Adolescent Idiopathic Scoliosis (AIS): An Overview of the Etiology and Basic Management Principles

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Abstract

In the past four decades, considerable progresses have been made in the understanding of the clinical behavior and the pathoanatomy of adolescent idiopathic scoliosis (AIS). Significant advances in the surgical treatment and instrumentation have also been observed. However, the definite etiology is still unclear and thus the current treatments are at best treating the complications of AIS rather than the direct underlying cause. The objective of this overview is to update our knowledge on the epidemiology, natural history of AIS, discuss a number of advances in the research related to the etiology of AIS and present a brief summary of the current concept of management.

Key words

Adolescent; Etiology; Scoliosis; Spinal brace

General Introduction of Adolescent Idiopathic Scoliosis

Definition and Classification

The term scoliosis was first used by Galen (A.D. 131-201). Idiopathic scoliosis is the most common form of deformity of the spine. By definition, it is a lateral curve of the spine in an otherwise healthy child, for which a currently recognisable cause has not been found. These children have no clinically observable muscular or neurological problem, other known etiology, and with no congenital vertebral abnormalities radiographically. The deformity occurs during the growing years and is customarily divided into three categories: infantile (aged 0-3), juvenile (aged 3 to 9), and adolescent (aged 10 or above). By anatomical level of the apical vertebra, scoliosis curve has been further described as cervical, thoracic, thoracolumbar and lumbar curves (Figures 1 & 2).

Epidemiology

Adolescent idiopathic scoliosis (AIS) is basically a clinical diagnosis with confirming radiological finding of scoliosis after excluding any known etiology clinically and radiologically. From school screening programmes, the incidence of AIS reported in literature varied from 2% to 13.6%.1-3 The ratio of female to male incidence varied directly with the severity of the curve from 1:1 for curves of 6 to 10 degrees, 5.4:1 for curves of more than 20 degrees and 10:1 for curves of more than 40 degrees.3 In the Chinese population, the reported incidence of AIS is 1.04% in Beijing, 1.07% Guangdong and 3.08% in Hong Kong (unpublished data).

Natural History

A clear understanding of the natural history of AIS is essential for planning evidence-based treatment and for research into the etiopathogenesis. It is generally recognised that the immature patients with larger curves carry a worse prognosis. Skeletal maturity can be assessed by the chronological age, Risser sign (radiological grading...
according to the stages of ossification of the iliac apophysis), growth velocity, menarche status for girl and Tanner staging. Bunnell\textsuperscript{4} found that the risk of progression was three times greater for children under 12 than for older children and approximately 50% before onset of menarche and Risser 2 or less which drops to less than 20% after menarche. Curves in girls are generally more progressive than boys. The vertebrae were also found to be more slender in girls than in boys.\textsuperscript{5}

Weinstein et al in their long-term follow-up study showed clearly that severe idiopathic curves could continue to progress in adulthood.\textsuperscript{6,7} Thoracic curve greater than 60 degrees at the completion of growth will progress continuously up to an average of 29.4 degrees on a follow-up of 40 years. Lumbar curves and thoracolumbar curves of 45 to 50 degrees will progress by an average of 15 to 20 degrees on a 40-year follow-up. More recent epidemiological studies have shown that the mortality rate of patients having idiopathic thoracic scoliosis is not significantly greater than the general population until the
curve reaches more than 80 degrees whereby cor pulmonale can result in shorter life span.\textsuperscript{6} Other studies have shown that the incidence of back pain in the adult idiopathic scoliosis case is not statistically different from that of the normal person except for those with thoracolumbar or lumbar curve of more than 45 degrees with substantial rotation and imbalance.\textsuperscript{8}

**Current Concepts of the Etiology of AIS**

Considerable advances have been made in the treatment of scoliosis in the past 40 years as a result of improved knowledge of the three dimensional deformity of scoliosis, the availability of new non-operative and surgical treatments and the parallel advances in related supportive techniques. Despite all these advances, the etiology of idiopathic scoliosis remains unsettled. Below is an attempt to give an overview of the various proposed links to the possible etiology of AIS.

**Genetics**

Clinical observations revealed the presence of higher incidence of scoliosis in relatives of large families.\textsuperscript{9,10} In 1934, scoliosis has been reported in five generations of a family.\textsuperscript{11} Twin studies have also shown the presence of idiopathic scoliosis in the family.\textsuperscript{12-14} Although the role of hereditary or genetic factors in the development of this condition is widely accepted, the mode of inheritance is still uncertain. More recently, the segregation analysis, candidate genes analysis and genome-wide linkage surveys have been utilized.\textsuperscript{15,16} Medical scientists are confronted with a number of obstacles including differences in the clinical definition of affected individuals, modification of the expression of the AIS genotype by environmental factors, variability in the age of onset of the disease and most importantly the lack of knowledge of the basic defect(s) in AIS leading to scoliosis.

**Growth and Hormonal Dysfunction**

**Growth Disturbances in AIS**

It has been observed that AIS typically occurred during the period of rapid growth and the rate of progression is closely related to the velocity of growth. In general, AIS patients are found to be taller and leaner.\textsuperscript{17-19} Height velocity is a good predictor of the curvature progress.\textsuperscript{20,21} The abnormal anthropometric parameters in AIS appear to be resulted from systemic disturbances in differential growth affecting both the limbs and the spinal column.

**Hormone Dysfunction**

Melatonin and growth hormone have been implicated in the etiopathogenesis of AIS. Willner et al\textsuperscript{22} found a higher GH and serum somatomedin level in the girls with AIS comparing with normal controls. Dymling and Willner\textsuperscript{23} reported rapid progression of the thoracic curve of a patient with AIS treated by GH over a 10-week period. When the GH was stopped, the curve remained stable. Skogland and Miller\textsuperscript{24} (1980) reported a significant higher sensitivity of the GH release mechanism in prepubertal (7-12 years) girls with IS. Willner and Johnell\textsuperscript{25} (1981) found increase in the morning fasting GH, Somatomedin A and 17-oxosteroids (metabolites of androgens in girls) level in AIS. On the contrary, Ahl et al\textsuperscript{26} (1987) was unable to detect any differences in 24-hour GH between scoliotic and nonscoliotic girls in pubertal stages 3 and 4. In stage 2 (pubertal), they measured significantly more GH in girls with AIS than in the controls. Whether the higher level of GH is of etiological importance is an open question which needs further studies.

Melatonin deficiency has been reported to be a possible cause of AIS. Several authors have produced idiopathic scoliosis-like deformity in pinealectomised chicken-model.\textsuperscript{27,28} The controversy however, still exists with the observed differences in the success rate of inducing scoliotic deformity in the chicken model and also between different animal species.

**Bone Mineral Density and AIS**

The association of generalised osteopenia and AIS were reported by several authors.\textsuperscript{9,29-31} In 1987, Cook et al\textsuperscript{29} investigated bone mineral status in 44 girls with the diagnosis of AIS aged 9 to 20. Bone mineral measurements were made using dual-photon absorptiometry and gadolinium-153 radiotracer source. Compared to age-, weight-, and race-matched girls, the scoliotic subjects had a significant delay in menarche and lower average bone mineral density (BMD) in the lumbar region. This group of subjects was followed-up longitudinally and shown to have persistent osteopenia after an average of 30 months. Recently, Cheng et al\textsuperscript{32,33} conducted a cross-sectional and longitudinal follow-up study to assess the lumbar spinal and proximal femoral BMD with Dual Energy X-ray Absorptiometry (DEXA) in AIS with age-, sex-matched normal controls. Eighty-seven percent of the scoliotic individuals have a significantly reduced BMD compared to normal controls. Moreover, 33.3% were 1 SD below and 20.1% 2 SD below the normal mean.

The same observation was found with peripheral
quantitative computer tomography (pQCT) with high resolution of 0.2 mm and reproducibility of 0.3%. The volumetric BMD measured at the bilateral lower extremities were significantly lower in AIS than normal controls.34 Low bone mineral status could be related to abnormal bone modelling (remodelling) in AIS. Histomorphometry study of bone biopsies from the iliac crest found significantly less osteocyte count in the trabecular bone accompanied by the presence of smooth and continuous borders in patients with AIS.35 Histomorphometry confirmed the lower static parameters such as reduced trabecular width and osteoblast numbers. The results correlated well with the decreased bone mineral density. This study showed a primary disturbance in the bone metabolism and growth. Further detail studies are necessary to explore further the link between abnormal osteoblast metabolism and bone mineralisation.

Abnormalities in Other Body Tissues

Abnormality in Connective Tissue

Possible defect within the connective tissue as an etiological factor of AIS has been hypothesized. Pedrini et al36 reported an abnormal proportion of collagen in the nucleus of intervertebral discs of patients with AIS. The result was not supported by similar studies focusing on the proteoglycan and collagen of the intervertebral discs.37 Tang38 in an immunohistochemical study showed the lower expression of two small proteoglycan, decorin and biglycan, in the iliac crest specimen of AIS patients.

The elastic fiber system is the second major component of the extracellular matrix. Echenne et al39 found that the skin of AIS was significantly different from normal subjects within the middle and deep dermis. In 1994, Hadley-Miller et al40 researched on the fibroblasts harvested from AIS and indicated a potential failure of matrix incorporation of elastic fiber components in a select number of AIS. Most researchers concede at this time that connective tissue abnormal in AIS is most likely to be secondary to the structural scoliotic deformity itself.

Skeletal Muscle Abnormality

By muscle morphology, histopathology, and biochemical study, numerous researches have been done on the paraspinal muscle of AIS patients. Abnormal findings include increased EMG activity on the convexity of the curve; decreased type II fibers near the apex and at the convex side; swollen mitochondria, myofibrillar damage, disruption of myofibrillar banding pattern and loss of myofilaments under electron microscopy; increased intracellular lipid and glycogen; increased intracellular calcium; decreased number of muscle spindles; abnormalities in muscle enzyme activity; abnormalities in muscle protein synthesis and decrease in zinc content in muscle.41-51 The current view held by most investigators is that the observed abnormalities in the muscle are more likely to be secondary to the spinal deformity rather than as a primary cause.

Abnormal Platelet Calmodulin Levels

Platelet has been used as a model in the study of AIS after it was found to contain actin and myosin similar to that in skeletal muscle. Abnormal reported findings in AIS included increase in calcium and phosphorus concentrations in the dense granules; poor aggregation with collagen specimen; longer bleeding time and increase in dense bodies.49,52-56 More recently, Kindsfater et al56 found that calmodulin, a calcium-binding receptor protein was significantly higher in AIS with progress curve. In another longitudinal study on 55 patients with idiopathic scoliosis, results showed increased calmodulin levels in all the patients with progressive curves (13/13), no change in 73% of the patients with non-progressive curves (11/15), and higher level in curves greater than 30 degrees.57 More large scale multicentre studies will be necessary to further delineate the role of calmodulin level in the etiopathogenesis of AIS.

Biomechanical Factors

Biomechanical factors probably play a secondary role in the etiopathogenesis of AIS. Altered material properties of the spine could affect its response to mechanical loading.58 In 1977, Harrington suggested that a minor deficiency in the disc collagen could cause scoliosis.59 Bone quality changes have been detected by DEXA and pQCT. Cook et al59 and Cheng et al52 found the generalised low bone mineral density in AIS when compared with normal controls.35

Central Nervous System Abnormality

Although AIS by definition has normal clinical neurologic examination, abnormal somatosensory evoked potentials (SEPs) and lower position of the cerebellar tonsil from MRI study have been reported.60,61 The incidence of scoliosis with syringomyelia from a study was 4.0% with 18.4% in boys, and 2.6% in girls.61 Syringomyelia and functional disturbance in the somatosensory pathway was found to be significantly more frequent in the group of patients with severe scoliosis curvature with an incidence of 31% and 27.6%, respectively.60 Recently, compared with
normal references, Cheng found that 17.9% of patients with AIS had tonsilar trips below the foramen magnum. Disorders in the somatosensory function may be one of the mechanisms linking tonsillar herniation to scoliosis.

**Basic Management Principles in AIS**

The basic principle in the treatment of AIS is to make the proper diagnosis, rule out other organic causes of the scoliosis and assess the severity of the deformity clinically and radiologically. The aim of non-operative treatment is to control the curve, to prevent progression, prevent the need for surgery and to improve cosmesis. The factors affecting the choice of treatment are most importantly, the patient's age and physiologic (not chronologic) maturity, curve magnitude, location of the curve and the risk for progression.

**Non-operative Treatments**

Observation or spinal orthoses treatment are the basic methods of non-operative management of adolescent idiopathic scoliosis.

**Observation**

It is generally accepted that if the curve is below 20 degrees in the immature patient and if the curves is below 40 degrees in skeletally mature patient, observation with regular follow-up is appropriate. In clinical practice, a majority of AIS: 80-90% is non-progressive and could be managed by observation alone.

**Orthotic Spinal Brace Treatment**

In the past few years many multicentre prospective studies showed that proper full time bracing programme treatment can be successful in up to 78% of AIS cases in controlling the curve progression in immature girls with 25 to 35 degrees curve. In the same group of patients with similar curve, age and maturity, a 68% chance of progression has been documented in those who has not received any bracing treatment.

The aims of brace treatment are to control the curve, to prevent progression, to prevent the need for surgery and to improve cosmesis. The indications are for growing child (Risser's 2 or less) with <25 degrees and documented progression and for cases of 25-45 degrees curves. The contraindications are when the growth is already completed, when there is significant thoracic lordosis and when the curve is already greater than 45 degrees. The most effective braces are the Milwaukee brace (CTLSO) for higher level curve and the underarm brace (TLSO) for apex of curve from T8 downwards (Figures 3 & 4). The bracing programme is most effective when worn for up to 20 hours a day except for sports activities and meals. The period of bracing will last till the growth stabilised generally around one and a half to two years of post-menarche.

**Surgical Treatment**

The decision for surgical treatment of AIS should be based on analysis of multiple factors; the curve size and characteristic in three planes, the bone age, the cosmetic component and the knowledge of the natural history of the curve concerned. The general indication for surgical instrumentation and fusion are curves over 45 to 50 degree Cobb's angle with high probability of progression or demonstrable progression. The aim of surgery for AIS is to arrest the progression of the scoliotic deformity, to correct the deformity, to restore trunkal imbalance with the shortest possible spinal fusion and to improve the self-image.

As scoliosis surgery is a very major surgery, a thorough preoperative evaluation includes haematological, biochemical, radiological, cardiopulmonary functional assessments. Proper psychological preparation for the operation and the postoperative aftercare programme need to be explained carefully to the patients and their parents to facilitate a smooth outcome of the surgery.

Surgical release and correction of the three dimensional deformity can be achieved by posterior approach, anterior approach or combined anterior-posterior approaches in very severe stiff curves. This would be followed by the insertion of spinal instrumentation and spinal fusion. The instrumentation system has evolved over the past 40 years from basic first generation posterior Harrington rod system to the latest 4th generation systems like ISOLA and TSRH systems (Figure 5). Modern instrumentations can achieve more significant 3D corrections and immediate postoperative stability to allow early mobilisation and back to school without the necessity of plaster immobilisation. Recently, in the era of minimal invasive surgery, advanced techniques on thoracoscopic corrections and instrumentation for selected thoracic curves have been tried and undergoing limited clinical trials.

Modern surgery has been made safer through the concurrent advances in preoperative imaging and assessments, anaesthestia, intensive care, blood salvaging techniques, bone substitutes and availability of introoperative spinal electrophysiological monitoring in advance centres.
Figure 3  Milwaukee scoliosis brace.

Figure 4  Underarm scoliosis brace.

Figure 5  AIS with severe major curves showing correction with ISOLA posterior spinal instrumentation.
References