

### Article 3

## Role of Growth Modulation in the Management of Idiopathic Scoliosis: A Narrative Review of literature

**Key words:** Idiopathic Scoliosis, Growth Modulation, Spinal Deformity, Lateral Bending

### Abstract

Scoliosis is a condition in which there is a lateral curve to the spine. The cause of scoliosis is unknown, but different aetiologies have been suggested, but mostly cause has been idiopathic in nature. Muscle spasms, cerebral palsy, Marfan syndrome, and tumours (neurofibromatosis) are some of the suggested aetiologies. Progressive adolescent idiopathic scoliosis (AIS) affects mainly girls and anterior spinal overgrowth during the second growth spurt appear to be a significant cause.<sup>1</sup> The diagnosis of scoliosis is primarily a clinical suspicion followed by an AP and lateral X ray of spine in standing position. Measurement of the Cobb angle is the standard method of assessing the curvature in a quantitative manner. It is the angle between two lines, drawn perpendicular to the upper endplate of the first vertebra involved and the lower endplate of the last vertebra involved. Cobb angles are followed for both curves for those with two curves. Risser classification grades the skeletal maturity on X rays and is considered along with the Cobb angle to making a decision towards surgery.<sup>2</sup> Indications for surgical correction of scoliosis is not clearly defined however, the treatment of scoliosis is based on the severity and progressive nature of the curve. Cobb angle above 40 degrees, rapidly progressing curve, major thoracic deformity affecting the function such as breathing and cosmetic reasons, are some of the indications for surgery. There are several modalities of surgical correction. Main method has been correction of the deformity and fixation with one or two rods and pedicle screws followed by bone grafting. Harrington rods were the primarily used system, but with time many spinal instrumentation systems and rods have been introduced to the market. <sup>3</sup> Apart from using rods some have tried anterior vertebral body stapling and anterior vertebral body tethering for correction scoliosis using the principle of growth modulation. <sup>4 5</sup>

We conducted a systematic review to answer the question, 'What is the role of growth modulation in the management of idiopathic scoliosis?' All articles / publications published from 2010 May to 2019 October were used as research data. A health, related database (PubMed) was used for the search. Search criteria revealed 99 articles initially and 37 articles after filtered based on title reading. Then 18 articles were selected for the final analysis after being filtered manually by reading summary and abstracts of each article.

**Level of Evidence:** Level II, systematic review

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## Introduction

A condition in which there is a lateral curvature of the spine is c scoliosis. The cause of most cases is unknown, but it is said that genetics and environmental factors play a role in it. The treatment is based on the severity and progressive nature of scoliosis. Based on that there are several modalities of treatment which includes watching periodically, applying a brace and surgical correction. The surgical correction of scoliosis involves many treatment formats out of which growth modulation is considered one. The growth modulation in managing Adult idiopathic scoliosis (AIS) is based on Hunter-Volkman law 6 This law tries to explain the mechanism of scoliosis. A compressive force usually halts the growth while traction force enhances it. In the vertebral column there is anteriorly a compression and posteriorly traction force. This is a possible reason for normal AP curvatures in scoliosis and a lateral bending that is significant. However, due to rotation of the vertebra, the direction of the traction and compression forces change creating disproportionate growth of vertebrae.

Heuter Volkman law-based growth modulatory surgical techniques include use of correctional implants such as Harrington rods, anterior vertebral body stapling and vertebral body tethering.

Harrington rods are used in the correction of curvatures in scoliosis and fixation of vertebra. They can be fixed with single or double rods. It's a stainless-steel rod fitted with hooks at both ends and a ratchet and is implanted through a posterior approach. Harrington rods reduce the curvature and provide more stability to a spinal fusion. Before the Harrington rod was invented, scoliosis patients had their spines fused without any instrumentation to support it; However, disadvantages of such fusions were required many months in plaster casts, and large curvatures progressed despite fusion.

Anterior vertebral body stapling is a new non fusion technique used to treat scoliosis, especially in skeletally immature patients. This concept of stapling the growth plates in achieving curve stabilization via growth modulation is known to be an effective method. Therefore, it is used as an alternative to bracing in patients with rapid progression of the curve and for patients who might need spinal fusion in the future.

Screws placed into the vertebral body modulating the growth of concave and convex sides of the spine and curve stabilization is the technique used in anterior vertebral body tethering. It is a newer method compared to stapling and it places a compressive force over the convex side of the spine with slowing growth and permits growth of the concave side ultimately creating a straight spine.

The basic principle in spinal growth modulation involves slowing the growth on the convex side and enhancing the growth on the concave side, resulting in gradual deformity correction.<sup>5</sup> In theory advantages include early recovery ability to use minimal invasive procedures, and motion preservation. This systematic review attempts to look at the published evidence of available growth modulation techniques and instrumentations.

## Materials and methods

The objective of the study was to find out the Role of growth modulation in the management of Idiopathic Scoliosis. A detailed systematic search of the database (PubMed) was done.

### Search strategy:

The following search strategy was carried out using PubMed database. The initial PubMed search was done using the terms "Growth modulation" OR "Scoliosis" which retrieved 145114 articles. Then a filter up to 10years (2010-2019) was added to the search and it retrieved 72972 articles. When a single term "Scoliosis"

was searched the result was 10716 hits. "Growth modulation" search of the database from 2010 to 2019 gave 62355 hits. Further search continued with the terms "Growth modulation" AND "Scoliosis" with the aim of filtering the number of articles for final analysis retrieved 158 results. Further filtering the search for 10 years (2010-2019) with terms "Growth modulation" AND "Scoliosis" retrieved 99 articles.

Search: **(growth modulation) AND (scoliosis)** Filters: **from 2010 - 2019**

(((((("growth and development"[MeSH Subheading] OR ("growth"[All Fields] AND "development"[All Fields])) OR "growth and development"[All Fields]) OR "growth"[All Fields]) OR "growth"[MeSH Terms]) OR "growths"[All Fields])AND((((("modulate"[All Fields] OR "modulated"[All Fields]) OR "modulates"[All Fields]) OR "modulating"[All Fields]) OR "modulation"[All Fields]) OR "modulations"[All Fields]) OR "modulator"[All Fields]) OR "modulators"[All Fields])) AND (("scoliosis"[MeSH Terms] OR "scoliosis"[All Fields]) OR "scolioses"[All Fields])

9900:22:23#12

Search: **(growth modulation) AND (scoliosis)**

(((((("growth and development"[MeSH Subheading] OR ("growth"[All Fields] AND "development"[All Fields])) OR "growth and development"[All Fields]) OR "growth"[All Fields]) OR "growth"[MeSH Terms]) OR "growths"[All Fields])AND((((("modulate"[All Fields] OR "modulated"[All Fields]) OR "modulates"[All Fields]) OR "modulating"[All Fields]) OR "modulation"[All Fields]) OR "modulations"[All Fields]) OR "modulator"[All Fields]) OR "modulators"[All Fields])) AND (("scoliosis"[MeSH Terms] OR "scoliosis"[All Fields]) OR "scolioses"[All Fields])

15800:22:02#11

This was used as the base for our search strategy. After going through the titles of the articles We manually removed 62 articles. (24 Non-human studies, 30 Studies not related to the topic, 8 duplicate studies) .Remaining 37 articles were retrieved for abstract reading. Using our exclusion criteria, we further reduced to 18 articles. 19 articles excluded after abstract reading as per exclusion criteria. (2 studies in other languages, 2 animal studies, 11 studies which were not topic related, 4 studies, including a pilot study, observational study, cohort study and a single surgeon study) (Fig 1) in Using data extraction form which included Title, type of study, research question, publisher/journal, impact factor of the journal, authors, patients, comparison and outcome we retrieved following information from all the final 18 articles. (Table 1)

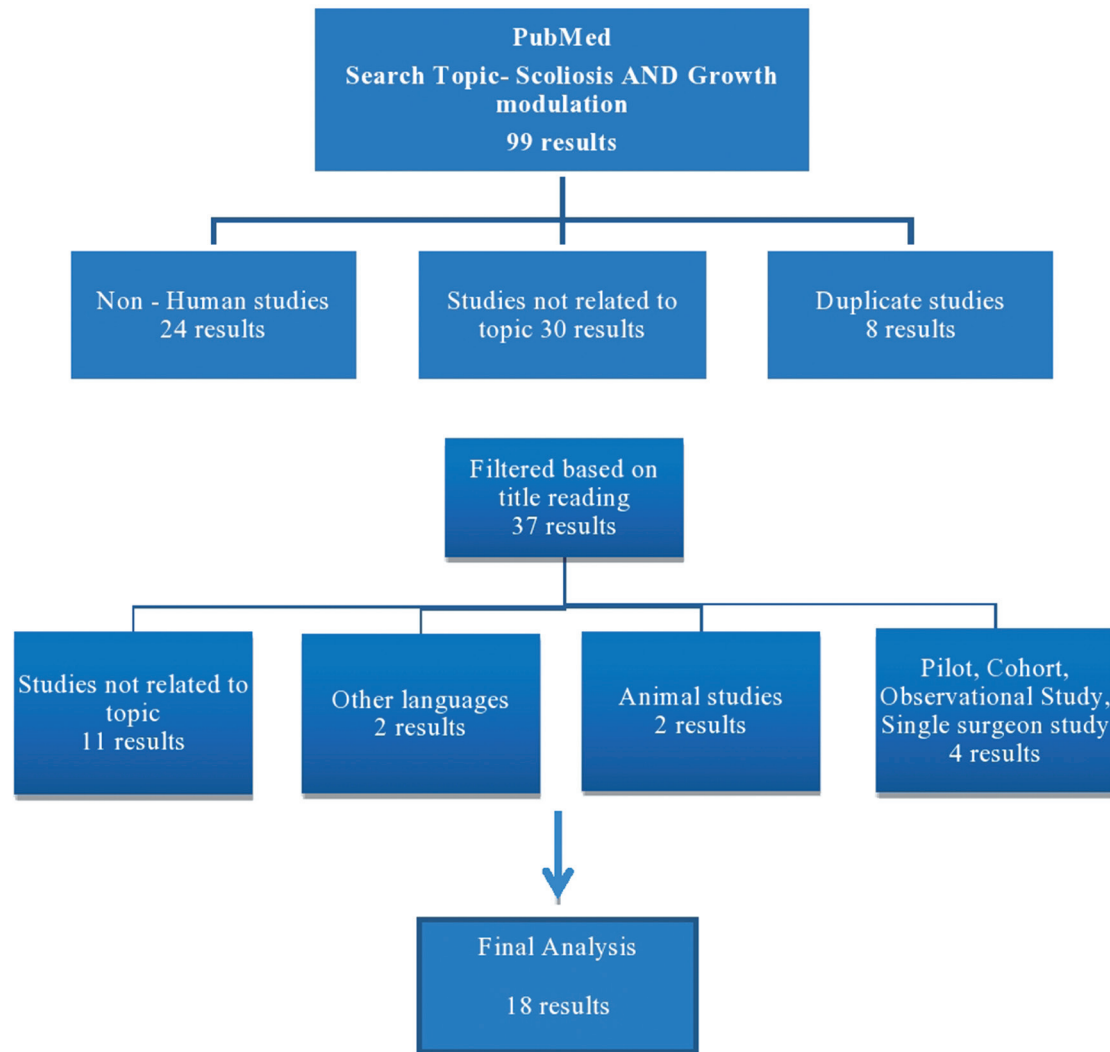
The inclusion and exclusion criteria which were used in the final selection of 18 articles are given below. (Fig 1)

### Inclusion criteria

- All articles published from 2010 May to 2019 October in the search site PubMed
- Articles published in English language
- Articles that were related to the research question

### Exclusion criteria

- All articles that were published in other languages
- All articles that were published before 2010 May and after October 2019
- Studies not involving humans
- Articles that were retrieved by the data base search, but were manually filtered reading the titles as they were not topic related
- Pilot studies, case series, cohort, observational studies and single surgeon studies were manually filtered
- Duplicate articles were removed manually.



**Fig 1** Flow chart of the search strategy-

## Results

Summary of final 18 articles are given below in table 1.

**Table 1** Summary of final 18 articles analysed

Title	Type of study	Publisher/Journal (Impact Factor)	Authors	Patients	Intervention	Comparison	Outcome Primary Secondary
1. Idiopathic scoliosis in children and adolescents: emerging techniques in surgical treatment <sup>7</sup>	Narrative review	World Neurosurgery (1.723)	Cheung et al <sup>7</sup>	Children and adolescents with idiopathic scoliosis	Emerging techniques in surgical treatment	None	Robotic-assisted pedicle screw placement, vertebral body stapling, vertebral body tethering, magnetically controlled growing rods, , and sublaminar polyester bands are the emerging techniques in surgical treatment.
2. Dynamic scoliosis correction as alternative treatment for patients with adolescent idiopathic scoliosis: A non-fusion surgical technique <sup>8</sup>	Narrative review	Zeitschrift für Orthopädie Und Unfallchirurgie (0.572)	Trobisch et al <sup>8</sup>	100 patients from different institutions	Dynamic scoliosis correction: A non-fusion surgical technique	None	Anterior dynamic scoliosis correction has promising short term results but there is a paucity of literature and optimal criteria for the best candidate has yet to be defined.

Title	Type of study	Publisher/Journal (Impact Factor)	Authors	Patients	Intervention	Comparison	Outcome Primary Secondary
3. Curve modulation and apex migration using Shilla growth guidance rods for early-onset scoliosis at 5-year follow-up <sup>9</sup>	Retrospective study	Journal of paediatric orthopaedics (2.046)	<i>Wilkinson et al</i> <sup>9</sup>	All patients with Shilla implants in place for ≥5 years yielded 21 patients	Curve modulation and apex migration using Shilla growth guidance rods	Coronal curve characteristics preoperatively, postoperatively, and at last follow-up to note changes in the apex of the primary curve.	Apex of the fused primary curve shifts in approximately 62% of patients, with nearly all of these (92%) involving a distal migration. Compensatory curves did develop after Shilla placement as well.
4. Prediction outcomes for anterior vertebral body growth modulation surgery from discriminant spatiotemporal manifolds	Narrative review	International Journal of computer assisted radiology and surgery (1.961)	<i>Mandel et al</i> <sup>10</sup>	Adolescents with idiopathic scoliosis	Anterior Vertebral Body Growth modulation	None	Achieved a higher prediction accuracy and improved the modeling of spatiotemporal morphological changes in surgical patients treated with AVBGM.
5. Anterior spinal growth tethering for skeletally immature patients with Scoliosis: A retrospective look two to four years postoperatively	Retrospective study	The journal of bone and joint surgery (4.84)	<i>Newton et al</i> <sup>11</sup>	Skeletally immature patients with thoracic scoliosis who underwent ASGT	ASGT with a minimum of 2 years of follow-up.	Skeletally immature patients with thoracic scoliosis	ASGT showed a powerful, but variable, ability to modulate spinal growth and did so with little perioperative and early postoperative risk
6. Scoliosis vertebral growth plate histomorphometry: Comparisons to controls, growth Rates, and compressive stresses	Retrospective study	Journal of Orthopaedic Research (3.14)	<i>Bylski-Austrow et al</i> <sup>12</sup>	Patients with Severe scoliosis	Hypertrophic zone heights and chondrocyte heights have been used to assess treatments that aim to modulate growth	To age matched autopsy specimens	Help assess theories of progression and potential treatments using growth modulation.
7. Thoracoscopic anterior instrumentation and fusion as a treatment for adolescent idiopathic scoliosis: A systematic review of the literature	Systematic review	Spine deformity (1.11)	<i>Padhye et al</i> <sup>13</sup>	AIS patients	Thoracoscopic anterior instrumentation and fusion	None	Advantages include less invasive, excellent curve correction, few levels fused, good satisfaction, and no long-term effect on pulmonary function. Drawbacks are, increased operative time and incidence of pulmonary complications.
8. Magnetic growth modulation in orthopaedic and spine surgery	Retrospective study	Journal of Orthopedics (1.463)	<i>Eltorai et al</i> <sup>14</sup>	Patients with the magnetically controlled growing rod system (MCGR)	The magnetically controlled growing rod system (MCGR) relative to traditional growing rod system (TGR)	To traditionally growing rod systems	MCGR is promising in that it involves less surgical procedures, shorter hospital stays, and lower long-term cost relative to TGR
9. What's new in paediatric spine growth modulation and implant technology for early-onset Scoliosis?	Systematic Review	Journal of paediatric orthopaedics (2.046)	<i>Wessell et al</i> <sup>15</sup>	Pædiatric age group with early onset scoliosis	Spine growth modulation	None	Summarizes the recently published literature regarding growth-friendly spinal implants, the status of their Food and Drug Administration approval labelling as well as the indications, applications, and complications associated with their implementation.



Title	Type of study	Publisher/Journal (Impact Factor)	Authors	Patients	Intervention	Comparison	Outcome Primary Secondary
10. 3D correction over 2years with anterior vertebral body growth modulation: A finite element analysis of screw positioning, cable tensioning and postoperative functional activities	Retrospective study	Clinical Biomechanics (2.248)	<i>Cobetto et al</i> <sup>16</sup>	Scoliosis cases	Anterior vertebral body growth modulation	Cable tensioning and screw positioning	Biomechanical possibility to adjust the fusionless instrumentation parameters to improve correction in frontal and sagittal planes, but not in the transverse plane. The convex side stresses increase in the supine position may suggest that growth modulation could be accentuated during nighttime.
11. Biomechanical simulations of costo-vertebral and anterior vertebral body tethers for the fusionless treatment of paediatric Scoliosis	Retrospective study	Journal of orthopaedic research (3.14)	<i>Aubin et al</i> <sup>17</sup>	Adolescent scoliosis patients	Fusionless treatment	CV and ANT	Biomechanical study captured the differences between a CV and ANT tether and indicated the variability arising from the patient-specific characteristics.
12. Growth tethering devices for idiopathic Scoliosis	Narrative review	Expert review of medical devices (1.784)	<i>Courvoisier et al</i> <sup>18</sup>	Idiopathic scoliosis	Growth tethering	None	This review discusses the recent developments in the field of spinal growth modulation techniques and discusses the pros and cons of the medical devices used in this indication.
13. Anterior vertebral body tethering for idiopathic Scoliosis: Two-year results	Retrospective review.	Spine (2.078)	<i>Samdani et al</i> <sup>19</sup>	Patients who underwent anterior VBT with 2-year follow-up	Anterior vertebral body tethering	preoperative, intraoperative, and most recent clinical and radiographical data	Anterior VBT is a promising technique for skeletally immature patients with idiopathic scoliosis. This technique can be performed safely and can result in progressive correction.
14. Surgical aspects of spinal growth modulation in Scoliosis correction	Narrative review	Instructional course lectures (0.6)	<i>Jain et al</i> <sup>5</sup>	Scoliosis	Spinal growth modulation		Surgical aspects of growth modulation described
15. Early onset Scoliosis: Modern treatment and results	Systematic review	Journal of paediatric orthopaedics (2.046)	<i>Tis et al</i> <sup>20</sup>	Early onset scoliosis	Modern treatment methods of scoliosis	None	Recent advances have improved the treatment of children with EOS. Treatment continues to be challenging with complication rates higher than treatment of idiopathic scoliosis.
16. Biomechanical comparison of fusion less growth modulation corrective techniques in paediatric Scoliosis	Comparative study	Medical& biological engineering and computing (1.82)	<i>Driscoll et al</i> <sup>21</sup>	Adolescent idiopathic scoliosis	Fusionless growth modulation corrective techniques	Non-instrumented and instrumented models	Initial implant compression achieved during instrumentation provided a significant influence on initial and long-term spinal profiles. The developed FEM provides an effective platform with which to explore, critique, and enhance fusionless growth-sparing techniques.

Title	Type of study	Publisher/Journal (Impact Factor)	Authors	Patients	Intervention	Comparison	Outcome Primary Secondary
17. Biomechanical analysis and modelling of different vertebral growth patterns in adolescent idiopathic Scoliosis and healthy subjects	Retrospective study	Scoliosis (0.89)	Shi et al <sup>22</sup>	Adolescent idiopathic scoliosis		Healthy subjects	Results from this analysis suggest that accelerated growth profiles may encourage supplementary scoliotic progression and, thus, may pose as a progressive risk factor.
18. Non-fusion treatment of adolescent idiopathic Scoliosis by growth modulation and remodelling	Retrospective study	Journal of Paediatric Orthopaedics (2.046)	Aronsson et al <sup>4</sup>	Patients with AIS		Non fusion treatment	A brace that applies the appropriate loading and is worn as prescribed may dramatically improve the results of brace treatment. A procedure using external fixation or adjustable anterolateral tethering may achieve a non-fusion correction of AIS.

Out of 18 articles we found three Systematic reviews 13 15 20, one Meta-analysis study 13, five Narrative Reviews<sup>5 7 8 10 18</sup>, nine Retrospective studies<sup>4 9 11 12 14 16 17 19 22</sup> and one Comparative study<sup>21</sup>.

The final 18 articles were critically analysed with the help of the data extraction form and individual articles.

## Discussion

Managing scoliosis has been a challenging problem in orthopaedics. Despite many research studies over the years the true understanding of the pathogenic factors leading to different onsets and progression of the disease all remains unclear. However, with modern advances in growth modulation techniques in managing idiopathic scoliosis has been published extensively. The results of our final 18 articles following the detailed systematic review have revealed following points. Each has been summarised below.

Article published by Cheung et al mentions major developments in surgical techniques that include robotic assisted pedicle screw placement, vertebral body tethering, vertebral body stapling magnetically controlled growing rods, and sublaminar polyester bands. All these are considered as fusionless growth modulation

techniques.<sup>7</sup> In 2019 Trobisch et al review article describing an innovative non-fusion option of scoliosis correction by insertion of segmental pedicle screws with flexible polyethylene cord anteriorly. In this review short term results of hundred patients were studied. Short term results concluded with over correction and cord rupture mentioned as noted complications.<sup>8</sup>

Shilla procedure was designed to manage early onset scoliosis in patients with growing spines.<sup>23</sup> Wilkinson et al found out from a retrospective review conducted with 21 patients 9 which was a single centre review demonstrated that apex of the primary curve shifts and most patients develop secondary curves following the procedure.

Anterior vertebral growth modulation (AVBGM) in adolescents with idiopathic scoliosis is described as a minimally invasive technique that gradually correct the deformity while preserving some lumbar mobility. However the patient selection for this procedure and predicting the outcome has been challenging. Mandel et al developed a 3D reconstruction computer model helping to answer this question with equal results to existing biomechanical models.<sup>10</sup> Newton et al in a retrospective look into anterior spinal growth tethering (ASGT) in patients with skeletally immature thoracic scoliosis found out that

scoliosis could be corrected while maintaining spinal flexibility and natural growth of the spine. This is a promising alternative technique compared to a rigid fixation for the skeletally immature spine.<sup>11</sup> Scoliosis vertebral growth plate histomorphometry was studied by Bylski-Austrow et al helping us to understand better the bio mechanics of the curve.<sup>12</sup>

Anterior instrumentation and usage of thoracoscopic procedures in managing AIS as compared to childhood scoliosis has been gaining popularity over last decade. In a systematic review conducted by Padhye et al using multi database searches a total of thirteen studies were identified. In a total of 530 patients thoracoscopic procedure was found to have an excellent curve correction, high patient satisfaction and no long-term effect on pulmonary function over the open procedure. However, longer surgical time and intra-operative pulmonary complications were higher in the thoracoscopic procedure.<sup>13</sup>

Distraction based techniques in managing early onset scoliosis (EOS) has been practiced widely. However Magnetically controlled growing rod systems (MCGR) has been relatively new as compared to the traditional growing rod systems (TGR). Eltoral et al reports promising results of MCGR as compared to the current gold standard of TGR in managing EOS.<sup>14</sup>

In managing EOS or paediatric scoliosis various newer growth modulation implants<sup>15</sup>, 3D correction devices with anterior vertebral growth modulation<sup>16</sup> and biomechanical simulation of costo-vertebral and anterior vertebral tethers attempting fusionless treatment<sup>17</sup> have all been tried with promising results.

The final analysis, had three more articles dealing with EOS or paediatric scoliosis. Systematic review by Tis et al describes the modern growth modulation models in comparison to classic rods used in surgery.<sup>20</sup> Driscoll et al published a biomechanical comparison of fusionless growth modulation surgical techniques in paediatric scoliosis. This increasing gives supportive

evidence towards using growth modulation principle to develop instrumentations.<sup>21</sup> Surgical aspects of growth modulation in EOS are well described by Jain et al in an article published in Instructional course lectures.<sup>5</sup>

Out of the eighteen articles analysed in the final selection we found three articles dealing with Adolescent idiopathic scoliosis (AIS) and using growth modulation techniques in managing these. In principle, growth modulation works better with paediatric scoliosis with flexible and growing spines that can be modulated. One study that looks at 2 year results of anterior vertebral body tethering in AIS shows promising results. However, even in this, patients were in an early adolescent group with a mean age of 12 years.<sup>19</sup> Biomechanical analysis on AIS studied by Shi et al<sup>22</sup>, a study similar to the one done by Driscoll et al<sup>21</sup> on paediatric scoliosis shows that abnormal growth profiles seen in AIS are a potential risk factor encouraging supplementary curve progression.

Bracing and non-operative techniques have been used relatively less in modern day practice due to poor patient compliance. However, specific braces designed and used in the principles of growth modulations, in managing AIS have been reported by a study done by Aronsson et al. In that they conclude a brace that applies proper loading and worn in the prescribed manner will equally improve the correction of scoliosis.<sup>4</sup>

This systematic review tries to evaluate the secondary evidence available within this context of managing scoliosis using growth modulation.

Our review had some limitations. We only used a single database (PubMed) for the search other sources such as books, conference proceedings, unpublished data, lectures and ongoing research were not included. Our language settings were limited to, articles published only in English language.

Using growth modulation in managing surgical correction of scoliosis appears to be



effective as traditional correction. With the development of modern instrumentation as mentioned in many studies above, we found out that high level of success rates can be achieved. The clear advantages of this remain that, gradual correction of the deformity while maintaining spinal growth and slow correction of soft tissues

around, making it more compliant to patient and achieving physiological and functional correction. The downside of this seems that limitation in achieving full cosmetic correction, less success rates in AIS. This works best in younger age group where there is further spinal growth namely the EOS.

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