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Original Article

Ring Chromosome 14 Syndrome: What the Dentist Should Know to Manage Children with r(14) Effectively

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Abstract

Introduction: Ring chromosome 14 syndrome, or r(14), is a rare genetic disorder characterized by distinctive facial features, intractable epilepsy, delayed development, intellectual disability, and autism spectrum disorder. With less than 100 documented cases worldwide, the disease is not well known or fully studied. Furthermore, the literature offers little guidance to aid dentists in the management of these patients as r(14) remains undocumented in the dental literature.

Aim: To investigate the manifestations and challenges faced by a group of subjects suffering from r(14), to raise awareness of this syndrome, and to provide tips and suggestions that dentists may find helpful to manage r(14) children effectively.

Materials and methods: A voluntary survey was administered to the caretakers of 13 r(14) patients who, as of 2019, were registered in the NORD (National Organization for Rare Diseases) global data bank (Ring 14 USA Outreach). The patients were assessed for age, gender, geographic distribution, phenotype, physical appearance, maxillofacial characteristics, presence of oral conditions and abnormalities, malocclusion, epileptic seizures, cognitive abilities, speech, muscle tone, nutrition, autism, and other developmental and behavioral points of interest.

Results: Of the 13 patients queried, 7 were male and 6 were female. The age of the patients ranged from 5 to 49 years. Ten patients were of European ancestry and three were Hispanic, all residing across the U.S. The majority of patients were diagnosed as infants, shortly after commencement of uncontrollable seizures. All the patients had microcephaly and presented with Class II malocclusions. More frequent occlusal anomalies and conditions included diastemata of the anterior teeth, congenitally missing teeth, crowding, and drooling. The majority of subjects was unable to speak, suffered from intractable seizures, and frequently exhibited behavioral outbursts.

Conclusions: A child with r(14) may present a considerable challenge to the dentist and staff, but the dental problems of r(14) children are, for the most part, like those of any other patient and can often be handled by the dentist. Depending on the severity of symptoms, some children with r(14) may be as treatable in the dental office as any other child.

Keywords

children, dental management, ring chromosome 14 syndrome, special needs

INTRODUCTION

Ring chromosome 14 syndrome [r(14)] is a rare chromosomal disorder distinguished by refractory epilepsy, intellectual disability, autism spectrum disorder, and a myriad of diverse health issues.[1] Recurrent seizures, developing in infancy or early childhood, are often intractable and resistant to antiepileptic drugs. Other challenges faced by r(14) children include various intellectual and learning disabilities, as well as developmental delays in speech and motor skills such as sitting, standing, and walking.[2]

Individuals with r(14) are typically short in stature and present with microcephaly and puffy hands and/or feet. Facial phenotype may also manifest with subtle differences. Recurrent respiratory infections due to immune issues are a common problem for many r(14) individuals. Abnormalities of the retina, which usually do not affect vision, have also been reported. Major birth defects are rare.[2,3]

The prevalence of r(14) is unknown, but less than 100 affected individuals have been reported in the literature worldwide. The syndrome is caused by one aberrant chromosome 14 whose broken ends fuse together to form a ring. In turn, the loss of several critical genes near the end of the long (q) arm of chromosome 14 (typically at band 14q32.2 or 32.3) during ring formation is believed to result in the major features of the syndrome **(Fig. 1)**.[2,3]

Individuals with r(14) have one copy of the abnormal chromosome in some or all of their cells.[3] However, the syndrome is almost never inherited and the ring chromosome probably occurs as a random event during early embryonic development or during the formation of male and female reproductive cells. Most affected individuals have no family history of the disorder, although at least two cases have been documented in which a ring chromosome 14 was passed on to the child from their mother.[3,4]

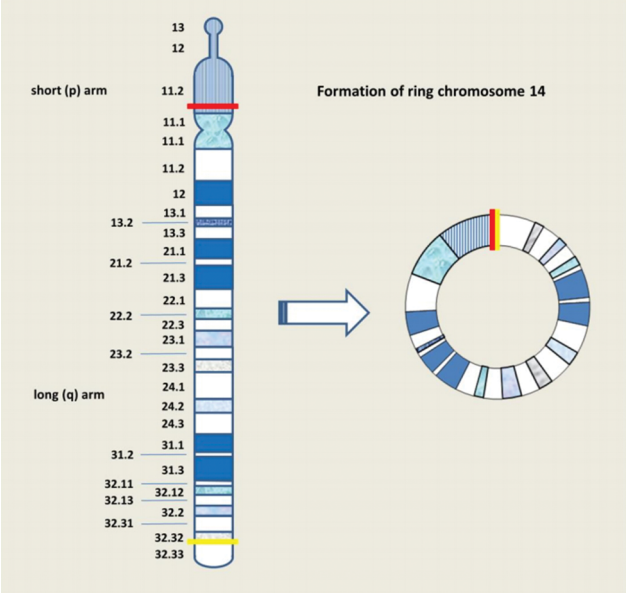

Figure 1. Breakpoints in chromosome 14 during ring formation can vary between patients. The p arm of chromosome 14 is small and may usually be deleted without consequence. The long q arm typically breaks at 14q32.2 or 14q32.3. Breaks at 14q31 and 14q24 may also occur. The loss of genetic material from the q arm is believed to cause the main features of r14.

The symptoms among r(14) individuals may vary in type and severity. Abnormalities may include prenatal and postnatal growth delays, intellectual disabilities, diminished muscle tone, and feeding difficulties. The specific type of epileptic seizures may also vary. Seizures may be myoclonic or tonic-clonic. They may also manifest as sensory or behavioral disturbances or loss of consciousness, as well as loss of bowel or bladder control or other voluntary functions.[5]

Children with r(14) may also present with a distinctive facial appearance, which results from characteristic dysmorphisms of the head and facial area. Besides microcephaly, these may include dolicocephaly, a high forehead, an elongated face, and a flat nasal bridge with a prominent nasal tip. The eyes may be widely spaced with downwardly slanting palpebral fissures and vertical skin folds covering the epicanthic folds. Affected individuals may also have a thin upper lip, downwardly turned corners of the mouth, a high-arched palate, micrognathia, and large, low-set ears **(Fig. 2)**.[1-5]

Since other chromosomal disorders may have similar features, chromosomal testing is necessary to confirm the diagnosis. Conventional cytogenetics can usually identify a ring chromosome once a terminal deletion of chromosome 14q is ascertained by molecular karyotyping.[5] In some cases, r(14) may be diagnosed prenatally by ultrasound, amniocentesis, and/or chorionic villus sampling.[5]

Dentists see patients with all kinds of special needs, developmental conditions and disabilities. Children with r(14) need dental care just like every other child. As with other autism-related disorders, r(14) children need sameness and continuity in their environment.[6-8] The dental literature, however, offers very little guidance to aid the dentist in the management of these children.

AIM

The article aims to make dentists aware of the disorder and provides tips and suggestions that dentists may find helpful to manage r(14) children more effectively.

MATERIALS AND METHODS

In 2019, a medical student and dentist reached out to Ring14 USA Outreach, a non-profit organization founded by a group of mothers whose children have r(14). The mothers advocate not only for the children but also the doctors, caregivers, friends, and family who help to care for these children. They also work to raise public awareness about the disorder. The medical student asked if the mothers would be willing to answer some questions about their experience with the disease in the form of a survey.

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Figure 2. The children were characterized as having a pleasant and affectionate demeanor. Most were short in stature and presented with distinctive features of the craniofacial area. Such features included microcephaly with a high forehead, an elongated face, widely spaced eyes, down-slanted palpebral fissure, thin upper lip, a flat nasal bridge with a prominent nasal tip, large low-set ears, micrognathia, and a high palate.

Participation by the mothers was voluntary and informed consent was obtained. The study conformed to the tenets of the Declaration of Helsinki as well as the requirements established by our institutional review board.

The survey was comprised of 26 questions, which included: five anthropometric questions related to gender, race, birth weight, current weight, current height; diagnostic tests conducted; type of doctor who delivered the diagnosis; onset of the disease; signs and symptoms at disease onset; current signs and symptoms; if other members of the family had the disease; whether microcephaly was present; and presence of lymphedema. Does the child experience any seizures? If so, when did they begin? How frequently do they occur? What type of seizure is experienced? Have any antiepileptic medications been administered? Was treatment effective in controlling the seizures? To what extent is the child capable of communicating?

Questions related to dentistry included: Has the child ever visited a dentist for an oral/dental examination? If so, how did the child respond to the dentist? At what age did the child begin to develop their permanent teeth? Does the child present with any oral abnormalities, for example, oral sores, ulcerations or patches, delayed eruption of teeth, bleeding and inflammation of the gums, missing or supernumerary teeth?

Two questions asked: Is the I.Q. of the child known? If so, what is the I.Q.? Finally, the mothers were asked: Are there any additional complications? What is the most challenging aspect of this disease for the child and the caregiver/parent/guardian? Is there any additional information, comments, signs, symptoms, behavioral patterns? If possible, the mothers were asked to attach photos demonstrating specific abnormalities related to their child's condition, for example, facial dysmorphisms, misaligned teeth, etc.

RESULTS

Of the 13 patients queried, 7 were male and 6 were female. The age of the patients ranged from 5 to 49 years. Ten patients were of European ancestry and three were Hispanic, all residing across the U.S. In all 13 cases, the onset of disease was marked by seizures at infancy, at about 3 months and as early as 3 weeks. No other family members had a history of the disease. All the patients suffered from 'global development delay', taking longer than other children their age to reach key developmental milestones, such as walking or talking, acquiring fundamental movement skills, and learning to interact with others. The ability of the children to communicate was limited, some with a vocabulary limited to a few words and most very good at communicating with facial expressions, cries, or simply pulling at their par-

ents to get their attention. Other complications included lung disease, scoliosis, tracheotomy, and feeding tube.

All the children were characterized as having a pleasant and affectionate demeanor. Most were short in stature, microcephalic, and presented with distinctive facial features. The face was generally elongated and presented with a high forehead. The eyes were widely spaced and distinguished by down-slanted palpebral fissures. The nasal tip was prominent and the nasal bridge was flat. The ears were set low and the upper lip was thin. Other craniofacial features included micrognathia and a high palate.

All the individuals suffered from epilepsy, which in most cases was drug resistant. The onset was varied, but usually presented during the first few months after birth. The seizures were mostly generalized, but could also be focal and spread to other areas. Seizures could occur when the children were awake or asleep. Cluster seizures were also possible, occurring over a period of 24 hours. However, status epilepticus was not indicated in any of the individuals. In two cases, the frequency of seizures gradually ameliorated by the time they became adolescents. In half the patients, however, the seizures were reported to be so intense that it would often set back previous gains in language and psychomotor skills.

Recurrent infections and episodes of exanthema could also trigger seizures. Seizures could eventually become less frequent, but they did not completely disappear. Antiepileptic drugs were frequently used, including carbamazepine, valproic acid, vigabatrin, topiramate, clobazam, and others. About half of the children developed some degree of drug resistance, while the other half had seizures under varying degrees of control. In two cases, where seizures seemed to disappear altogether and effective antiepileptic drugs were stopped, the seizures returned but would not respond to former medications.

One patient experienced complications of insomnia, mood disorder, neurogenic bladder, autism spectrum disorder, mild cerebral palsy, global development delay, chronic dehydration, chronic constipation, keratosis pilaris, allergies, and microcephaly. Her mother stated, "She can carry a simple conversation, but she cannot read or write and the pronunciation of the words is not always correct." Another patient had low muscle tone, feeding issues, global delayed development and sometimes expressed aggressive behavior. One child was born with a heart murmur, high bilirubin, hypothyroidism, and feeding difficulties. Another child with brain malformations had GI issues, severe reflux, low tone, esophagitis, dysphagia, neuronal migration disorder, and global developmental delay. The child was completely non-verbal.

Moderate to severe intellectual disability was a consistent feature among the r(14) children studied. This condition appeared to correlate with seizure severity and time of onset. Autism spectrum disorder presented in children who experienced their first seizure very early on. Most of the children achieved postural control by their first birthday, while those who could walk took their first steps by 3 years of age. Unfortunately, two patients were not able to walk at all.

Language was the most common developmental disability. Behavior disorders were also reported in many of the children. Although the children were described as usually good natured, tantrums were also noted. Behavior characteristics of autism included anxiety, restricted or repetitive motor movements, obsessive routines, hyperactivity, and heightened or lessened excitability to sensory input.

Additional issues included feeding issues, slow gastric emptying, and pump feeds at night. One child, reported as having sensory processing disorder, was delayed in expressing when he feels pain. Another child, reported as having intractable epilepsy, OCD, sensory processing disorder (SPD), autism, pronated ankles, mental and growth delay, and compromised immune system was completely non-verbal. Behavior patterns such as sensory seeking seemed very common. Others suffered from strabismus, renal issues and were tube fed. In addition to seizures, some children experienced ataxia and body tremors, while others suffered from joint contractures.

Hypotonia was also common with the children and often involved the axial muscles. Physical therapy could help to gradually improve muscle tone in many. However, impaired motility beginning during infancy could result in muscle contractions, scoliosis, and flat foot.[1]

Many of the r(14) children suffered from frequent upper respiratory infections, though cases of recurrent pneumonia were rare. Since many of the children also suffered from gastrointestinal issues, malnutrition was a serious concern. At times, the condition could be life threatening, especially when factoring in the role of seizures.[1-5] Refractive issues such as myopia and astigmatism can also be observed in r(14) syndrome.[1-5] However, strabismus was most often reported. Less frequently observed conditions included sleep disorders and arthritis, as well as congenital heart defects.

Dental

All the children had visited a dentist at least once for a dental examination. The children varied widely in their ability to understand and cooperate during dental treatment. Three patients were very overwhelmed and the dentist was able to do an exam but not a cleaning. One patient had a cleaning under sedation. In contrast, two patients were very cooperative. Another patient was so cooperative that he regularly presented for biannual recall prophylaxis. Virtually all the children displayed late eruption of the permanent teeth, in some cases as late as by 3-6 years. Most frequently encountered dental problems included (Class II) malocclusion, crowding, and congenitally missing teeth. Poor muscle tone, incessant chewing, teeth grinding, sleep bruxism[9], and tongue thrusting were contributing factors. Malocclusion was often accompanied by difficulty swallowing and drooling, which may contribute to difficulties in verbalization. Gastroesophageal reflux and dyspepsia reported in many of the children, predisposes the teeth to erosion.[7,8]

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DISCUSSION

The r(14) children in this study have varying ability to comprehend dental treatment and cooperate with the dentist. Thus, detecting caries and other dental issues by means other than observation may be problematic. Obtaining an accurate dental history may be difficult due to limitations on the child's ability to communicate effectively. R(14) children with autistic traits may have a higher pain threshold and, consequently, may not indicate to the dentist when they are experiencing major discomfort. Behavioral issues, including hyperexcitability and bursts of aggression may also hamper the delivery of treatment.[10-15] Temper tantrums and other violent behaviors, triggered by invasive dental treatments, may expose the child to the risk of self-injury. Thus, in some cases, general anesthesia may be necessary to execute full mouth rehabilitation and allow the dentist to provide comprehensive treatment in a single appointment safely and without rushing.[7] The child's parents must also be made aware of the importance of routine dental check-ups and follow-ups. A successful long-term care plan should include routine oral prophylaxis, effective oral hygiene homecare that may require assistance from the parents, fluoride treatments, and consumption of non-cariogenic healthy foods such as cheese, nuts, and plain milk.[7]

The parents' perspective

Caring for a child with r(14) syndrome is challenging and often stressful. However, the parents in this study embraced the opportunity with unconditional love. There are many factors that make caring for an r(14) child difficult. Because the syndrome is so rare, it is difficult for family physicians to recognize. Furthermore, r(14) children can present with multiple symptoms, which are often overlapping and not directly induced by the disease. Due to their cognitive and language disabilities, children with r(14) syndrome cannot always express their pain and discomfort. Thus, the parents must in effect be their eyes and ears to continually monitor and voice their condition to physicians for them. The disease can also have profound effects on the entire family. As one parent often sacrifices their career in order to tend to the child, this can add further emotional and financial stress in adapting to the new situation. Caring for an r(14) child can also be a full-time job. The attention, time, and effort dedicated to these special needs children may unintentionally be diverted away from the parents' other healthy children, whose lives are also profoundly affected. Parents often find themselves learning to live in the moment of their r(14) child, but emerge from the experience with an extraordinary ability to anticipate seizures and see things that others may not understand. During this uncharted journey of unexpected and unplanned personal growth, the parents ultimately evolve into key intercessors and counselors in the dynamics of the child's management.

Medical management

Management depends on the symptoms in each child and often requires a team of specialists to address each medical issue. Because symptoms and severity can vary, the prognosis depends mainly on the health issues present and complications that may arise.[1] Medical management focuses on feeding problems, treatment of infection, control of seizures, and supportive measures.

A developmental evaluation may be conducted to assess the child's motor, cognitive, social, and vocational skills. Treatment might include a feeding specialist, occupational therapist, and speech pathologist. A child development specialist might evaluate the r(14) child with autism spectrum disorder for early intervention programs that may help to manage abnormal behaviors and meet the child's developmental needs.

A prognosis for expected lifespan in r(14) individuals has yet to be established, although one patient in our survey was 49 years old. Considering clinical variability, prognosis depends primarily on individual comorbidities and medical complications. Seizures, infections, and nutritional deficiencies are major determinants. Treatment typically requires a multidisciplinary team of pediatricians, neurologists, orthopedists, physical therapists, and other health care professionals[1], including dentists.[7]

In some cases, treatment with anticonvulsant drugs may help prevent, reduce, or control seizures. Regular follow-up visits to evaluate seizures are important. It is also important not to interrupt effective antiepileptic therapy even if the symptoms appear less severe. Treatment may also include measures to help prevent or treat respiratory infections. Respiratory complications are frequent in r(14) patients, primarily because of diaphragmatic weakness, aspiration, and recurrent infections. Thus, respiratory physiotherapy is individualized for each patient. This may include antibiotic prophylaxis for recurrent pulmonary infections and oxygen therapy for more severe conditions. In addition, orthopedic and physical therapy may help prevent or correct contractures. Physical therapy should be started early to reduce scoliosis and other hypotonic conditions.[1] In individuals with congenital heart defects, surgical correction may also be required.

In most cases, r(14) children are extremely underweight, anorexic, and inclined to malnutrition. Therefore, nutritional evaluation by a dietician or nutritionist may be appropriate. Enteral tube feeding is recommended with severe anorexia or when aspiration occurs during swallowing due to dysphagia. When oral feeding is not possible, a nasogastric tube may be used. In severe cases of dysphagia, a gastrostomy may be necessary to continue administering drugs to treat epilepsy and frequently occurring gastrointestinal conditions, including dyspepsia.[1]

Although the communicative skills of the children varied greatly, the current survey showed that only four out of 13 children with r(14) syndrome could use words to communicate and only two of them could speak fluently.

Some children relied on gestures or kinesics to communicate. The mothers of non-verbal children also reported a higher number of challenging behaviors. The communication skills of many of the children were also affected by the presence of autism. As with other children with autism spectrum disorders, intensive behavioral therapy may help to reduce challenging behaviors. A trained therapist can assess the child regularly for speech and language development and tailor therapy based on the child's age and individual needs.[1,7]

Dental management

Routine oral prophylaxis, regular brushing, and fluoride treatments are indispensable for the r(14) child's dental treatment and well-being. Dental examinations should routinely monitor for dental issues, including malocclusion and crowding. As extended bottle feeding, continuous antibiotics therapy, and gastric acid reflux can result in poor enamel formation, r(14) children should be monitored regularly for accelerated tooth decay.[6] Chewing problems and difficulties with swallowing may be alleviated with oral-motor therapy. Orthodontic treatment may be necessary to correct malocclusion. Nutritional evaluation may help r(14) children suffering from dyspepsia and recurrent gastric acid reflux. Infants suffering from gastric acid reflux may be helped by smaller feedings and positioning, as well as feeding the infants with thickened formula. Older children with GER might benefit from avoiding eating two to three hours before bedtime, as well as abstaining from spicy foods. Still other patients may benefit from appropriate medication, including antacids.[7] A sleep study might be appropriate for children suffering from sleep disturbances to assess for sleep apnea/hypopnea.[7,8] Melatonin may also be considered to improve disturbed sleep.[9]

Tips for dentists

The severity of the patient's symptoms will undoubtedly impact the general dentist's decision to treat individuals with r(14) at the office. The patient's ability to cooperate, as well as the dentist's experience with special needs patients will also determine whether or not to refer the child to a pediatric dentistry specialist. As each patient is different and the circumstances will vary, the dentist must weigh the benefits versus the risks of treatment, keeping in mind that the safety of the patient is a priority. Without dental guidelines specific for r(14) patients, the same treatment principles recommended for other special needs children with developmental and intellectual disabilities may be appropriate for r(14) patients as well.[7]

Children with r(14) need sameness and continuity in their environment. Therefore, it may be prudent for the dentist to plan a desensitization appointment before any dental care is given, to help familiarize the child with the office and staff. Since the child may be easily overwhelmed by loud noises, sudden movement, and things that are felt, a slow gradual exposure to the dental office and staff may benefit the r(14) child. A short and positive first appointment, which permits the parents and the child to tour the dental office, ask questions and touch the dental equipment, will also help acclimate the child to the new environment, as well as to build trust. Permitting the r(14) child to bring a blanket, favorite toy, or other comfort item may further have a calming effect on the child. The parent or caregiver can also be consulted for additional recommendations and tips on how best to manage the child.[10-15]

Explaining the procedure beforehand, as well as inviting the child to sit alone in the dental chair can help them adjust to the treatment environment. The child should always be approached in a quiet, non-threatening manner and treatment should be provided using a "tell-show-do" approach **(Table 1)**. Showing the instruments that will be used may satisfy the child's need to know what will occur next, as it would be wrong to assume that the child does not or cannot comprehend. Thus, the dentist should try to explain what is being done so it makes sense to the child and every treatment should be explained before it occurs. The child should not be crowded and should always be told where and why the dentist needs to touch them, especially when using dental instruments. The dentist should also try to speak in short and direct phrases. As with autistic children, children with r(14) may take everything literally. Thus, it is important to watch what the dentist says and to avoid words or phrases with double meanings.[10-15]

To reduce the risks of accidental injury to the child, the area around the dental chair should always be kept clear and free of clutter. In the event of a tantrum or aggressive behavior, immobilization techniques to keep the child from potential injury may be used only with parental consent. Using the same staff, dental operatory, and appointment time

Table 1. Tips for the dentist to manage r(14) children[6,7]

Begin the oral examination slowly, using fingers only.
Switch to a dental mirror or toothbrush, for further access.
Keep light out of the child's eyes and dental instruments out of sight.
Minimize sounds, odors, and other sensory input. Avoid cologne or aftershave.
Avoid interruptions and minimize staff in the operatory.
Reward cooperative behavior with positive verbal reinforcement and ignore poor behavior.
Watch for sudden body movements to prevent accidental injury.
Invite the parent to hold the child's hand during the procedure if the child becomes agitated.
Moderate pressure may calm some children with autism. • Drape a lead apron over the child. • Place a weighted blanket over the child. • Place your hand on the child's forehead while working. • Distract the child visually with toy or video • Massage to help reduce sensitivity.

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during each visit may also help to maintain the child's need for sameness in the surrounding environment and ultimately reduce the child's anxiety. For more complex surgical or restorative treatment, some children may need sedation or general anesthesia which should always be preceded by consultation with the child's physician. Follow-up appointments should also be kept short and to the point.[10-15]

Dental treatment and prevention

As with autism, higher functioning r(14) children with severe bruxism or self-injurious behavior may need to be prescribed a mouth guard.[10-15] For some of these children, powered toothbrushes may need to be avoided as they may be too stimulating; while other children may find the vibration of a powered toothbrush more tolerable than a regular brush. Therefore, powered toothbrushes should only be recommended after determining if the child will tolerate one.[10] In the event of an epileptic seizure during treatment, all dental instruments should be removed from the mouth. The dentist should stay with the child and turn the child to one side, while continuously monitoring the airway to mitigate the risk of aspiration. If the seizure continues for more than 3 minutes, the dentist should immediately call EMS, as the status is potentially life threatening.[10]

Seizures at the dental office or elsewhere pose a risk for tongue injuries[16], TMJ damage[17], or aspiration of a tooth[18]**.** TMJ dislocation, though rare during status epilepticus, may also cause hypersalivation, impaired swallowing, and breathing difficulties. If immediate TMJ reduction cannot be done, the patient should be intubated to protect the airway.[17]

Children with epilepsy, in general, are also susceptible to decreased oral health and dental status. The high prevalence of caries, injury, and periodontal disease among epileptic children is in great part due to neglect, inadequate oral hygiene, and oral injuries.[19] Consequently, management of the special needs epileptic patient is an extraordinary challenge for the dentist and, therefore, requires a well-thought-out treatment plan and strategy.

Dentists should note that patients taking carbamazepine for extensive periods of time are at risk of thrombocytopenia. In addition to excessive bleeding and delayed healing, common oral side effects include increased microbial infections and xerostomia. Reduced salivary flow, deficient oral hygiene, and cognitive disabilities, in turn, can make the mechanical removal of dental biofilm difficult and, consequently, predispose the child to caries and gingivitis. Therefore, the dentist should routinely provide the child with regular fluoride treatments and reinforce oral hygiene instructions at every visit.[17]

Due to the danger of possible aspiration and injury during seizures, fixed prostheses should take precedence over removable appliances.[20,21] Problems with prostheses are usually related to loss of retention or occlusal changes caused by jaw growth.[22] Therefore, parents should be informed about these potential changes and that a permanent restoration can be fabricated after the jaw and the permanent dentition are fully developed.

For patients requiring surgical, endodontic and prosthodontic treatment, conscious sedation and general anesthesia can be used in patients with epilepsy and are not contraindicated. Nitrous oxide or intravenous sedation may also be used to safely and effectively provide treatment.[21] In lieu of sedation, the dentist may optionally try the "tell-show-do" approach to condition the child before treatment.[22] To minimize the risk of stress induced seizures, treatment should also be scheduled during a time of the day when seizures are less likely to occur.[20] The use of dark glasses can shield the child's eyes from the intense overhead light which, in turn, may potentially trigger a seizure. Treatment should also be carried out only after the child has taken their antiepileptic medication.[20] Finally, the child's pediatrician should also be consulted about the planned treatment before its commencement.

Unfortunately, antiepileptic drugs can also induce gingival hyperplasia. Gingival hyperplasia is reported to occur in half of the patients who take phenytoin.[23] Antiepileptic drugs may also cause xerostomia, making patients more susceptible to tooth decay. Therefore, the dentist should monitor for signs of gingival hyperplasia or xerostomia, and recommend appropriate oral hygiene measures to help prevent caries and gingival disease. New generation antiepileptic medications such as vigabatrin have improved seizure outcome in pediatric patients with intractable epilepsy.[24] However, common side effects include visual field defects, increased appetite, and obesity.

In the event a seizure occurs at the dental office, it is important for the dental team not to panic. Most epileptic seizures end so rapidly, there is really not much time to intervene. Once the seizure ends, the dentist simply needs to check the child for possible injuries. Tonic-clonic seizures, which are the most pronounced and disconcerting of the seizures, are usually longer in duration compared to other seizures. If the child experiences a seizure in the dental chair, the Epilepsy Foundation has created valuable first aid tips to help them through it **(Table 2)**.[25,26]

CONCLUSIONS

The dentist and dental staff may find the challenge of managing a child with r(14) to be daunting. However, a good starting point may be to first familiarize the child with the office surroundings, as well as the planned procedure. If there is any doubt about proceeding with treatment, the dentist should consider referral to a pediatric dentistry specialist. Notwithstanding, r(14) children still need dental treatment like any other child and many dentists are quite adept at handling patients with special needs, despite the fact that many of these children may be limited in their ability to communicate and interact with others. R(14) children may find the dental office to be quite overwhelming at first, especially when considering the sensory overload of

Table 2. Seizure first aid (Epilepsy Foundation First Aid Tips)[25,26]

DOs	DON'Ts	Status Epilepticus
Stay with the child until they are awake and alert. Time the seizure. Remain calm. Keep the child safe. Move them away from harm. Turn the child onto their side if not awake and aware. Keep airway clear. Loosen tight clothes around their neck. Put pillow under their head.	DO NOT restrain. DO NOT put objects in their mouth. DO NOT get help.	Call 911. Monitor the child's breath and pulse. If breathing without a spinal cord injury, carefully roll them on their side to keep airway open. If breathing with a spinal cord injury, leave them as is so they can breathe. If they vomit, carefully roll them on their side while supporting the neck and back. Keep them warm.

the lights, smells, and sounds peculiar to the dental office environment. However, these are things that all can be dealt with to manage the child successfully and should not deter the parent of a child with r(14) from seeking the help of the dentist. It is especially important for the dentist to address the oral hygiene needs of the child; and taking a measured approach to dental exams and cleanings may be prudent and very effective. Sedation can also be helpful when the child presents with more complex treatment, including general anesthesia if the treatments of the child are more extensive and protracted. However, this should always be planned in consultation with the child's physician. Since the medical conditions between r(14) children may vary significantly, the approach to treatment for each child may be different also. In less severe cases, some r(14) children may be treated at the dentist office the same as any other child.

Given the rarity of r(14) in the general population, it is essential to establish standards and best practices to improve the clinical and social issues affecting these children, as well as their families. The tips provided in this essay are, therefore, offered as suggestions which are intended to guide dentists in the absence of any rule books. It is hoped that this study will encourage researchers focused on the study of r(14) to expand their efforts further to include the dental needs of these children as well.

Author contributions

Dr. Chris S. Ivanoff and Dr. Athena E. Ivanoff equally contributed to the design and execution of the study, collection and analysis of data, background research, and preparation of the study for publication.

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Синдром кольцевой хромосомы 14: что должен знать стоматолог, чтобы эффективно лечить детей с r(14)

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Резюме

Введение. Синдром кольцевой хромосомы 14, или r(14), представляет собой редкое генетическое заболевание, характеризующееся отличительными чертами лица, трудноизлечимой эпилепсией, задержкой развития, умственной отсталостью и расстройством аутистического спектра. Во всём мире зарегистрировано менее 100 задокументированных случаев, болезнь недостаточно известна или полностью не изучена. Кроме того, литература предлагает мало рекомендаций, помогающих стоматологам в лечении этих пациентов, поскольку r(14) остаётся незадокументированным в стоматологической литературе.

Цель: Изучить проявления и проблемы, с которыми сталкивается группа лиц, страдающих r(14), повысить осведомлённость об этом синдроме и дать советы и предложения, которые стоматологи могут счесть полезными для эффективного лечения детей с r(14).

Материалы и методы: Был проведён добровольный опрос лиц, осуществляющих уход за 13 пациентами с r(14), которые по состоянию на 2019 г. были зарегистрированы в глобальном банке данных NORD (Национальная организация по редким заболеваниям) (Ring 14 USA Outreach). Пациентов оценивали по возрасту, полу, географическому распределению, фенотипу, внешнему виду, челюстно-лицевым характеристикам, наличию заболеваний и аномалий полости рта, неправильному прикусу, эпилептическим припадкам, когнитивным способностям, речи, мышечному тонусу, питанию, аутизму и другим аспектам развития и поведения. представляющих интерес.

Результаты: Среди 13 опрошенных пациентов 7 лиц мужского пола и 6 – женского пола. Возраст больных колебался от 5 до 49 лет. Десять пациентов были европейского происхождения, трое были латиноамериканцами, все проживали в США. Большинство пациентов были диагностированы в младенчестве вскоре после начала неконтролируемых припадков. Все пациенты имели микроцефалию и аномалии прикуса II класса. Более частые окклюзионные аномалии и состояния включали диастемы передних зубов, врождённое отсутствие зубов, скученность и слюнотечение. Большинство испытуемых не могли говорить, страдали от трудноизлечимых припадков и часто демонстрировали поведенческие всплески.

Заключение: Ребёнок с r(14) может представлять собой серьёзную проблему для стоматолога и других лиц медицинского персонала, но проблемы с зубами у детей с r(14), по большей части, такие же, как и у любого другого пациента, и часто с ними может справиться стоматолог. В зависимости от тяжести симптомов некоторые дети с r(14) могут лечиться в стоматологическом кабинете так же, как и любой другой ребёнок.

Ключевые слова

дети, лечение зубов, синдром кольцевой хромосомы 14, особые потребности