 DOI: 10.18231/2395-499X.2017.0030

Syndromes and General concepts of their orthodontic management: A review

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Abstract

Oral health is important for all children but is especially important for children with syndromes. Syndrome has a complex array of special features and functional challenges. Good oral health and proper dental follow up is an important element in the overall care pathway for these children.

Diagnosis of the syndrome in childhood is basically through oral abnormalities and Orthodontists may be the first to detect these cases by playing important role in early diagnosis. Oral symptoms are the main basis for diagnosis in childhood and adolescence, which is the time most patients receive orthodontic treatment and some of the most frequent clinical features of the syndrome are discovered through radiographs normally used in routine orthodontic procedure.

Orthodontic management for syndromic patients require correction of interarch and intra arch tooth relationships to restore near to normal masticatory as well as esthetic functions.

Literature regarding oral conditions in patients with various syndromes often covers the periodontal and carious aspects, but less literature was found describing orthodontic aspect. This review is compilation of various features requiring orthodontic corrections and a special emphasis is given on their orthodontic management.

Keywords: Syndromes, Orthodontic treatment and Oral care

Introduction

Biological variation is a natural consequence of sexually reproducing organisms. Such variation has allowed populations to genetically adapt to changing environments. The human face probably has more basic divergent kinds of facial patterns than most other species, as can be seen; there is a wide spectrum of human craniofacial morphologies that are all within the range of normal human variation. This diversity is produced by an interaction of normal genetic and epigenetic factors such as developmental acclimatization to extreme environments.(1) Craniofacial anomalies should be interpreted from the viewpoint of developmental anatomy and pathology. Depending on the developmental timing and severity of the primary craniofacial anomaly, consistent patterns of multiple anomalies may be observed. These are referred to as syndromes or sequences.(2)

A syndrome is a pattern of multiple anomalies that are pathogenetically related and not known to represent a single sequence.(2,3,4)

Syndromic individuals are children or adults who are prevented by a physical or mental condition from full participation in the normal range of activities of their age groups. They usually exhibit high orthodontic treatment needs because of an increased prevalence and severity of malocclusions.(5)

The main goal of orthodontics is to improve the alignment and occlusion of the teeth and thus, directly improve functional efficiency and indirectly improves facial appearance.

Since regular ongoing dental care is an important part of good medical care for a child with syndrome. The American Academy of Pediatric Dentistry recommends the first dental visit be around one year of age. This provides an opportunity to have a base line evaluation, have your questions addressed and with the dentist develop a long term plan to assure the child will grow with good dental health. In a child with complex long term health and developmental needs it is even more important to get a very solid and early start on good oral health.(5,6)

This article is a review of literature available regarding syndromes and by means of this a compilation is done of oral features and a light is thrown on the oral health care regime along with general Principals of orthodontic management of the syndromic patients are here by highlighted.

Craniofacial development in the embryo

Recent advances in molecular biology and in human genetics have had a considerable influence in the understanding of orofacial genetics. The Orthodontic speciality is faced with the evidence that genetic factors play a predominant role in the aetiology of malocclusion.(7)

Some insight into the genetic mechanisms involved in craniofacial morphogenesis at the molecular level in the embryo assists our appreciation of the role of genetics, not only in the aetiology of craniofacial abnormalities, but also in the regulation of maxillary, mandibular, and tooth morphology.

Facial development in the embryo is demarcated by the appearance of the pre-chordal plate (the cranial end of the embryo) on the fourteenth day of development. One of the most unusual features of vertebrate facial

development is the origin of the facial mesenchyme which arises from neural crest cells. Unusually, they disrupt the ectodermal-mesodermal junction and migrate into the underlying tissue as ectomesenchymal cells. Migration and division of neural crest cells are extremely important in facial development. During their migration they undergo a number of interactions with the extra-cellular matrix, and with adjacent epithelia to determine the nature and patterning of the neural, skeletal and connective tissue structures they will form.

Among the derivatives of the cephalic neural crest cells are the maxilla, mandible, zygomatic, nasal bones, and bones of the cranial vault.

Although the cessation of neural crest cell migration and the factors that cause neural crest cells to localize in particular regions are not yet completely understood, their migration into the branchial arches occurs in a highly regulated manner. This process is presumed to be under the control of genes known as ***homeobox genes***, which endow neural crest cells (NCC) with a positional identity, which mediates aspects of craniofacial morphogenesis and patterning.

The role of homeobox genes

Homeobox genes are genes which are highly conserved throughout evolution of diverse organisms and are now known to play a role in patterning the embryonic development. These can also be regarded as master genes of the head and face controlling patterning, induction, programmed cell death, and epithelial mesenchymal interaction during development of the craniofacial complex.

Those of particular interest in craniofacial development include the Hox group, Msx1 and Msx2 (muscle segment), Dlx (distalless), Otx (orthodontical), Gsc (goosecoid), and Shh (sonic hedgehog).[7,8]

The role of cell adhesion molecules:[7,8]

Cell adhesion molecules such as cadherins, integrins, immunoglobulins, and proteoglycans are glycoproteins on the external surface of the cell membranes, and are thought to be important in embryogenesis, particularly organ formation. In craniofacial development the precise positioning of the neural crest cells in the branchial arches may involve changes in expression of cell adhesion molecules are expressed and down regulated in neural crest cells during their pre-migratory and migratory stages.

Molecular genetics in oral and craniofacial dysmorphology:[8]

Molecular genetics studies using animal models for human malformations enables elucidation of pathogenetic mechanisms.

For example, mice with retinoic acid syndrome (RAS) have illustrated major neural crest cell involvement (Sulik *et al*., 1988) and in similar human syndromes such as hemifacial microsomia neural crest involvement is implicated. Craniosynostosis- premature closure of cranial sutures, is a common birth defect in humans, occurring in approximately1:2500 live births (Cohen, 1993) and premature suture closure has also been found to have its origins in neural crest cell disorders.

The Role of Epigenetic Factors

A crucial objective in studying a multifactorial trait in man is to contemplate the effect of genotype-environment interaction. The effect of a particular environmental factor on phenotype will vary depending on the genetic background because of the influence of the latter on the response.

Growth and the final morphology of the dentofacial structures is undoubtedly influenced by environmental factors, a classical case of gene/environment interaction. It is important to realize that the functional matrix encompasses neuromuscular activity which is influenced by genetics, as well as environmentally-influenced behavioural and postural adaptations.

It would, therefore, be erroneous to believe that craniofacial size and shape are entirely determined either by genetics or by environmental factors, but by the complex interaction of both and every malocclusion will occupy a unique slot on the gene/ environment spectrum. This will have a direct bearing on the more important issue from an orthodontic viewpoint, which is the determination of the extent to which a particular malocclusion can be influenced by therapeutic environmental intervention, i.e. the prognosis for orthodontic correction.

Correlations Between Syndromes and malocclusion[7,8]

The malocclusions with severe skeletal discrepancies might be accompanied by a genetic syndrome. Some of the genetic syndromes are known to influence the development of craniofacial complex. Chromosomal aberrations, deficiencies, transpositions, breakage, deletions, or enlargements usually lead to abnormal development of the first branchial arch. This genetic situation results in micrognathia, malocclusions, facial asymmetry, facial and oral clefts, oligodontia and other dentofacial disorders accompanied by different types of deformities and deficiencies in other parts of the body. When the balance between the genetic and the environmental influences exceed a certain threshold the malformation occurs. The further the threshold is exceeded, the more severe the malformation. Syndromes affect development of either one jaw or both jaws causing disparity in growth and leads to abnormal interarch and intraarch relationship.

Diagnosis of the syndrome in childhood is basically through oral abnormalities.

Orthodontists may be the first to detect these cases and early diagnosis is of extreme importance. Some of the most frequent clinical features of the syndrome are

discovered through radiographs normally used in orthodontics.

It is surprising that although oral symptoms are the main basis for diagnosis in childhood and adolescence, which is the time most patients receive orthodontic treatment.[9]

Describing syndromes in detail is beyond the scope of this paper and other articles available quotes same features of various syndromes, only the management part differs, so relevant syndromes available in dental literature are tabulated here with their cardinal features and mode of inheritance. (Tables 1-5)[9-32]

Classification of various syndromes according to maxillary and mandibular features

Table 1: Syndrome having maxillary deficiency

S. No.	Condition	Etiology	Striking Features
1.	***Van der Woude syndrome (VWS).***	Autosomal dominant/recessive and environmental	- Cleft lip and palate or palate only - Lower lip pits, - Partial syndactgl of fingers and toe, - Dental anomalies including under developed maxilla, collapsed maxillary dental arch and - Sparse hair,
2.	Cleidocranial dysplasia	Autosomal dominant	- Underdeveloped or absent clavicle, - Prominent face head, - Hyper telorism, - Brachycephaly, - Over retained deciduous teeth, - Supernumerary teeth, - Reduced height of lower third of face, - Underdeveloped maxilla (skeletal class3 tendency)
3.	Papillon-lefevre syndrome	Genetic	- Palmer planter keratosis, - Early onset form of aggressive periodontitis - Gingival enlargement - Ulceration and pocket (vertical) formation, - Retrognathic maxilla, - Retroclination of mandibular incisors and - Upper lip retrusion, - Decreased lower facial height
4.	Sticker syndrome	Autosomal dominant/autosomal recessive	- Midface hypoplasia, - myopia, - anteverted nares, - hearing loss, - cleft of soft palate, - fairly small SNA and SNB angles, - steep mandibular plane - incisors of both arches retroclined, - large overjet and overbite
5.	Down syndrome	Trisomy of 21^{st} chromosome	- Mental retardation, - epicanthal folds, and - flat facial profile, - abundant neck skin, - simian crease, - congenital heart disease, - gap between first and second toe, - brachycephaly, - folded or dysplastic ears, - open mouth, - protruding tongue, - hypotonia.

			- flat nasal bridge, - high incidence of ANUG - lower decay rate, - deficient maxilla may have class 3 (32-70%) class2 malocclusion - anterior or posterior cross bite, - open bite
6.	Occlusofaciocardiodontal syndrome	x-lined dominant	- Congenital cataract, - hypertelorism, - glaucoma, - nasolacrimal duct obstruction. - long narrow face high nasal bridge, - broad or pointed nose, - bifid nose, - ear deformity, - cleft palate. - atrial septal defect, - ventricular septal defect - mitral valve defect. - Radiculomegaly (canine or multiple), - open apexs of maxilla and mandibular premolars, - dilacerations of roots, - oligodontia, - constricted maxilla, - maxillary and mandibular dentoalveolar heights are greater than normal
7.	Kabuki syndrome	Multifactorial	- Flatness of cheeks below the eyes, - lower face is disproportionately long, - may class 1, 2, 3 malocclusion, - high arch palate, - cleft palate, - lexity of TMJ, - central incisor – shovel shaped
8.	Freeman Sheldon syndrome	Multifactorial	- Stiff immobile flat midface and elongated philtrum, - rounded cheeks and small nose - dimpling of chin, - microstomia
9.	Crouzon's syndrome	Mutation of gene	- Exorbetism, - retromaxillism - paradox retrognathia, - class3 malocclusion, - high arch palate, - hearing loss

Table 2: Syndrome having mandibular deficiency

S No.	Condition	Etiology	Striking Features
1.	Pierre- robin syndrome	Matter of debate but some support compression mechanical or positional theory	- Mandibular retrognathia esp in ramal height (bird faces) - cleft palate, - glossoptosis, - severe upper airway obstruction at birth.
2.	Treacher- Collins syndrome	Autosomal dominant	- Symmetrically hypoplastic - lowest call, - docon slanting palpebral fissures,

			- mandibular hypoplasia, - cleft palate(30%)
3.	Silver Russell syndrome	Most cases sporadic/ autosomal dominant	- Pseudohydrocephaly, - frontal bossing, - triangular facies, - small and pointed chin with hypoplastic mandible, - high arch palate, - congenital absence of lateral incisors and premolars, - upper lip vermillion is thin, corners of mouth cone turned down.

Table 3: Syndrome having mandibular prognathism

S. No.	Condition	Etiology	Striking Features
1.	Gorlin syndrome	Autosomal dominant	- Basal cell carcinoma, - widened, fused or rudimentary ribs, - frontoparital bossing, - hypertelorism, - mandibular prognathism, - crynecomastic, - mandibular and maxillary - odontogenic keratocyst (twice as frequent in mandible esp in 8^{th} molar and canine area) - carnivorous teeth with shovel canine and premolar, - cleft lip and palate.
2.	Marfan syndrome	Autosomal dominant	- Marfanoid habitus, - dolichostenomelia, arachnodactyly, - ectopia lentis, - fusiform and dissecting aneurysm of aorta, - mandibular prognathism.
3.	Hemifacial microstomia	Autosomal dominant/recessive	- Unilateral or bilateral asymmetrically hypoplastic ears and mandibular ramus, - ear tags/ or pits, - micrognathia, - variable cleft lip and palate, - epibulbar dermoid - vertebral anomalies, - cardiac defects, - renal anomalies and other abnormalities.

Table 4: Syndromes having both maxillary and mandibular deficiency

S. No.	Condition	Etiology	Striking Features
1.	Turner syndrome	Numerical / structural aberration of x-chromosome	- Low posterior hair line, - webbing of neck, - broad chest and widely spaced nipples, - coarctation of aorta, - short stature, - facies showing premature aging - Strabismus, - blue sclera, - color blindness, - total length of cranial base is reduced, - retrognathic maxilla and mandible to anterior and posterior lower facial heights, - upper posterior facial heights, - protruded maxillary central incisors.
2.	OMENS plus syndrome	Vascular insult leads to hematoma formation Disruption of mesodermal cell migration	- Hypoplastic orbit, - zygomatic region, - maxilla and mandible, nose asymmetry, - philtrum oblique, - mouth had a cleft like extension of left angle, - microdontia - partial anodontia, - non pnuematization of sinus

Table 5: Syndrome having maxillary deficiency and mandibular prognathism

S. No.	Condition	Etiology	Striking Features
1.	Saethrechotzen syndrome	- Autosomal dominant	- Palpabral ptosis, - myopia, - eagle nose with deviated system, - malformed ear with low insertion - cardiac and renal anomalies, - cryptorchidism, - deafness, - maxillary retrusion with mandibular prognathism, - upper lateral incisors sharp or missing, - TMJ ankylosis

Treatment consideration from general dentistry point of view

The aim of the pretreatment visits is three-fold:[8]

1. To raise the patient's level of confidence in the dental environment.
2. To assess the patient's and parent's compliance in dental homecare.
3. To evaluate the expected degree of cooperation that will finally be forthcoming

Therapeutic Access: Therapeutic access to these patients is impeded by the following several specific obstacles:

1. General behavior is often problematic because of reduced understanding and increased apprehension, short attention span, and limited tolerance.
2. Uncontrolled limb and head movements and an inability to sit still—making it difficult even to seat the child in the dental chair.
3. Level of cooperation during treatment is usually significantly impaired.
4. Exaggerated gag reflex, apparently related to dental/ medical phobia.
5. Markedly increased incidence of drooling in many cases.

These factors contribute to significant difficulty in performing otherwise routine procedures, such as impression taking and intraoral radiography. Accordingly, successful treatment delivery often requires different behavior management approaches, starting from simple behavior modification techniques through conscious and deep sedation to general anesthesia.

Oral care of syndromic patients: Important role in everyday care of syndromic patients are played by their parents. They provide oral care, feeding and fulfil other needs helping them to sustain normal life. Tooth brushing is not usually practiced by such children and considerable collections of food from recent meals may be seen in several areas of the mouth, including around the teeth. A lessened activity of the oral musculature, common in several debilitating conditions, and a lack of manual dexterity may contribute significantly to the stagnation. So education of the parent and, whenever possible, the child to recognize plaque and gingival inflammation and to teach them the correct way to brush the teeth is very essential as it's the first step towards successful dental treatment.

Proper brushing is the first and fore most important step in initiation of any dental treatment. Due to improper brushing and less oral hygiene maintenance syndromic kids are more prone to caries. Restorations of such lesions are done before starting orthodontic treatment as if left untreated they can lead to periapical pathogenesis. If root canal treatment is indicated to save the tooth it should be performed before the orthodontic treatment but capping of tooth should be done afterwards so that bonding of bracket is not hampered on the tooth surface.

Treatment consideration from orthodontic point of view

Adapting Orthodontics to the syndromic patients

1. Realistic Treatment Goals**:** when conditions are compromised by the existence of adverse factors, then treatment must be redirected toward more limited goals, more suited to the circumstances that the patient's condition dictates.
2. Treatment Provided in Modules: It is wise to establish reasonable goals on a modular basis, and to reassess them after each stage, being prepared to make the necessary changes if needed based on the treatment experience with the previous stage, for the particular disabled individual.

Modification of orthodontic treatment steps according to the syndromic patient comfort

1. **Simple Treatment plan:** treatment planning includes choosing very simple mechanics, where ever possible go for removable appliance rather than fixed appliance. The problems encountered with fixed appliances were generally more severe than with removable appliances. If fixed appliances are mandatory then prefer straight wire appliance or tip edge appliance so as to avoid complex wire bending. If expansion or any other adjunctive therapy is required then it should be given in short modules rather than in combination to fixed treatment as it will complicate the oral hygiene maintenance and can increase discomfort to the patient.
2. **Choice of impression material**: Impression taking is the first step to start the orthodontic treatment. It is required to make study models which are used to assess the arch length tooth material discrepancy and plan the treatment procedure. Alginate impression material is the commonest among the all but in case of syndromic patients it has its own draw backs. It can cause gag reflex, its moisture unfriendly, setting time is prolonged and can easily distort while retrieving the cast. The choice of impression material is elastomeric impression material as its patient friendly, less or no gag reflux and multiple casts can be retrieved from single impression.
3. **Use of newer generation of etchants and moister controlled primers:** Syndromic patients have drooling problem and less control over their musculature. Recently developed primers that enhance the strength of bonding even in wet environments are particularly useful in patients with excessive salivation. These, together with the use of anti-sialogogue drugs and special devices to maintain dryness, such as the Dry system are also helpful.
4. **Indirect bonding procedure**: From the orthodontist's point of view, fixed appliances are more difficult to place, especially in these children, because they require specific conditions, such as the need for the patient to sit still for long periods of time to enable the precise positioning of the brackets and with complete dryness of the teeth. Indirect bonding of brackets is faster and is preferred. High quality and accurate bonding must be assured to avoid the need for subsequent rebonding without sedation. The most reliable and proven bonding materials should be employed.
5. **Use of simple and comfortable appliances**: Tip edge appliance permits the insertion of heavier arch wires that are less likely to deform in the early stages. In such cases complex wire bending should be avoided as it can cause discomfort to the patient and can hinder in maintaining oral hygiene. Straight wire appliances and self ligating brackets should be preferred. Self-ligating brackets omits the use of ligature wires and modules to tie wire in the bracket slot thus reduces chair side time, any laceration with stainless steel ligature wire as well as stress to maintain oral hygiene with modules.
6. **Short activation schedules**: Adjustment of removable appliances is made extra orally and does not disturb the child. Orthodontic appliances with a

longer range of action, requiring less frequent visits, are to be preferred. As described above self-ligating brackets should be preferred in such patients.

7. **Long term or permanent retention:** There are many subgroups of children in whom the etiology may not be eliminated during the treatment. Thus, children with skeletal discrepancies, particularly the vertical discrepancies seen in cerebral palsy and the various congenital myopathies, or with large tongues, may never achieve stability. This should be predictable before treatment is undertaken and, once treatment is completed, retention must be for an extended period of time. Removable retainers will hold the alignment of teeth within the maxillary or mandibular arch, but cooperation must be assured. Where this may be in doubt, bonded lingual splints are preferred, even though this may involve a further sedation session for its reliable placement. A tendency for relapse in Class II and open bite cases abounds among these patients. "Active retention" may be essential.[8]

Post treatment Satisfaction: Most parents of syndromic patients are satisfied with the results of orthodontic treatment because of positive facial/dental changes and improvement in oral functions, the swallowing pattern, the related drooling, speech, and even mastication. Additionally in those children who were aware of the improved appearance, this resulted in associated improvements in esthetic self-satisfaction and self-confidence.

Conclusion

An overview of genetically determined disorders is presented, that will help us in understanding the complex interactions of various factors both genetic and epigenetic involved.

All treatment goals should be set keeping in mind that treatment is done to remove the obstacles in performing day to day work rather than to make kids equivalent to non-syndromic kids. So, high expectations should be avoided by the clinicians as well as the parents. The key to successful treatment of these patients is interdisciplinary coordination and sequencing. The management of a patient with a complex facial deformity has been presented in order to demonstrate the type of outcome that can be achieved using a comprehensive, multidisciplinary approach.

The major advances in diagnostics, materials and techniques have provided the tools that allow the various specialties to significantly improve the quality of life for these individuals who have frequently been ostracized from normal societal interactions. The outcomes achieved not only benefit the patients we serve but provide enormous satisfaction to all those involved in their care.

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