturbed and produced buckling and rotation, which are two components of scoliosis [20]. It was then speculated that buckling-

Fig. 2 Canal asymmetry following the neuro-central cartilage (NCC) growth arrest of the porcine spine. Unilateral pedicle screws applying compression on the NCC of immature porcine spine (**a**, **b**) yields smaller pedicle and hemi-canal area after 4 months. (From reference [15] with permission)

lordotic deformity was followed by rotation of the spinal column, which resulted in three-dimensional deformity of the spine [21–24]. Porter claimed that smaller canal length compared to anterior spinal length yielding spinal buckling via posterior canal tethering was the key mechanism to spinal scoliosis [25]. Vertebral wedging at the scoliotic segments became the interest of research and it was found that wedging was mainly in the frontal plane and was seen mostly at the apex of the curve. Height was mostly

diminished at the concavity site [26, 27]. Stokes et al. stated that, whatever the initiator mechanism of the asymmetrical loading, a vicious biomechanical cycle is created and results in a progressive deformity. Deformity induces non-physiological, increased loading on the concave (short) side that leads to more suppressed growth and, in turn, on the concave side. Stokes et al. also put forward the concept of vertebral symphyseal dysplasia, which starts the vertebral wedging and feeds forward the vicious cycle of asymmetrical loading-induced growth arrest [5, 28].

Mechanical loading studies on long bone and vertebral physis revealed that full-time loading was more effective in the suppression of growth compared to intermittent loading. Further work investigated the histological changes at the growth plate under mechanical loading. The results showed that: (1) growth suppression or induction following mechanical loading/distraction was related to the number of proliferative chondrocytes per unit width of growth plate, and (2) the final chondrocytic height in the hypertrophic zone and chondrocytic enlargement gave a greater contribution to the altered growth rates [29, 30].

Blount was the pioneer who defined the growth modulation concept for the treatment of long-bone angular deformities in the 1940s [31]. Logic behind the long-bone deformity treatment concept could have been applied to the spinal deformities. It was stated that convex-side compression would result in the improvement of scoliotic deformity. Smith used bone staples to achieve compression, whereas others criticized that bone staples were not suitable for the cancellous vertebral bone [32, 33].

Spinal growth modulation is studied in bovine models and antero-lateral tethering with a body screw and flexible cable system yielded scoliosis with concavity on the implantation side. Asymmetrical spinal segment motion was noted as well. Furthermore, for a single tethering system and a double tethering system applied antero-laterally in a bovine model, a significantly greater scoliotic deformity in the double tethering group and a kyphotic deformity in both of the experimental groups were reported [34, 35].

A goat model was also successful in producing scoliosis by the application of either flexible or rigid asymmetric tethering systems, together with convex-side rib resection. This led to wedging at the apical vertebrae, which can be explained by the Hueter–Volkmann law. Shape memory alloy staples were tested in the rigid tethering model for anterior fixation and reversal of the curvature. A correction in moderately severe type scoliosis and a halting in the progression of a more malignant fusion were reported. Convex-side growth was retarded and concave-side growth was accelerated. Stapling resulted in growth modulation on both concave and convex sides. In addition, apical vertebral wedging was improved when compared to untreated

groups. Staple back-out rates were reported to be 27%. Histological and biological analysis revealed significant differences among groups [36–41]. Endoscopic spinal hemiepiphysiodesis, via custom spine staples, was performed in pig vertebrae and was shown to modify the spinal growth effectively. No staple back-out was reported [42].

Asymmetrical static loading rat tail was shown to create vertebral wedging [29]. Subsequently, a new technique was established that produced dynamic loading on the rat tail vertebrae and studies revealed that dynamic loading induced a more potent growth modulation compared to static loading [43]. A greater effect on the gene expression of aggrecan and collagen type II with dynamic loading was reported [44].

Posterior tethering without fusion was studied in a sheep model as well. It was found that significant sagittal plane deformity was experienced following posterior tethering. Facet joint stiffness was also noticed in both instrumented and non-instrumented segments due to heterotrophic ossification [45].

Shape memory alloy implants have experimental applications in posterior systems. Nitinol is a nickel titanium alloy which has a shape memory. Six-millimeter Nitinol rods are used in an experimental study to correct scoliosis of a goat model. Scoliosis correction in goats is shown to be effective. The technique provided neurological monitoring during correction. Forces transmitted to the spine can be estimated by the amount of rod curvature and temperature. The technique seems to be effective, but clinical studies are needed to confirm the findings [46].

Rib procedures for spinal growth modulation

The thoracic cage is composed of the sternum, ribs, and the vertebrae; thereby, scoliosis should be considered as a complex deformity of all of these structures. Ribs act as a bridge between the posterior and the anterior cage and, therefore, may have a role in the growth modulation of the vertebrae through costo-chondral and costo-vertebral articulations. Kawakami et al. postulated the effect of ribs on spinal growth modulation by reporting spinal deformity development in patients following several rib resection surgeries. They then described a chicken scoliosis model created by rib resections [47, 48]. Rib procedures are studied in scoliosis etiology and rabbit scoliosis models with intercostal nerve denervation leading to convex-side short-rib scoliotic curves being reported [49, 50]. A biomechanical study utilizing a finite element model to evaluate the effects of concave- and convex-side rib procedures reported that convex-side lengthening or concave-side shortening improved the thoracic and lumbar curves [51].

Clinical application of spinal growth modulation

Principles of growth modulation can be used to treat spinal deformities. As the spine has the most growth potential until the age of 5 years, early-onset scoliosis patterns can be treated with the similar philosophy of long-bone deformity treatment. The growth potential of the retarded side and the efficacy of the mechanical suppression force applied to the near-normal or normal growing site affect the outcome of the technique. Convex growth suppression with or without concave-side distraction and convex-side fusion may be the alternative method of choice.

Smith et al. reported the results of convex-side growth arrest via stapling. They did not report improvement with the stapling technique, presumably due to weak cancellous bony structure of the body that might not be able to conduct a compressive force over the vertebral endplate [7]. Another probable explanation may be that a lower growth rate of the vertebrae was experienced compared to the long bones. Thus, the staple technique was inspired from the long-bone deformity treatment via staple-induced passive tethering and growth modulation. Therefore, convex growth arrest (CGA) has gained popularity against staple epiphysiodesis over time.

Anterior vertebral body stapling has been popularized by Betz et al. after previously disappointing clinical experiences. Theoretically, convex apical vertebral body stapling produced acute and probably reversible suppression of anterior growth. Nitinol staples were used and promising results were reported by Betz et al. [10, 11]. Nitinol staples are composed of a shape memory nickel titanium alloy. The staple prongs are straight when cooled, and clamp down into the shape of a “C” when warmed to body temperature [8]. A biomechanical study evaluating spinal flexibility following Nitinol staple instrumentation revealed that staples significantly limited the motion of the spine, especially in the axial and coronal planes [9]. First, large clinical series on anterior vertebral body stapling revealed promising results and the authors claimed that the technique was feasible, safe, and successful in controlling the curve. Patients were not brace-compliant and deformities were progressive. Almost 90% of the patients older than 8 years of age and with curves less than 50° showed as small as 10° of curve progression. The surgical indications may be summarized as age less than 13 years in girls and 15 years in boys, along with Risser 0 or 1 and/or 1 year of growth remaining on the wrist radiograph. Ideal deformities seem to be the curves of less than 45° with minimal rotation and flexibility to less than 25° on bending radiographs. Sagittal plane deformities should not exceed 40°. Early results are encouraging [10, 11].

Rib procedures are also performed during the management of the growing spine deformities, mainly for cosmetic

Fig. 3 Convex growth arrest in the treatment of a complex congenital anomaly. A 3-year-old female patient with congenital scoliosis is presented. The Cobb angle is 40° preoperatively (**a**). The curve

regressed to 20° (**b**) in two years. Lateral X-rays show improvement in the sagittal deformity at follow-up (**c, d**)

reasons. However, lengthening of the convex side and/or shortening of the concave side may change the load distribution along the vertebral endplates because the rib cage acts as a bridge for the forces to be transferred from the sternum to the spine. These forces are thought to be affective in the growth modulation of the spine [51]. Rib procedures have been shown to be effective for delaying fusion procedures of the spine. Xiong and Sevastik reported good results of concave-side rib shortening in a 6-year-old female idiopathic scoliosis patient [52].

The CGA procedure based on this concept has been popularized due to its safety, efficacy, and simplicity compared with other surgical alternatives [53–58]. The original technique described by Winter [53] and Andrew and Piggott [57] consists of anterior and posterior interventions to the spinal column. In 1963, Roaf reported his surgical technique and results with unilateral growth arrest for congenital scoliosis. Combined convex anterior and posterior growth arrest has been used in patients with congenital spinal deformity. This technique has helped suppress the progression to, in turn, improve or even correct the deformity with residual growth potential of the spinal column. According to the theory, control of the relatively longer convex-side growth would stop the progression and may even lead to a spontaneous correction with the help of the growth potential of the concave side [51].

Roaf and Piggott reported results of anterior and posterior convex hemiepiphysiodesis for congenital scoliosis; the rate of change of the Cobb angles were decreased, but not reversed, when deformity was due to an unsegmented bar. For complex anomalies, they reported an increase in the final Cobb angles. The rate of progression reversed or decreased in 97% of the hemivertebra patients. Moreover, lumbar anomalies and younger patient age resulted in better corrections [53, 59].

Uzumcugil et al. reported the results of anterior and posterior approaches in 32 patients. Forty-one percent of

the patients had true epiphysiodesis effect (Fig. 3), 47% of the patients had fusion, and only 12% of the patients showed an increase in the curvature in an average follow-up of 40 months. The authors also reported that anomalies of hemivertebrae, instead of unsegmented bars, had better outcomes. Unsegmented bar is believed to obscure the growth of the concavity. On the other hand, it has also been shown that fusion of one upper and one lower segment of the bar may result in an improvement of the deformity [60].

To achieve a successful CGA, the preoperative curve magnitude was reported to be less than 50–60°, whereas there are other studies showing that curves less than 70° also have favorable results. The best results were reported with curves that affect five consecutive segments or less [55–57]. On the other hand, longer curves have been successfully treated with CGA as well [60]. The upper age limit set for an effective CGA was reported to be 5 years, since 95% of the vertebral growth occurs before this age. However, the procedure is shown to be effective in children older than 5 years of age without signs of advanced skeletal maturity [55–60]. CGA is accepted as a safe procedure that generally does not result in serious complications, except for infections (wound or chest) and traction neuropathias of either the intercostals or thigh cutaneous nerves, which are related to anterior surgery. More significant problems include unpredictability of the curve behavior after the procedure and incapability to control the spinal balance, which is very important [60].

Cheung et al. reported their results using convex hemiepiphysiodesis with concave-side distraction. They suggested that this procedure could be recommended for children with severe deformities and decompensation in the lower thoracic spine. Distraction of the concavity produces immediate improvement in the coronal balance, such that there is no need to wait for uncertain growth-mediated correction in patients who undergo only convex fusion [61].

Fig. 4 Instrumented convex hemiepiphysiodesis in congenital spinal deformity. The preoperative radiograph shows the complex congenital deformity (**a**). Deformity improvement following epiphysiodesis effect is observed (**b**). Although posterior convex fusion was performed alone, convex side disc spaces were not visible in the follow-up radiographs, probably due to spontaneous anterior fusion (**c, d**)

Another modification that has been proposed by the Hacettepe group is the addition of posterior instrumentation with transpedicular screws [62] (Fig. 4). Specifically, transpedicular screws were shown to control the growth of the vertebral column in both longitudinal [15] and transverse planes [63] in animal studies. Transpedicular screws were placed in all of the vertebrae that were fused to

eliminate the need for an anterior surgery and acute compression–rotation maneuvers were employed to correct the deformity in ten patients. Added posterior instrumentation provided an initial correction, thereby, decreasing the unpredictability of the curve. This procedure controls the progression of the curve and provides a correction of the deformity, although trunk balance is not achieved in every

Fig. 5 Instrumented posterior convex hemiepiphysiodesis with concave-side distraction. Preoperative radiograph of a 1.5-year-old female (**a**). Complex deformity is managed with instrumented posterior convex hemiepiphysiodesis (**b**). Concave-side distraction is added to the hemiepiphysiodesis to obtain better trunk balance. Later distraction procedures will help maintaining the correction (**c**)

Fig. 6 Growth stimulation effect of the growing rod technique. Eight-week-old domestic pigs underwent posterior growing rod instrumentation. When preoperative (a), postoperative (b), and following the third operation radiographs are compared, the vertebral

height is showed to be increased compared to preoperative measures and distracted vertebrae yielded increased height compared to uninstrumented segments (c)

case. Therefore, recently, concave distraction without fusion has been added to convex compression and fusion as it might better achieve trunk balance in patients (Fig. 5).

Growing rod and vertical expandable prosthetic titanium rib are recently developed techniques used in early-onset scoliosis treatment. These methods produce distractive forces on the deformity and primarily aim to let the spine grow while correction of the deformity is maintained. Both techniques produce distraction temporarily; we assume that these distractive forces have a growth-stimulant effect [64–69]. This growth-stimulant effect has not been proven clinically, but supporting experimental data is available [70] (Fig. 6).

Conclusion

Experimental studies have proven that spinal deformities can be produced and treated by means of growth modulation. Clinical trials show that the new techniques are promising; however, well designed new clinical studies are needed to support the use of growth modulation as a standard treatment philosophy.

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