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ORIGINAL ARTICLE

Early dental management of patients with Mobius syndrome

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OBJECTIVE(S): The aim of this study was to evaluate the orofacial manifestations in patients with Mobius syndrome (MS), establish an early adequate dental treatment and discuss the possible etiology of all cases examined based on information about the gestational intercurrences.
DESIGN: Prospective study.
SETTING: Special Care Dentistry Center, School of Dentistry, University of Sao Paulo, Brazil.
SUBJECT(S) AND METHODS: Twenty-nine patients with MS aged 0 to 4 underwent prospective dental examination as well as early orthodontic treatment.
RESULTS: All patients presented micrognathia, lack of lip seal, high arched palate and weak soft palate. The use of orthopedic appliances was recommended to all 29 patients, but only 13 adhered to treatment and were monitored for at least 24 months. We observed that, after 24 months of treatment, the palate was expanded and micrognathia became less severe in the majority of the cases. Pregnancy-related complications were reported by 27 (97%) of the 29 mothers.
CONCLUSION(S): The early use of orthopedic appliances was important to prevent malocclusion and glossoptosis. Attempted abortion with misoprostol is associated with an increased risk of MS in infants.
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Keywords: Mobius syndrome; micrognathia; glossoptosis; misoprostol

Introduction

Although von Graefe described a case of congenital facial diplegia in 1880, Mobius syndrome (MS) was reviewed and further defined by Möbius in 1888 and 1892. Because of these contributions, Möbius is now the eponym used to describe the syndrome (Rubin, 1976; Verzijl *et al*, 2003).

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Mobius syndrome is characterized by agenesis or aplasia of the sixth and seventh cranial nerves, limb malformations and sometimes mental retardation. Clinically, the patient presents total or partial facial paralysis, with lack of facial expression and severe functional problems. Immediately after birth, the patient presents feeding and breathing difficulties, which are related to micrognathia and glossoptosis (Rubin, 1976; Verzijl *et al*, 2003; Domingos *et al*, 2004).

Mobius syndrome is a rare disorder whose incidence has not yet been determined. In Brazil, according to the Mobius Association of Brazil (AMOB), a non-governmental organization, epidemiologic data show that there were approximately 300 subjects with MS in 2004 (http://www.unicamp.br).

Etiology and pathogenesis of the syndrome are still unclear, but two explanations have been proposed: a primary genetic and a primary ischemic cause. Teratogenicity is suggested as an important etiologic factor in both. The postulated etiologic mechanisms are based on limited pathologic observations, which include agenesis or hypoplasia of cranial nerve nuclei, atrophy of cranial nerve nuclei secondary to peripheral nerve involvement, and primary muscle involvement without abnormalities in the brainstem or cranial nerves (Verzijl *et al*, 2003).

Many variants and atypical features of orofacial structures have been described in MS patients, such as high caries incidence, paralysis and hypoplasia of the tongue, weakness of the soft palate and micrognathia (Campistol *et al*, 1980; Rizos *et al*, 1998; Serpa Pinto *et al*, 2002; Harriete *et al*, 2003; Sensat, 2003).

The purpose of this study was to identify the main craniofacial alterations in MS children aged 0 to 4, as well as to propose therapeutic and preventive protocols.

This study is justified because we have already treated 61 MS patients in our outpatient clinic (Special Care Dentistry Center of the University of Sao Paulo). The majority of these patients were referred to our clinic by the Mobius Association of Brazil, and approximately 50% were aged 0 to 4.

Materials and methods

We studied 29 unrelated MS patients (18 men, 11 women) who had been referred to the Special Care

Dentistry Center between 1994 and 2004, with a mean age of 15 months (2–4 years), and whose diagnosis was established by a pediatric geneticist using clinical criteria. The patients' guardians signed an informed consent form, and this project was approved by the Research Ethics Committee of the School of Dentistry, University of São Paulo (FOUSP).

The data obtained during anamnesis and clinical examination, which included information about the gestational period as well as general and oral characteristics, were compiled in a form specially designed for this study. The data obtained from the 29 patients through anamnesis and clinical examination are summarized in Tables 1 and 2.

For the evaluation of micrognathia we used a jaw index propose by Van Der Haven *et al* (1997), defined as: alveolar overjet X maxillary arch/mandibular arch measured in millimeters, which sizes are obtained with the help of a simple measured tape. The normal index is 4,2 ± 1,8. Mathematically, the jaw index is increased in cases where micrognathia is present.

When micrognathia, weakness of the soft palate or glossoptosis were observed, early orthopedic treatment was recommended, and two appliances were used: a specially designed acrylic plate for babies (0–2 years) and/or a maxillary expander with a Hawley arch for children over 2 years of age. Preventive and curative treatment of caries and periodontal disease was performed in all patients.

The plate for babies was manufactured with acrylic resin, according to the procedures proposed by Lopes, who suggested an acrylic jig with a vestibular screen, to which a velar extension was added (Lopes and Andre, 1980; Lopes *et al*, 1991). When necessary, a Castillo Morales plate with additional devices to stimulate lip seal was applied (Glatz-Noll and Berg, 1991).

In patients older than 2 years, an acrylic-splint maxillary expander was used in an attempt to correct the high arched palate. This splint had a shape similar to the plate used for babies, with an expansion screw and Hawley arch.

For fast set alginate impression, stock trays were used when possible, and individual ones were used when necessary.

Patients undergoing treatment were monitored for at least 24 months. During this period, adherence to treatment, position of the mandible (through analysis of the soft tissue profile), occurrence of glossoptosis and lip seal were observed.

Table 1 Data obtained from the 29 patients through anamnesis

Pregnancy-related data
Reports of medication use to induce abortion
Reports of medication use for other purposes
Bleeding
Infectious diseases
Blood pressure problems
Electric shock
Hypothermia
Hyperthermia
Cases of Mobius syndrome in the family
Medical history
Feeding problems
Breathing problems
Glossoptosis

Table 2 Data obtained from the 29 patients through clinical examination

General characteristics	*Number of patients affected*
Strabismus, absence of blinking	25
Foot limb malformation	29
Upper limb malformation	2
Micrognathia	29
Deformed tongue	29
Cleft palate	4
Weakness of the soft palate	29
Lack of lip seal	29
High arched palate	29

Results

Pregnancy-related data are presented in Table 3 and show that 27 (97%) of the 29 mothers reported some kind of problem during pregnancy. Medication intake was the most frequently reported problem. Ten mothers (34.4%) had taken misoprostol to induce abortion. Five (17.2%) had taken other drugs such as cimetidine, antihistaminic, corticoids, or tetracycline to treat diseases. Six mothers (24.1%) reported occurrence of Down's syndrome in the family and three (10.1%) reported cases of cleft palate in the family.

The mean age of the 29 patients who participated in this study was 18 months; the youngest was 45 days old, and the oldest was 3 years and 6 months old. In our sample, 18 patients were male, 27 were white and two were black.

All mothers reported babies' feeding difficulties and breathing problems early after birth. No patient presented any kind of congenital heart disease. Foot malformation was observed in all patients and upper limb malformations were observed in two patients. All patients presented with strabismus and absence of blinking. All patients presented with or had a history of respiratory problems such as upper respiratory infections, bronchitis, or recurrent pneumonia.

All patients presented micrognathia, lack of lip seal, high arched palate, and weakness of the soft palate. Cleft palate was observed in four patients (13.8%). Twenty-nine patients (100%) presented some degree of

Table 3 Problems during pregnancy reported by the 29 mothers

Problems during pregnancy	*Number of cases (%)*
Use of misoprostol to induce abortion	10 (34)
Medication use without abortive purpose	5 (17)
Electric shock	1 (3)
Exposure to biological agents	3 (10)
Blood pressure problems	5 (17)
Bleeding	3 (10)
No reports of problems	2 (7)

paralysis and hypoplasia of the tongue. Sometimes the tongue was lobulated.

The use of orthopedic appliances was recommended to all 29 patients, due to the presence of micrognathia and risk of glossoptosis, but only 20 started the treatment. Among them, 13 adhered to treatment and were monitored for at least 24 months. Four of them have been followed up for 8 years. Among the nine patients who did not undergo orthopedic treatment, two died of asphyxia caused by glossoptosis.

After 4 months of orthopedic treatment, the palate was expanded in 10 patients (77%). After 24 months of treatment, micrognathia became less severe in 100% of the cases. Table 4 shows the initial and final jaw index used to diagnosed micrognathia. In four of the 13 patients who underwent treatment, lip seal was improved.

Discussion

Special Care Dentistry Center is an excellence center for the treatment of medically compromised patients and patients with disabilities. Between 1992 and 2004, a total of 61 patients with MS were seen at our outpatient clinic, and 30 were aged between 2 months and 4 years.

The data obtained through anamnesis in our study corroborate the important role of teratogenic agents in the etiopathogenesis of MS. Among the 29 mothers interviewed, 10 (34%) reported the use of misoprostol to induce abortion. Misoprostol is a prostaglandin E_1 analog that has been approved by the Food and Drug Administration (FDA) to be taken orally for the prevention and treatment of gastric ulcers associated with the use of nonsteroidal antiinflammatory drugs. It has also become an important drug in obstetrical and gynecologic practice because of its uterotonic and cervical-ripening actions (Goldberg *et al*, 2001; Serpa Pinto *et al*, 2002; Sensat, 2003). The information about the use of misoprostol was obtained by means of a query. Mothers were asked once whether any kind of medication had been used during pregnancy to induce abortion. In case the answer was no, the question was not asked again.

Table 4 Initial and final jaw index (after 24 months of treatment) of orthodontically treated patients

		Jaw index (mm)	
Patients	*Age*	*Initial*	*Final*
1	2 years	9.5	6.5
2	1 year and 2 months	13.5	5.6
3	5 months	8.0	6.3
4	45 days	12.00	4.2
5	9 months	9.8	6.8
6	4 months	12.8	3.9
7	10 months	13.0	5.1
8	6 months	14.9	7.0
9	3 years and 6 months	6.0	2.3
10	2 years and 9 months	9.0	2.1
11	2 years and 10 months	9.6	3.5
12	2 years and 7 months	10.3	3.4
13	2 years and 2 months	10.5	5.0

Respiratory problems were very frequent in the population studied, especially breathing difficulties associated with upper respiratory infections, apnea and dyspnea occurring separately or concurrently, and a high incidence of pneumonia. Respiratory problems are closely related to anatomical aspects observed in patients, especially severe microretrognathia. Mobius patients present with hypoplastic tongue, sometimes with lateral deviation. As a result of microretrognathia, the hyploplastic tongue tends to become retracted, leading to glossoptosis.

We believe that early use of orthopedic appliances may prevent glossoptosis. The presence of micrognathia and a hypoplastic tongue must be carefully analyzed, for the more severe the micrognathia, the more retracted the tongue. MS patients usually present high, triangular-shaped palate, which contributes to mouth breathing.

Micrognathia becomes more severe due to low tone of the lateral pterygoid muscle. According to Petrovic *et al* (1973), the low tone of this muscle hinders mandibular growth. Our patients were unable to suck during their first month of life because of hypotonia, commonly observed in MS patients. The most severe case of inability to suck was observed in a 2-year-old girl with a tracheostomy tube and an oxygen cylinder for breathing, and a gastric tube for feeding. She also presented with ankylosis of the temporomandibular joint and severe micrognathia.

The related literature reports cases of MS patients with cleft palate. Four cases of cleft palate associated with MS were observed in our study. These patients presented a U-shaped cleft of the posterior palate, similar to that observed in the Pierre-Robin sequence. The presence of the cleft reduces the risk of asphyxia caused by glossoptosis. Therefore, surgical intervention for correction of the cleft palate must be concurrent with mandibular expansion in order to enable a better positioning of the tongue and reduce the risk of glossoptosis.

Among the 20 patients who underwent orthopedic treatment, only 13 adhered to treatment and were monitored for at least 24 months. Four of these patients have been followed up for 8 years. Among the nine patients who did not adhere to treatment, two died of asphyxia caused by glossoptosis.

Treatment adherence problems were mainly related to socioeconomic factors. It was difficult for parents to take their children to Special Care Dentistry Center. Many patients lived in other cities or states, or had a nasogastric tube in place, and thus the use of public transportation was difficult. In addition, the knowledge that treatment should continue up to adolescence was a discouraging factor for some guardians.

Orthodontic–orthopedic treatment of MS patients is usually difficult because of technical problems – particularly impression – and treatment adherence problems. Alginate impression in patients with MS may be difficult because many of them present microstomia. In our

study, many patients needed custom-made impression trays. Babies were placed on an adult's legs, lying on their stomachs, to avoid flow of the molding material into their oropharynx.

Weakness of the soft palate, clinically observed in all patients, associated with glossoptosis may lead to asphyxia. In order to avoid that, a plate with a velar extension was used by patients. This extension elevates the soft palate, preventing contact with the dorsum of the tongue and consequent asphyxia. A mark was made on the anterior region of the plate to make patients position their tongues more anteriorly, as a result of proprioceptive stimulation. It is important to remember that, in MS patients, motor skills are affected, not sensory ones. The plates were periodically changed, and had to be worn away as teeth erupted. When the upper incisors erupted, a Hawley arch was attached to the appliance to prevent overjet. An expansion screw was also used for effective correction of the high arched palate. The surface of the plate was smooth and allowed projection of the lower jaw, which stimulated its growth.

After the first 18 months of treatment using the plate, a better positioning of the tongue and palatal expansion was observed.

Another oral health problem observed in our study was the high caries incidence in MS patients. A cariogenic diet and the inactivity of perioral muscles contribute to a high caries incidence. We must point out that MS children have difficulty feeding from birth, and sometimes a gastric tube is necessary for nutrition of neonates. When babies leave the hospital, they are fed semisolid food rich in carbohydrates. Based on a cultural belief that foods high in sugar and starch, and semisolid foods taste better, guardians feed their children with a highly cariogenic diet. Inactivity of perioral muscles contributes to poor mouth hygiene, increasing the risk of rampant caries in MS children, especially in the anterior teeth region.

Most of our patients were bottle fed. Bottles are well accepted by children, even when they are sleeping, as bottles prevent contact between the tongue and the palate, and make breathing easier. However, they increase the risk of rampant caries and worsen the high palate problem.

Dentists must provide instructions on diet and oral hygiene. It is difficult to convince guardians about the importance of diet control and proper oral hygiene, but a detailed explanation illustrated by the good results obtained with other patients might be effective.

All patients in our sample presented lack of lip seal, which contributes to a higher risk of caries and overjet. The maxilla generally presents forward and downward growth in subjects with normal facial development. In MS patients, the absence of muscle activity in the upper lip causes excessive forward growth of the maxilla, whereas downward growth is arrested. We thought that the use of a vestibular screen would stimulate the labial muscles, promoting lip seal. However, after 18 months of monitoring, most patients still did not present lip seal.

Early functional orthopedics proved to be feasible, effective and important for prevention of future sequelae caused by facial paralysis in MS patients. Older patients should also undergo orthodontic and orthopedic treatment to minimize occlusal problems, particularly micrognathia due to a neuromuscular deficiency.

Patients with MS are unable to show happiness, sadness or anger through facial expression, which frequently results in severe introversion and a reclusive personality. Therefore, early treatment is recommended, with a multidisciplinary approach to diminish the impact of sequelae on the lives of MS patients and their families.

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