COMMUNICATION DEVELOPMENT OF A YOUNG CHILD WITH FOETAL RETINOID SYNDROME: A SEVEN-YEAR FOLLOW-UP STUDY

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ABSTRACT

The aim of the article is to describe the communication development of a child with Fetal Retinoid syndrome (FRS) from six months to seven years of age. Little is known about this rare acquired syndrome and its long-term implications, especially on a child's communication development. A descriptive, ex post facto research design was used to study the participant's communication development from 1996 when the family enrolled in an early communication intervention programme. Annual serial assessments of the participant and her family were conducted and the data were stored in a research database after each assessment. The results are described according to a 4-level assessment framework and indicated consistent, but moderate to minor delays in the participant's communication development with a mild hearing loss in the right ear, associated with ear anomalies. Although prenatal exposure to isotretinoin may have serious effects on the unborn fetus and even cause death, the participant did not display all the symptoms of FRS described in the literature. The favorable family circumstances, early commencement of intervention, and supporting early educational environments were protecting factors that could have contributed positively to the participant's communication development. The importance of knowledge accumulation about rare syndromes such as FRS in Communication Pathology and Audiology is discussed and guidelines for early identification, assessment and treatment applicable to the case are proposed as an intervention option.

Key words: Fetal retinoid syndrome, communication development, rare syndrome, early communication intervention, longitudinal study

INTRODUCTION

Since its licensing in 1982, isotretinoin, the main compound in Roaccutane®, has successfully been used for the treatment of cystic acne that occurs predominantly in women between the age of 15 to 44 years (Honein, Paulozzi & Erickson, 2001). The increase in use of isotretinoin among women of this childbearing age group raised serious concerns regarding the possibility of pregnancy during the use of this powerful teratogen. Experimental studies on animals and descriptive research utilizing human subjects found serious implications for embryonic and foetal growth when isotretinoin was used by the mother (Moerike, Pantzar & de Sa, 2002). The complex of symptoms in infants prenatally exposed to isotretinoin is known as Foetal Retinoid syndrome (FRS) or retinoic acid embryopathy and these infants may display an array of morphological, sensory and developmental disorders (Adams, 1990; Moerike et al., 2002).

Isotretinoin is classified as a Category X drug, i.e. contraindicated during pregnancy (Kassis, Sunderij & Abdul-Karim, 1985) and its use is rigorously controlled. Although a pregnancy prevention programme was initiated by the drug distributor in 1988 (Leach, Dominguez, Ruszkowki & Rudy, 2001), isolated cases of pregnancy during the use of the drug are still reported (Atanackovic & Koren, 1999). According to Kuznar (2001) pregnancies during the use of isotretinoin may occur as a result of false-negative pregnancy tests or lack of information about contraceptive methods. Christiansson (personal communication, 1997) added that isotretinoin, although an expensive drug, was also known to be used by women to induce the abortion of an unwanted pregnancy. The misuse of the drug for these purposes may now have stopped since the legalization of abortions in South Africa in 1996.

It is, however, useful to document rare cases of FRS in order to contribute to the limited knowledge base of the syndrome and to use the information for prevention, early identification, individualised early intervention services and to facilitate family-to-family contact where children are affected by by this rare syndrome. Knowledge about FRS is particularly important to speech-language therapists and audiologists, since limited data exists on the long-term influence of prenatal exposure to isotretinoin on a child's speech, language and hearing development.

Shprintzen (1997) describes FRS under a category of syndromes related to speech, language, hearing and cognitive disorders, and reports that children with FRS are expected to display serious conductive hearing loss, speech and language delays, as well as learning difficulties. The only study on the development of children with FRS reported that 52% of the subjects had low intelligence levels (Adams, 1990). In contrast with the dearth of studies on developmental aspects of children with FRS, the teratogenic effects of the drug on prenatal development are described in detail.

Knowledge about the chemical composition of isotretinoin may assist in understanding the congenital anomalies caused by the drug. Isotretinoin is an analogue of vitamin A, which implies that vitamin A and isotretinoin are similar in terms of chemical composition, but differ in characteristics. Vitamin A is the alcohol retinol, which metabolizes to form the aldehide retinal, which metabolizes to form retinoic acid. The natural form of retinoic acid is an all-trans derivate, tretinoin, which is a potent Vitamin A derivate. Isotretinoin is the 13-cis form (this form changes directly to the all-trans form) that differs stereo-chemically from tretinoin, i.e. in terms of the direction of the acid tail. The acid tail is the non-polar tail region of the molecule (Rosa, Wilk & Kelsey, 1986). Since isotretinoin and vitamin A have the same chemical composition, both influence the structures that develop from the neural crest cells in early embryonic life. Excessive consumption of vitamin A during pregnancy may cause anencephaly, ocular abnormalities, morphological abnormalities of the limbs, labial

clefts and abnormalities of the kidneys and adrenaline glands in the infant (Carlson, 1999). Consumption of *isotretinoin* during pregnancy, however, causes different abnormalities in the developing embryo and fetus.

The origin of morphological and sensory impairments, and subsequent communication disorders in children with FRS, can be traced to the effects of isotretinoin during embryogenesis (during the 3rd to 8th week of gestation). Transcription factors are one of the groups of molecules responsible for initiating patterns of gene expression resulting in the extensive developmental changes characteristic of embryogenesis. Hox genes are some of the most important transcription factors that attach to specific Deoxyribonucleic Acid DNA sequences in order to assist in regulating the development of a specific area in an organism that produces proteins. There are approximately 60 amino acids regulating gene expression or expression of transcription factors in such an area (Emery & Mueller, 1992). Hox genes are arranged in a specific sequence on the chromosome, and gene expression occurs along the cranio-caudal axis of the embryo in this sequence. Mutations of these gene sequences may cause a change of direction in gene expression. An excessive amount of retinoid acid causes the cells of a specific *anterior* rhombomere (segments of the embryological hindbrain giving rise to motor nuclei of certain cranial nerves) to form the structural equivalent of a *posterior* segment. The change in direction of gene expression causes morphological abnormalities of the rhombomeres as well as changes in the neural crest cells (Carlson, 1999). The teratogenic capacity of isotretinoin therefore may cause a mutation of the gene expression sequences.

According to Monga (1997) and Webster, Johnston, Lammer and Sulik (1986) isotretinoin disrupts the normal activity of the cephalic neural crest cells as well as the migration of the mesenchymal cells (loosely organized embryonic connective tissue, regardless of its origin). The disruption manifests itself clinically, since the majority of structures affected in children with FRS originate in the mesenchymal and neural crest cells, causing neural tube defects, as well as ear, craniofacial and heart anomalies (Sadler, 1995).

Mesenchymal cells originate from the mesoderm, the middle germinal layer of the embryo and give rise to the pharyngeal arches (Jacobs & Meiring, 1997). The cascading effect of isotretinoin, that disrupts the migration of mesenchymal and neural crest cells, may therefore influence the development of the pharyngeal clefts and arches, specifically causing ear and craniofacial anomalies.

The typical pattern of symptoms of infants prenatally exposed to isotretinoin involves the craniofacial structures, heart, thymus gland, brain and cranial nerves. The morphological and sensory impairments that can be expected in children with FRS are summarized in Table 1.

Table 1: Possible congenital anomalies in children prenatally exposed to isotretinoin.

Structure or system	Possible anomalies described in the literature
Craniofacial structures	• Micrognathia: Unusually small mandible or maxilla • Midfacial hypoplasia • Facial asymmetry • Hyperthelorism • Facial nerve hypoplasia • Isolated cases of cleft lip and palate
Hearing and vestibular system	• Absence of the pinna or microtia (small pinna) • Constricted external auditory meatus • Protrusion of bone marrow in the middle ear cavity • Abnormal ossicles • Absence of the chorda tympani and stapedius muscle • Abnormalities of the membranous labyrinth in the vestibule • Impairment of the auditory nerve • Hypoplastic lateral semicircular channel • Enlarged vestibular aquaduct and endolymphatic sac
Cardiovasular system	• Defects of the aorticopulmonary septum
Thymus gland (part of the lymphatic system)	• Ectopia (abnormal position of the thymus gland) • Hypoplasia of the thymus gland
Central nervous system	• Abnormal genesis of the cerebellum • Hydrocephaly • Microcephaly • Impairments of cranial nerves (Optical, occulomotor and trochlear nerves) • Neural tube defects
Skeletal system	• Shortened limbs or digits

(Sources: Guirgis, Wong, & Tychsen,, 2002; Ishijima & Sando, 1999; Moerike et al., 2002; Sadler, 1995)

It is clear from Table 1 that many of the characteristic of FRS may also be associated with other syndromes displaying cranio-facial anomalies. As a result of the rareness of the syndrome, it may not be diagnosed correctly during a physical examination at birth. Anomalies of the external ear, and concomitant hearing impairment, however, may be detected during newborn hearing screening. Paediatric audiologists may therefore play an important role in identifying infants with FRS early and facilitate the process of diagnosis and appropriate early communication intervention (ECI).

According to Table 1 prenatal exposure to isotretinoin may cause a diversity of anomalies in children. Lammer et al. (1985) found that exposure to isotretinoin mostly occurs very early in pregnancy, before completion of organogenesis. According to Monga (1997) the critical periods for exposure to isotretinoin are before 28 days gestation and after 63 days of gestation, and it appears that the timing of exposure to the drug is the determining factor, and not so much the dose of exposure.

FRS is therefore an acquired congenital disorder caused by a powerful teratogen, resulting in the mutation of gene sequences, which produces a unique pattern of impairments that may hold long-term consequences for a child's development. Although the morphological impairments of FRS are present in an infant at birth, these infants may be identified late since the syndrome is so rare. The dearth of research on the long-term consequences and development of children with FRS may add to delayed identification, diagnosis and intervention of these children. In addition, insufficient knowledge about genetic disorders is a self-identified need among speech-language therapists and audiologists in South Africa (Khan, 1999). Opportunities to study young children with genetic disorders should therefore be used in order to increase knowledge and early intervention options.

The rationale for the study is based on the need to accumulate long-term data on the communication development of children with FRS. Documenting cases

of rare syndromes such as FRS may contribute to the knowledge base of the syndrome, assist speech-language therapists and audiologists in providing appropriate ECI services to families with young children with FRS, and contribute to its ultimate prevention. The following research question was posed: What is the characteristic nature of communication development over a seven year period in a specific case of a young child diagnosed with FRS?

METHOD

Main aim

The main aim of the study was to describe the communication development of a single case of a young child diagnosed with FRS, from six months to seven years, in order to contribute to the limited knowledge base about the developmental consequences of exposure to isotretinoin in children.

Sub-aims

- To describe the physical appearance of the young child with FRS
- To describe the hearing abilities and changes over time of the child from six months to seven years of age
- To describe the communication development of the child with FRS, from six months to seven years, over seven data collection sessions

Research design

A longitudinal case study design was used since it provides for multiple measurements of the participant's communication development over time. Since the measurements were carried out over seven sessions of early communication assessment and entered into an electronic research database after each session, the principles of an ex post facto method were applicable. No manipulation of variables occurred. Data were collected by means of observation, studying of available documents, audiovisual material and interviews with the family. A rich description of the case in terms of different child development and family variables, and possible causes or contributing factors over a seven year period, was achieved (de Vos, Strydom, Fouché & Delport, 2002; Leedy & Ormrod, 2001). The research database utilized was specially designed to store longitudinal data of infants at risk for communication disorders and their families and has been in operation for the past nine years (Kritzinger, 2000).

Research participant

Convenience nonprobability sampling was used to select the participant as she presented to the researchers when the parents sought early intervention services (Leedy & Ormrod, 2001). The following two criteria were applied in selecting the participant for the study:

- The participant presented with prenatal exposure to the teratogen isotretinoin and the diagnosis of FRS was made by a geneticist
- The parents of the participant gave written informed consent for the conduction of the research and publishing of the results

Description of the participant and family

In order to provide a basis for the interpretation of the results of the study, and consistent with a family-centered and asset-based approach to ECI, family strengths and resources in addition to risk factors are reported. A rich description of the participant's characteristics and her family is provided in Table 2. The different characteristics are provided in the middle column of the table, with the corresponding risk and protective factors for communication development identified in the left and right columns.

Table 2: Characteristics of participant and family indicated as risk and protective factors.

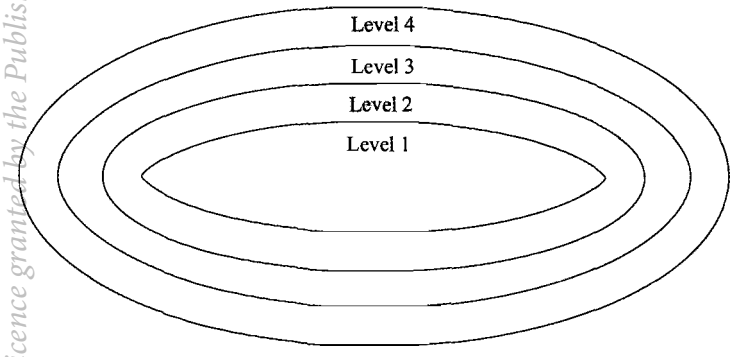
Risk factor (Rossetti, 2001)	Characteristic	Protective factor (Werner, 2000)
Use of isotretinoin during pregnancy by biological mother	1. *Prenatal history*	• None
Not married Father unknown	2. *Circumstances of biological parents*	• Age of mother 23 years, i.e. within ideal age category (Rossetti, 2001)
None	3. *Duration of pregnancy*	• Full-term
None	4. *Birth weight*	• Normal, 2900g
5 days of vomiting (withdrawal from isotretinoin) 5 days tube feeding	5. *Perinatal conditions*	• Normal birth • Normal Apgar scores: 7/10 and 9/10 (Rossetti , 2001) • Initial feeding problems resolved after five days
Biological mother voluntarily gave her up for adoption 8 weeks in hospital without attaching to a single caregiver	6. *Mother-infant attachment*	• Adoptive mother started visiting participant in hospital 10 days after birth • Placed in foster care with adoptive parents at age 8 weeks
None	7. *Role of adoptive parents as primary caregivers*	• Stable attachment and home environment since placed in foster care • Adopted by foster parents
None	8. *Role of siblings*	• Adoptive brother and sister are involved and supportive • Close relationships
Established risk for CNS and sensory impairments, and developmental delay (Moerike et al., 2002)	9. *Diagnosed with FRS at 6m*	• Identified early • Early commencement with intervention: Speech-language and occupational therapy • Good health
Risk for learning difficulties	10. *Roles of day mother and teacher in nursery school and primary school*	• Stable and supportive relationship with day mother • The same teacher is involved from nursery school until primary school • Small class in a private school

According to Table 2 there were many protecting factors in the participant's life, even though the risks for development include the fact that she was prenatally exposed to isotretenoin and given up for adoption. It appears that the serious risks associated with prenatal exposure to a teratogen, such as abrupti placentae, intra-uterine growth retardation, still birth, foetal distress, preterm birth and low birth weight (Rossetti, 2001) did not occur in the participant. It is clear that her adoptive family, early commencement of intervention and supportive educational environments played protective roles (Werner, 2000) and that chronic health problems and emotional adjustment problems often associated with young children in foster care, did not occur in the participant (Vig, Chinitz & Shulman, 2005).

Material

Since data were collected by an experienced early communication assessment team and stored in an early intervention database, the reliability of the data was increased and could therefore be used retrospectively. The CHRIB Assessment Protocol (Kritzinger & Louw, 2002) was used and adapted to assess the client and family during seven serial assessment sessions, when the participant was aged 6 months, 12 months, 20 months, 29 months, 45 months, 74 months and 84 months respectively. The CHRIB Assessment Protocol mainly consists of a collection of criterion-referenced assessment instruments that allow a flexible and appropriate description of a young child's communication development according to a continuum of expected sequences or developmental criteria. Norm-referenced methods, which compare a child's development to a specific population of typically developing children, are used to a limited extent in this assessment protocol (See Kritzinger & Louw, 2002 for a complete list of early communication assessment instruments included in the CHRIB Assessment Protocol).

The CHRIB Assessment Protocol was used to collect data on the participant's different developmental areas and a 4-Level Early Communication Assessment Framework (See Figure 1) was used to describe her communication functioning in a holistic manner.



Level 1: Describe physical appearance and determine sensory abilities
Level 2: Describe communication functioning and feeding skills
Level 3: Describe general development
Level 4: Determine risk and resilient factors

Figure 1: 4-level early communication assessment framework.

According to Figure 1 the first level forms the basis of an early communication assessment and usually involves a multidisciplinary evaluation, which proved to be necessary in this case of a child with FRS. Knowledge about a young child's physical appearance and sensory abilities allows the identification of a genetic syndrome or sensory impairment, which determines the outcome of the next three levels of the assessment framework. Assessment data from different disciplines, such as a clinical genetics, pediatric audiology and speech-language therapy were integrated to determine the participant's underlying conditions.

The second level involves the description of all communication skill areas, i.e. communication functions, listening skills, receptive language, expressive language (which included the phonetic repertoire, babbling patterns, phonological development, vocabulary and sentence structures), early literacy skills, mother-child communication interaction and feeding skills. Since the main goal was to conduct a communication assessment of the participant, the description of Level 2 comprised the focus of the evaluation.

Level 3 includes assessment areas that may be used to compare the outcomes of the communication assessment with and determine the extent of the participant's developmental difficulties. General developmental areas such as fine and gross motor, self-help and social skills, cognition, play patterns, and general behaviour are included, and typically assessed by an occupational therapist and educational psychologist. Based on the systematic description and outcomes of Levels 1 to 3, in Level 4 all risk and resilient factors within the participant as well as in her environment were considered. The participant's environment may change her development and her development may change her environment over time, thereby acknowledging the reciprocal relationship between a child's environment and constitution (Rossetti, 2001). Level 4 therefore permits a realistic view of a child at a certain point in time, where risks are identified but resilient or protective factors may be used to plan communication intervention and guide parent support efforts (See also Table 2).

Procedures

Validity and reliability

The CHRIB Assessment Protocol has been used extensively for clinical purposes (Kritzinger & Louw, 2002) and in previous research studies (Bam, Kritzinger & Louw, 2003; Höne, 2000; Kriek, 2002; Kritzinger, Louw & Hugo, 1996), thereby contributing to the validity and reliability of the data collection instrument and process. The collection of instruments that comprises the CHRIB Assessment Protocol was carefully selected and found to measure the different components of early communication skills that it intended to measure. The *Genetic Screening Checklist* (Kritzinger & Louw, 1998), one of the assessment instruments of the CHRIB Assessment Protocol, added to the suitability of the data collection procedures, since this instrument allowed a full description of the physical characteristics of the participant's syndromic anomalies.

Guidelines for early communication assessment recommended by Rossetti (2001) and Coggins & Timler (2000) were followed. Preference was given to criterion-referenced measuring instruments over norm-referenced, standardised assessment procedures. The CHRIB assessment protocol also proved to be consistent and dependable as a measure of the participant's communication developmental levels and to track her progress over seven years.

Although the nature of the study was retrospective, data were entered into the database shortly after each data collection session, thereby ensuring comprehensive and detailed data storage. The same researcher entered the data into the database at each data collection time.

Ethical considerations

Since the nature of the enquiry was intrusive and sensitive information was revealed, careful consideration was given to informed consent, confidentiality and the right of the family to withdraw from the research if they so wished (de Vos et al., 2002). The adoptive parents were invited to participate in the research and the implications were discussed with them. They gave written consent to the researchers to carry out the longitudinal study and publish the results.

Data collection procedures, storage and analysis

A play-based arena assessment approach was used, where one researcher acted as a facilitator to elicit and observe communication behaviours from the participant (Rossetti, 2001), while another researcher interviewed the parents to allow them to report their views about the participant's progress. The remainder of the team observed from behind a one-way mirror, and the team's findings were discussed with the parents as integrated recommendations for further intervention. The team consisted of two speech-language therapists, a paediatric audiologist, an occupational therapist and a community health nurse.

Data were recorded on the data collection sheets of each assessment instrument used in the CHRIB Assessment Protocol. Data were then stored in the CHRIB electronic database, as well as in a paper-based file and on video recordings. These three data sources were used as triangulation of measures (de Vos et al., 2002) to analyze and describe the participant's developmental progress over seven years.

RESULTS

Sub-aim #1: Physical appearance of the participant

Using the 4-Level Early Communication Assessment Framework (See Figure 1) as a guideline, a detailed description of the physical appearance and genetic anomalies of the participant is provided in Table 3. The results were obtained by means of clinical observations, guided by the *Genetic Screening Checklist* (Kritzinger & Louw, 1998) and a report from the clinical geneticist who diagnosed the participant with FRS. Information about internal structures and systems of the participant was unavailable since instrumental procedures, such as X-rays, were not used to obtain data.

According to Table 3 most of the participant's physical features were similar to the profile of children with FRS described in the literature (Kassis et al., 1985; Moerike et al., 2002; Monga, 1997). Both the participant's ears displayed anomalies, with the right ear more affected than the left. According to Charkins (1996) the right ear is often more affected when both ears display anomalies in children with genetic syndromes since Nervus Facialis is often not in the expected location. Disruptions in the embryological development on the dorsal ends of the first and second pharyngeal clefts could have caused the extensive anomalies of the pinnae (Sadler, 1995). The participant is currently undergoing a series of reconstructive surgical procedures on the pinnae.

The participant also displays morphological features that appear to be unique to her and not ascribed to FRS. Of all the craniofacial structures involved, the pinnae appear to be most affected in the participant. According to Charkins (1996) the kind of morphological anomalies occurring in the participant have the potential to affect her self-image.

Table 3: Morphological anomalies present in the participant.

Structure or system	Anomalies in the participant
Craniofacial structures	• High forehead • Brachycephaly • Retrognathic maxilla • Eyes: Small, epicanthal folds and asymmetrically positioned • Hypertelorism • Midfacial hypoplasia
Hearing and vestibular systems	• Low-set pinnae • Ears asymmetrically positioned • Dysmorphic and dysplastic ears • Atresia of the external auditory meati • Difference in ear canal volumes • Only bottom part of right pinna developed, absent top part • External rotation of right pinna • Mircrotia of the left pinna • Total absence of the concha and antihelix of the left pinna
Central nervous system	• Microcephaly
Other physical features present in participant, but not described in the literature	• Small stature • Fine textured hair • Strabismus of the eyes • Upper lip thin, poorly defined philtrum • High arched palate • Simian hand crease pattern • Tapered fingers • Thumbs can rotate 360 degrees • Both feet are narrow • Clonus of the right foot

Sub-aim # 2: The participant's hearing abilities and listening skills

Prenatal exposure to isotretinoin may cause a characteristic pattern of dysmorphic features of structures that originate from the first and second pharyngeal arches and the first pharyngeal cleft. These structures involve the pinnae, external auditory meati, tympanic membranes, middle ear cavities and the ossicles (Carlson, 1999; Lammer, 1991; Sadler, 1995). As part of Level 1 of the 4-Level Early Communication Assessment Framework (See Figure 1), the results of the otoscopic examinations, middle ear functioning and measurements of the external auditory meati are displayed in Table 4.

As indicated in Table 4 the otoscopic examinations carried out at the data collection sessions revealed the participant's narrow external ear meati, one of the known symptoms of FRS and described in Table 3. The narrow ear canals made visual inspection of the tympanic membranes impossible and it was only during an examination by a medical doctor at 20 months and using a larger otoscope, that the tympani were visible for the first time.

As further indicated in Table 4 the tympanograms indicated normal middle ear functioning most of the time, but also a tight conduction system (Type As tympanogram) and possible serous otitis media (Type B tympanogram). The failure to obtain a tight seal in the external meati in order to perform tympanometry, could be attributed to the narrow ear canals and their unusual configuration. The ear canal volumes that could be measured also confirmed unusually small ear canals with values under the norm of 0,5 cc in children. The participant was referred to an Ear, Nose and Throat (ENT) specialist every time abnormal middle ear measurements were obtained, but otitis media was never diagnosed.

Table 4: Otoscopic examinations, tympanograms, volume measurements of the external auditory meati, and audiometric results at six* data collection sessions.

Type of measurement	Age at data collection sessions					
	6m	12m	20m	45m	74m	84m
Otoscopic examination: Left	Tympanum not visible**	Tympanum not visible	Medical examination: Tympanum visible	Tympanum not visible	Tympanum visible	Tympanum visible
Otoscopic examination: Right	Tympanum not visible	Tympanum not visible	Medical examination: Tympanum visible	Tympanum not visible	Tympanum visible	Tympanum not visible
Tympanogram: Left	Type B	Ear sensitive	Type B	Type As	Type A	Type A
Tympanogram: Right	No closure obtained	No closure obtained	Type A	Type B	No closure obtained	No closure obtained
Volume: Left	No results	No results	0.4 cc	0.39 cc	0.2 cc	No results
Volume: Right	-	-	0.5cc	0.15cc	-	-
Hearing test: Left	Calibrated noise makers: Normal responses	Not done	Not done	VRA*** 25 dB HL	VRA 0 dB HL	Play Audiometry 5 dB HL
Hearing test: Right	Calibrated noise makers: Normal responses	Not done	Not done	VRA 30 dB HL	VRA 5 dB HL	Play audiometry 12 dB HL

* At 29 months of age no hearing measurements were carried out on the participant
** A-typical findings are indicated in shaded cells
*** VRA = Visual Response Audiometry

The participant, however, contracted otitis externa, an inflammatory condition as a result of a fungal infection (Northern & Downs, 2002). It is postulated that the structural anomalies of the participant's ear canals may cause retention of moisture, which may have resulted in an inflammatory condition.

The audiometric results indicated in Table 4 showed normal hearing abilities at 6 months and 74 months of age. Elevated thresholds were measured at 45 months in the participant, which could be attributed to the middle ear condition that was evident at that time. At 84 months of age a minimal hearing loss was diagnosed in the high frequencies in the participant's right ear. Apart from the fluctuating middle ear conditions that were evident in the tympanograms and audiometric results over the years, the difference in results over the different data collection sessions may also be attributed to the different audiometric procedures that were used. As the participant's age increased, and conditioned responses could be elicited from her, visual response audiometry and play audiometry procedures could be used. The latter also yielded ear specific audiometric information, as indicated in the results at 84 months. Follow-up hearing evaluations were necessary to monitor these results, since hearing abilities were likely to influence the next three levels of the participant's functioning (See Figure 1).

In order to determine the effect of the middle ear and audiometric results on the listening skills of the client, a basic requirement for language development (Level 2 of the 4- Level Early Communication Assessment Framework), the *CHRIB Listening Scale* (Hugo, Louw, Kritzinger & Smit, 2001) was used. The results are indicated in Table 5.

Sub-aim #3: Communication development of the participant

Table 5: Listening skills during hearing testing and communication assessments.

	12m	20m	29m	45m	74m
Listening skills during hearing testing					
Conditioning to sound	1*	No data**	No data	2	2
Localization responses	1	No data	No data	1	1
Consistency of responses	2	No data	No data	2	2
Listening behaviour	1	No data	No data	2	2
Distractibility	2	No data	No data	2	2
Listening skills during communication assessment					
Environmental noise	1	1	1	1	2
Non-speech sounds	1	1	1	3	2
Whispered speech	2	1	1	3	1
Speech	1	1	1	2	2

* Key: 1= good; 2= inadequate; 3 = poor
** No hearing testing was done at 20 and 29 months, see Table 4

As indicated in Table 5 it appears that the participant's listening skills were the poorest at 45 months, when abnormal middle ear measurements were obtained (See Table 4). At 74 months her listening skills were still not adequate, despite normal middle ear measurements (See Table 4). At 84 months when the mild hearing loss was diagnosed (See Table 4), unfortunately no listening skill evaluation was carried out. The parental report and remarks from the teacher, however, confirmed that the participant was distractible.

Further components of the participant's communication development included those skills measured by the *Rossetti Infant-Toddler Language Scale* (Rossetti, 1990) until she reached a three year developmental level, which is the age limit of the scale (See Figure 2).

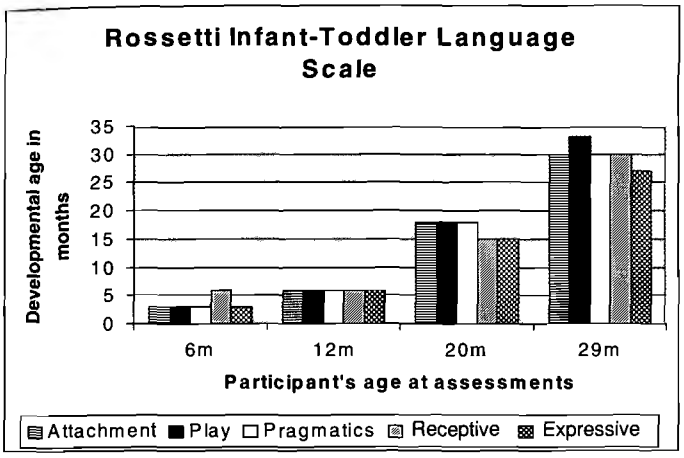


Figure 2: Participant's progress from 6-29 months on the *Rossetti Infant-Toddler Language Scale* (Rossetti, 1990).

According to Figure 2 the participant displayed delayed development in attachment to her primary caregiver, play skills related to language development, pragmatics, as well as receptive and expressive language skills during her first year of life. From 20 months it appeared that the participant showed a gradual increase in developmental levels and displayed catch-up development at 29 months for most components of communication development. The participant displayed a pattern of communication development which therefore changed gradually from abnormal to normal development where an increase in skills was observed, although still below her chronological age, until a pattern of catch-up development was observed for most components of communication development at 29 months (Rossetti, 2001).

According to Figure 2 a minor delay in expressive language development was still present at 29 months – a delay that could still be detected at 84 months. *The Bus Story Test* (Renfrew, 1997), a test of narrative speech, indicated short-term memory difficulties in the participant. The short-term memory problems were also confirmed by the Pendulum Test. A transcription of the participant's language sample revealed a decreased type-token ratio (Shipley & McAfee, 1998), indicating a decreased variety of words in her expressive vocabulary. The participant's type-token ratio was 0.395 and the norm for children of her age is between 0.45 to 0.50 (Shipley & McAfee, 1998). At the age of 84 months the participant was no longer receiving any speech-language therapy and the difficulties she was experiencing indicated a need for intervention in order to accommodate the academic demands of the school environment.

Descriptive observations of the participant's phonetic development displayed a gradual increase in her vowel and consonant repertoire over the seven serial assessments. At 29 months, cluster reduction, omission of consonants and phoneme specific nasality on [p], [t] and [s] were recorded. At 45 months the phoneme specific nasality was only noticed on one consonant, by 74 months distortion but not nasality was noticed on the [s] and [r] was omitted or substituted with [l], but at 84 months the participant had neither articulation errors nor phonological processes. The cause of phoneme specific nasality could never be established, except that it could be related to a mild hearing loss and concomitant affected listening skills that the participant experienced (See Tables 4 & 5).

Further components of the participant's communication development included a description of behaviour regulation, social interaction, shared attention, conversational structure, means of communication and non-verbal aspects of communication, based on Wetherby and Prizant (1989). See Table 6 for a summary of the new communication functions that developed and were added to her existing repertoire at each data collection session.

Table 6: Participant's communication development based on Wetherby and Prizant (1989).

Communication feature	6m	12m	20m	29m	45m
Regulation of another's behaviour	Protest →		Request object and action →		
Social interaction	Request attention and routine →	Greet →	Call → Show off → Imitate → Acknowledge →		Request permission
Shared attention	Not observed →			Comment Request information →	Request clarification
Conversational structure	Respond mostly →		Initiate more →		
Means of communication	Eye contact Vocalisation →	Gesture →	Verbal →	Posture Facial expressions →	

Table 6 indicates that the participant showed a gradual increase in the variety of communication functions between 6 and 12 months, with a marked increase since 20 months, until she was communicating actively at the age of 45 months. The pattern of delayed communication development in the first two years of life corresponded with the developmental pattern identified in the results of the *Rossetti Infant-Toddler Language Scale* (Rossetti, 1990).

Since caregiver-infant communication interaction provides the basis of communication development (Billeaud, 1998), it was necessary to analyse the quality of the participant's interaction with her adoptive mother. See Table 7 for the results of two scales that were used to measure the quality of the mother-child communication interaction.

Table 7: Quality of mother-child communication interaction.

Communication interaction scale	6m	12m	20m	29m	45m	74m
Mother-Infant Communication Scale (Raack, 1989) 5-point scale (1 = poor; 5 = excellent)	4	5	5	5	5	5
Observation of Communication Interaction (Klein & Briggs, 1987) 4-point scale (1 = poor; 4 = excellent)	3	4	4	4	4	3

According to Table 7 it is clear that the participant was consistently exposed to favourable mother-child communication interactions, which could have contributed to the catch-up pattern of communication development observed in the previous results. According to Vig et al. (2005) young children in foster care are at risk for attachment disruptions and may have complex medical, mental health and developmental needs. As a result of placement stability and permanence in the participant's life from a very early age, the adoptive mother could establish optimal patterns of communication interaction with the participant, which could have enhanced her language development.

The last component related to Level 2 skills of the assessment framework indicates the participant's development in feeding skills. See Table 8.

Table 8: Development of the participant's feeding skills according to the *Oral-Motor/Feeding Rating Scale* (Jelm, 1990).

Manner of feeding	6m	12m	20m	29m
Bottle feeding				
- Lip and cheek movements	5*	4		
- Tongue movements	5	4		
- Jaw movements	5	2		
Spoon feeding				
- Lip and cheek movements	5	3	3	
- Tongue movements	5	4	4	
- Jaw movements	5	4	4	
Cup drinking				
- Lip and cheek movements		5	3	0
- Tongue movements		5	4	0
- Jaw movements		5	4	0
Chewing				
- Lip and cheek movements			2	0
- Tongue movements			2	0
- Jaw movements			2	0
Straw drinking				
- Lip and cheek movements				0
- Tongue movements				0
- Jaw movements				0

* 5-point scale: 0 = normal functioning; 5 = more than 75% a-typical functioning

As depicted in Table 8 the participant showed serious feeding difficulties until 12 months, with a gradual improvement in feeding skills until she displayed no problems at 29 months. The feeding difficulties displayed a similar pattern as the delayed communication development during the first two years of the participant's life.

In conclusion, the participant's functioning on general developmental skills over six data collection sessions indicated her skills on Level 3 of the 4-Level Early Communication Assessment Framework (See Figure 1). Table 9 displays her development as measured on the Development Activities Screening Inventory II DASI-II (Fewell & Langley, 1984), a standardised test of cognitive and fine motor skills.

According to Table 9 the participant's cognitive development showed the same developmental pattern as communication development. The initial developmental delay during infancy was replaced by age appropriate development by 29 months of age. At 74 months, however, there appeared to be a flattening in the developmental pattern, and her functioning was no longer age appropriate.

Table 9. The participant's general developmental progress according to the DASI-II (Fewell & Langley, 1984).

Measurement	6m	12m	20m	29m	45m	74m
Developmental age in months	2	6	14	29	46	58
Developmental quotient	30	50	69	97	102	78
Interpretation of measurements	Poor	Poor	Below average	Average	Average	Below average

The results of the participant's general development corresponded with the difficulties she experienced with language skills at the same age.

DISCUSSION AND CONCLUSION

The study highlighted the long-term effects that prenatal exposure to isotretinoin may have on the communication development of a young child and her environment. Due to reasons not known, she was abandoned by her biological mother at birth. Within a relatively short period of two months, she was placed in the foster care of her prospective adoptive family, where mother-child attachment and interaction, as well as integration within the family were successful. Supportive daycare and educational environments, early communication intervention and occupational therapy, as well as the participant's good health, added to the advantageous reciprocal relationship between the participant and her environment over the years of the study. Positive environmental factors are known to enhance a child's development (Werner, 2000), and appeared to have provided the participant with resiliency in her early development.

The participant, already diagnosed with FRS at the beginning of the longitudinal study, displayed numerous observable anomalies. The anomalies were markedly expressed in her pinnae and external auditory meati, which explained the occurrence of otitis externa. The involvement of the first two pharyngeal arches and first pharyngeal cleft during embryogenesis were evident. The minimal high frequency hearing loss of 12 dB HL and concomitant distractibility detected at seven years of age (84 months), may suggest additional internal ear anomalies that could not be observed during the assessment sessions.

The participant displayed a gradual pattern of catch-up development in communication skills over seven years, but still demonstrated a minor expressive language delay at seven years. Her original articulation and phonological difficulties were resolved, but the remaining expressive language delay may be related to the inadequate listening skills and minimal hearing loss. The remainder of the communication developmental delay in the participant may be the cause of ongoing learning difficulties at school. Although her communication skills have developed, the prognosis for her cognitive-academic language development may be poorer.

Although the results of a single case study cannot be generalized, the study provides an example of a holistic description of the long-term effects of a rare genetic syndrome on a child's early development – information often missing in databases on genetic syndromes. Descriptions of syndromes often only focus on genetic analysis of the syndrome and its corresponding morphological features, and omit data on the affected children's development. Descriptions of developmental outcomes of children with genetic syndromes provide important information for clinicians involved in intervention services and vital knowledge to the families of these children.

The study also emphasised the importance of research on the development of young children with rare syndromes. It is the responsibility of clinicians involved in early intervention to carry out this kind of research, so that knowledge can be accumulated to increase evidence-based interventions and provide parents with valid and reliable information to make informed decisions on the future development and education of their children. Research results may therefore be used as a means to enhance family-centered practice in early intervention.

Lastly, the use of the 4-Level early communication assessment framework in the study represented an effort to make sense of the complexities of FRS and the resulting trajectory of early biological events on a young child's morphological features and communication development. Rossetti (2001) has identified the reliable and accurate assessment of a young child and family as the most challenging clinical activity in early intervention. The holistic assessment of communication skills implies detailed interdisciplinary observations of the dynamic, interactive and interdependent systems involved in early communication development. Early communication assessment is both a challenge, and an inevitable goal in order to determine the child's level of communicative functioning, to facilitate treatment planning and to evaluate the intervention efforts (Coggins & Timler, 2000). Clinicians owe it to our clients and the professional discipline of early communication intervention to do the best we can.

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