

ORIGINAL ARTICLE

Dental status and oral function in an adult group of subjects with thalidomide embryopathy – a clinical and questionnaire study

ANDERS EKFELDT¹ & GUNNAR E. CARLSSON²

¹*Mun-H-Center, Odontologen, National Orofacial Resource Centre for Rare Disorders, Gothenburg, Sweden; Department of Prosthetic Dentistry and Oral Function, Faculty of Dentistry, University of Oslo, Norway and* ²*Department of Prosthetic Dentistry, Institute of Odontology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*

Abstract

Objective. The purpose of the study was to present the results of an oral examination of individuals with thalidomide embryopathy in relation to dental conditions and functional aspects of the masticatory system, with a special focus on tooth wear. **Material and Methods.** All 108 subjects with thalidomide embryopathy living in Sweden were invited to participate in a comprehensive investigation, and approximately one-third, 31 subjects (13 F and 18 M, aged 45–49 years), took part. The methods included a questionnaire and clinical and radiographic examinations. **Results.** Most of the subjects had regular dental care, which they in general considered sufficient. All except one always brushed their teeth themselves. One subject had limited mouth opening (25 mm). There were no great deviations from normal anatomy and function of the masticatory system. Caries and periodontal conditions were also normal. Regurgitation was reported by 42% of the subjects. Tooth wear was more extensive than in comparable age groups. About a third of the subjects had Class III or edge-to-edge occlusion. **Conclusions.** In general, subjects with thalidomide embryopathy had no great deviations in dental conditions from people of the same age in the general population except for an increased rate of tooth wear and a higher prevalence of prenatal jaw relations. Tooth wear was related less to use of the teeth as tools and more to dental erosion associated, among other things, with a high rate of regurgitation.

Key Words: Caries, dental erosion, malocclusion, regurgitation, tooth wear

Introduction

The potent sedative drug thalidomide was withdrawn from the market in 1961–62 after having been sold on the market for a couple of years. Serious malformations in children were shown to be associated with the mothers' intake of thalidomide during pregnancy. The most common malformations were defects of the arms, legs and eyes, but other organ systems were also involved [1–3]. Thousands of children with thalidomide embryopathy were born in countries all over the world (the USA was saved from this medical catastrophe since the drug had not been approved by the authorities). A couple of years after withdrawal, thalidomide was approved again in some countries because it has a potent immune regulating effect and can be used for some oncologic and dermatologic conditions. Unfortunately, probably because of the habit of sharing medications, three new cases of thalidomide

embryopathy have recently been recognized and reported in Brazil [4].

Even though structures in the head (e.g. ears and cranial nerves) were also affected in some subjects suffering from thalidomide embryopathy, only a few studies have been published regarding orofacial and dental conditions in children. In a group of 40 Swedish children, mean age 3 years and 3 months, the prevalence of hypodontia and enamel hypoplasia was higher than in a Swedish normal material, whereas the caries situation was normal [5]. A study of 127 German children, mean age 4 years and 4 months, did not report any remarkable abnormalities of form or number of deciduous teeth, but an increased prevalence of some other dysgnathias [6]. Both these studies thus observed some developmental disturbances and it was suggested that this was associated with thalidomide embryopathy, but with differing results. However, both had observed an

Correspondence: Anders Ekfeldt, Department of Prosthetic Dentistry and Oral Function, Faculty of Dentistry, University of Oslo, P.O. Box 1109 Blindern, NO-0317 Oslo, Norway. Tel: +47 22 85 20 00. Fax: +47 22 85 23 44. E-mail: anders.ekfeldt@odont.uio.no

(Received 29 April 2008; accepted 27 June 2008)

ISSN 0001-6357 print/ISSN 1502-3850 online © 2008 Informa UK Ltd. (Informa Healthcare, Taylor & Francis As)
DOI: 10.1080/00016350802307638

increased risk of trauma to the teeth and recommended specialist dental care for the children suffering from thalidomide embryopathy. A search in PubMed (February 2008) could not identify any more articles on dental conditions associated with thalidomide embryopathy during the past four decades.

There are approximately 100 subjects with thalidomide embryopathy in Sweden today, and they are now around 45 to 50 years of age. As part of an extensive investigation of this group, oral aspects were also included. The purpose of this article is to present the results of a study of some of these individuals regarding dental conditions and functional aspects of the masticatory system, with a special focus on tooth wear. It was hypothesized that a high rate of tooth wear would be found in the subjects, as it has been suggested that they use their teeth as tools as a result of their deformities.

Material and methods

The members of the Swedish association of subjects with thalidomide embryopathy were invited to participate in a comprehensive investigation including neuropsychiatry, odontology, ophthalmology, orthopedics, and speech pathology. A flow-chart in Figure 1 gives the number of the original group (108) and the drop-outs. Among the 33 subjects who responded affirmatively to the invitation, two could not attend the examination. Owing to severe neurological disability, one of them was living at an institution, while the other had a stroke just before the examination was to take place. Finally, 31 subjects (13 F and 18 M, aged 45–49 years) took part in the investigation performed during 2007 for all but two, who were examined in November 2005. This article presents the odontological part of the study, which comprised a questionnaire and clinical and radiographic examination.

Questionnaire

Besides general socio-economic conditions (such as age, gender, occupation, education), the questionnaire comprised questions on dental and oral problems, as well as on experiences and use of dental care. Since one of the aims was to evaluate tooth wear in the study group, several questions focused on factors possibly related to attrition, abrasion, and erosion of the teeth, such as oral parafunctions, use of the teeth as tools, dietary habits, regurgitation, and vomiting. Furthermore, questions were asked regarding function and dysfunction of the masticatory system in order to assess the Helkimo anamnestic index, Ai [7].

Clinical examination

The clinical dental examination included registration of jaw relations, number of teeth, caries, and periodontal conditions. All teeth were examined and the numbers of decayed (D), missing (M), filled (F), and teeth (T) were recorded in accordance with the World Health Organization (WHO) criteria for the definition of DMFT/DFT [8]. Periodontal conditions were recorded according to a current classification system [9]. Teeth probably extracted for orthodontic reasons were not counted as missing. Enamel and other dental defects, erosive lesions as well as non-carious cervical lesions (NCCL) were also registered. The scale used for NCCL was (0 = no sign of lesion, 1 = tendency for lesion, 2 = lesion cavity < 1 mm, 3 = lesion cavity > 1 mm). The type of lesion (concave or wedge-shaped) was also recorded. Tooth wear was recorded in accordance with a 4-point scale [10]: 0 = no or minimal wear; 1 = wear of enamel down to dentine spots; 2 = wear of the dentine down to one-third of the crown height; 3 = wear of the dentine more than one-third of the crown height. Individual tooth wear was assigned and calculated according to the attrition index devised by

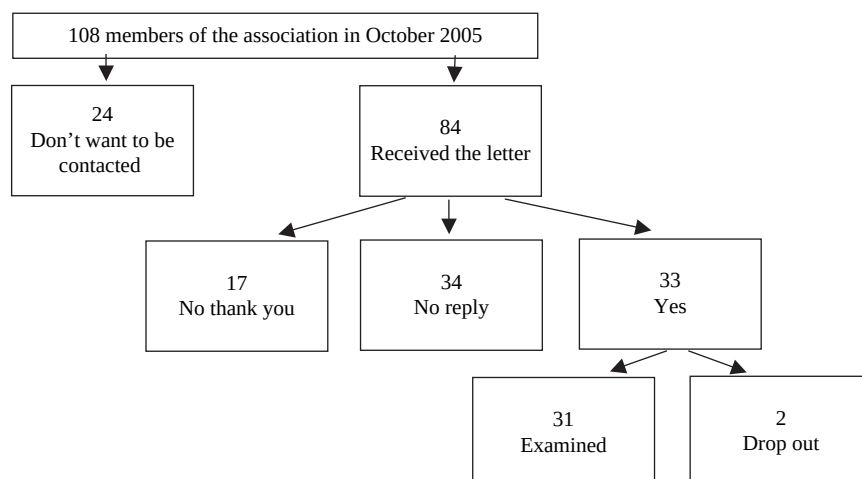


Figure 1. Flow-chart. Numbers of the original sample, the drop-outs, and participants in the final examination.

Ekfeldt et al. [11] using the following formula: $(10G_1 + 30G_2 + 100G_3)/(G_0 + G_1 + G_2 + G_3)$, where G_0 , G_1 , G_2 , and G_3 = number of teeth with occlusal wear scores of 0, 1, 2, and 3, respectively.

The functional capacity of the masticatory system was assessed according to the clinical dysfunction index (Di) of Helkimo [7]. The dental conditions of each subject were also documented by means of intra-oral photographs, casts of the jaws, and a panoramic radiograph. At the periodontal examination "bleeding on probing" was recorded as gingivitis, and "pocket depth" was measured for each tooth surface. All clinical examinations were carried out by one of the authors, except for one person who was registered by another senior consultant using the same criteria. The visible body anomalies/gross malformations were registered.

Student's *t*-test and, where appropriate, the chi-squared test were used for statistical analyses of differences. $P < 0.05$ was considered statistically significant. The study design was approved by the Ethics Committee of the Medical Faculty of the University of Gothenburg (Ö 556-03, 18 December 2003). Before the clinical and questionnaire examination, all subjects gave their informed consent to participation in the study.

Results

Questionnaire

Social conditions. Twenty-five of the subjects (81%) had married, and one was now divorced. The group had altogether 41 children. All of the subjects had full-time or part-time work. At the time of the examination, and for various reasons, six subjects were no longer in work. Ten (33%) claimed that they had had to reduce the amount of work because of their disability. Three had autism and had had reading and writing problems at school. Another three subjects had problems at school because of impaired hearing.

Dental care. Most of the 31 subjects considered that the dental care they had received was sufficient, while two were dissatisfied. The majority had regular dental care at least once a year, and all but three had their own dentist. One subject received occasional help with toothbrushing. All the others reported that they brushed their teeth themselves.

Tooth wear and oral function. Three subjects reported that they used their teeth as tools extensively (e.g. to catch and lift things); 10 did so to some extent (mainly to open various packages), whereas the remaining (18/31) denied using the teeth in this way. To the question whether they considered that

their teeth were worn, three answered "much", 12 "to some extent", and 16 "not at all". Six (19%) reported that they had suffered trauma to the maxillary incisors (Table I).

The majority (21/31) were unaware of nocturnal tooth grinding; 9 said it occurred a few times each week and one reported that it occurred every night. Only three subjects had noted tooth clenching in daytime hours. Fatigue in the jaws was reported by 9 subjects (Table II). Regurgitation was reported by 13 (42%; 38% of the women, 44% of the men, NS); two experienced regurgitation every day, nine about once a week, and two every second week. One of these subjects also admitted "vomiting about once a week", all the others said they "never vomited". The majority (22/31) preferred to drink water, milk, coffee, or tea when they were thirsty. Eight subjects often drank juice and/or soft drinks (three reported this on a daily basis) and one subject ate three or four apples a day. Seventeen of the 31 subjects (55%) did not report any symptoms of temporomandibular disorder (TMDs) and were classified as Ai 0; 6 had mild (Ai I) and 8 had severe symptoms (Ai II) according to Helkimo [7] (Table II).

Clinical examination

Anomalies. The most frequent malformations affected were the upper limbs. Twenty-five subjects had various anomalies of the upper limbs affecting the thumbs, other fingers, the wrists, and/or a general reduction of the length of the arms. In five subjects who had no visible malformations of the limbs, two were diagnosed with autism (one also with slight mental retardation). Four of those without limb anomalies had congenital facial palsy and two had impaired hearing, one of whom had an implant retained external ear prosthesis to replace a congenitally missing ear.

Table I. Prevalence (*n*, %) of some occlusal and dental anomalies in 31 subjects with thalidomide embryopathy. For comparison, percentages of the same variables in a population of Swedish schoolchildren [14] (S%), and a German population of adult dentate subjects [13] (G%).

Variable	<i>n</i>	%	S%	G%
Postnormal occlusion	3	10	14	33
Prenormal occlusion	3	10	4	4
Large maxillary overjet (≥ 6 mm)	3	10	8	—
Deep bite (overbite ≥ 5 mm)	1	3	8	—
Open bite frontally (< 0 mm)	3	10	4	3
Open bite laterally (< 0 mm)	1	3	0.2	—
Edge-to-edge bite	8	26	1	6
Cross bite	11	35	11	28
Hypodontia	2	6	6	—
Hyperdontia	0	0	1	—
Trauma to maxillary incisors	6	19	1	—

— Not reported.

Table II. Prevalence (n , %) of some variables related to function and dysfunction of the masticatory system in 31 subjects with thalidomide embryopathy. For comparison, percentage values of the same variables in 35-year-old subjects from a Swedish population sample [18] are presented (S^{35} %).

Variable	n	%	S^{35} %
Fatigue in jaws	9	29	18
Nocturnal bruxism	10	32	33
Daytime clenching	3	10	46
Anamnestic index 0	17	55	55
Anamnestic index I	6	19	–
Anamnestic index II	8	26	–
Clinical dysfunction index I	10	32	43
Clinical dysfunction index II	3	10	4
Clinical dysfunction index III	0	0	3

– Not reported.

Dental conditions. Most subjects had complete or almost complete dentition; the median number of teeth was 27 (mean 26.5, SD 1.5; 3rd molars were not included). Missing teeth in two subjects were diagnosed as tooth agenesis/hypodontia: the maxillary lateral incisors and one premolar in each mandibular quadrant were missing in one subject; in the other subject, one premolar in each quadrant was missing. The other missing teeth had probably been extracted for orthodontic or caries reasons.

The jaw relations varied a great deal, although most of the subjects had neutroclulsion (Angle Class I), three were postnormal (Class II), and three prenormal (Class III) according to the Angle classification. The prevalence of edge-to-edge bite and cross bite was high (Table I). The vertical overbite varied between 1 and +8 mm (mean 1.6, SD 1.6). The overjet varied between –5 and +10 mm (mean 2.3, SD 1.9). Three subjects showed enamel hypoplasia, two enamel hypomineralization, but no other tooth malformation.

All subjects demonstrated teeth with some degree of tooth wear; most assessed as score 1 or 2. The mean numbers of teeth, on a patient basis, with grade 1 and grade 2 were 13.6 (SD 5.7) and 8.4 (SD

5.1), respectively. Only one subject had teeth with grade 3 wear (7 teeth). There was wide variation in the wear index according to Ekfeldt et al. [11], i.e. from 4.6 to 41.8 (mean 15.6, SD 5.0). The women had a lower mean index (12.8) than the men (17.7; $p < 0.05$). In 10 subjects (32%), certain signs of dental erosion were recorded (Figure 2). In 15 persons with an individual tooth wear index (IA) close to or above average (15.6), there were obvious signs of erosion in 8, erosion and wear facets in 1, and wear facets in 3. Two others in this group were using smokeless tobacco.

Of 10 subjects with a varying number of teeth exhibiting non-carious cervical lesions (NCCL), 2 had wedge-like lesions (on 4 and 2 teeth, respectively).

An association between tooth wear and use of the teeth as tools was judged as certain in one subject, probable in five, and possible in three (Figure 3).

The caries experience of the group expressed as DMFT index varied greatly. The number of decayed teeth per person ranged from 0 to 6, although the median value was 0 (mean 1.1, SD 1.2). There were few missing teeth (median 0, mean 0.4, SD 0.6). All subjects had many teeth with restorations (median 13, mean 14.5, SD 4.9). The mean DFT was 15.6 (SD 6.8), with only small differences between the genders (14.8 in women, 16.2 in men). Six subjects (19%) had varying numbers of crowns (1, 2, 3, 3, 6, and 14, respectively), which means that 3.5% of all teeth in the group were crowned. One subject had a dental implant replacing a missing maxillary canine.

All subjects had some gingivitis (bleeding on probing), with prevalence varying from 10% to 100% (mean 32%, SD 17%) without significant difference between the genders. The periodontal situation was favorable in most subjects. Four were diagnosed with moderate generalized chronic periodontitis, two of whom also had teeth with localized severe chronic periodontitis.



Figure 2. Anterior view of a subject who reported eating 3–4 apples a day. Note the erosion of the labial tooth surfaces.



Figure 3. A subject with thalidomide embryopathy exhibiting very little tooth wear but with small enamel fractures on the maxillary incisors because they were used as tools to open bottles and cans.

Oral function. Only two subjects had a mouth opening less than 40 mm (36 mm and 25 mm, respectively). The mean value for the whole group was 50.9 mm (SD 6.7), with a range from 25 to 65 mm. As expected, the women had a smaller mouth opening (mean 47.5 mm) than the men (mean 53.3 mm; $p < 0.05$). The great majority had no or only mild TMD signs; three had moderate (all women) and none had severe dysfunction according to the Helkimo clinical dysfunction index. Women exhibited higher dysfunction index values than the men ($p < 0.05$).

Radiographic examination

No major pathology of the jaws, including the mandibular condyles, was observed on the panoramic radiographs. Four subjects had retained/impacted 3rd molars.

Discussion

The examined subjects demonstrated a variety of malformations typical of thalidomide embryopathy, but in general had a well-functioning masticatory system with no great deviations from normal anatomy and function. Most seemed to live in good social conditions. Four-fifths had been married and the divorce rate was low (4%). The group had in all 41 children, all of whom had been examined earlier and found to be free of functional malformations and anomalies like those of their parents with thalidomide embryopathy [12].

Distribution of the orthodontic (Angle) classification of jaw relations was similar to what is described in epidemiological samples of the general population, except for the high prevalence of Class III (10%) and edge-to-edge bite (26%; Table I). Large German and Swedish population samples have reported the prevalence of Angle III to be 4%, and edge-to-edge bite as 1% and 6%, respectively [13,14]. This indicates a tendency to more prenatal jaw relations in the thalidomide embryopathy group. An explanation for this finding might be given in the craniometrical results of a group of German

children found to have maxillary retrusion "in almost every case" [6].

The prevalence of hypodontia/tooth agenesis varies between 6% and 10% in Scandinavian studies [14,15]. In the present material, the prevalence was within that range (6%) and the missing teeth were the same as those reported most frequently missing, i.e. premolars and maxillary lateral incisors. In the early study on thalidomide embryopathy children [5], the prevalence was 8%. This was much higher than figures published at that time (0.4%), which, together with the high prevalence of disturbance of tooth mineralization (49%), led to the conclusion that "thalidomide did, in fact, also cause a disturbance in tooth development". The present findings and more recent prevalence results do not support this conclusion, as the prevalences of tooth agenesis and mineralization disturbance are within expected limits. The means for the vertical mouth opening of men and women were slightly smaller than those of Swedish population samples [16]. The percentage of subjects with a maximal opening of < 40 mm (6%) is identical to that found in the age group 40–49 years in a Swedish population sample [17]. Only one subject had a markedly reduced opening capacity (25 mm), which had made normal dental care difficult to perform. The reason for the severe reduction was not clear, but it was suggested as being more psychological than anatomical. The prevalence of signs and symptoms of temporomandibular disorders was within the ranges presented for epidemiological samples [13,17,18]. The higher prevalence in women is in accordance with data presented in reviews and recent results [19–21].

There seems to be an increased risk of accidents resulting in damage to the maxillary front teeth in subjects with thalidomide embryopathy. The reported prevalence of such trauma was 19%, compared to 1% in a Swedish population sample [14]. However, in a study of Swedish children with thalidomide embryopathy [5], trauma affecting the maxillary incisors was registered in 20% (8/40 children).

The caries situation of the thalidomide embryopathy subjects did not deviate markedly from Swedish

population samples of the same age. The mean DFT of the present group (15.6) was slightly higher than that of 40 and 50-year-old groups in the latest (2003) Jönköping study (11.5 and 15.0, respectively) [22]. The prevalence of gingivitis (bleeding on probing) was 32% of examined surfaces, a value double that presented for the 40 and 50-year-olds in the Jönköping study. To some extent this might be explained by the handicap of the thalidomide group, which made toothbrushing difficult. However, the periodontal conditions seemed otherwise comparable with population samples of the same age in Sweden, although detailed comparisons are not possible because of differences in examination methods [22]. The frequency of existing teeth with crowns was 3.5%, which is within the range 1.7–6.8% for 40 and 50-year-old individuals in the Swedish population sample [22].

Regarding tooth wear, there was a difference between the thalidomide embryopathy group and population samples. However, the high average wear rate was probably more related to erosive factors and in just a few cases the tooth wear could be related to the use of their teeth as tools according to the hypothesis. The mean value of the tooth wear index was 15.6, whereas it was 2.5 and 3.8 among 40 and 50-year-old subjects in the 1990 study by Ekfeldt et al. [11]. In a German epidemiological study using the same tooth wear index, the corresponding value was 13.1 for the 40 to 49-year-old group [13].

The etiology of tooth wear is multifactorial [23,24] and the subjects displaying the highest wear score of I_A showed signs of both erosion and wear facets. Furthermore, two subjects in the high-wear group used smokeless tobacco, which also has been found to be associated with increased rate of tooth wear [11].

The recent literature has emphasized erosion as an important wear factor [24,25], and this is probably an essential explanation for the average high level of tooth wear in the thalidomide embryopathy group. The etiology of erosion is usually divided into extrinsic and intrinsic factors. Among extrinsic factors, a high consumption of acidic beverages has been observed as a cause of increasing rate of erosion, especially in children and adolescents. Even though some of the thalidomide subjects had a high intake of soft drinks, consumption of the entire group seemed to be within normal limits. Important intrinsic factors include gastrointestinal and eating disorders associated with regurgitations of the very acidic gastric content that may lead to erosion [26]. The prevalence of regurgitation among the thalidomide embryopathy subjects was extremely high compared to population samples [13]. This may be the reason for the evident signs of erosion noted in several of these subjects. It is tempting to assume that the high rate of regurgitations in the

group may be associated with the thalidomide embryopathy.

The relatively high prevalence of NCCL also indicates that erosion is common in thalidomide embryopathy subjects. The traditional opinion that cervical lesions are mainly caused by toothbrushing abrasion has been questioned recently, and the important role of erosion in NCCL has been emphasized [24,27]. It is difficult to think that excessive toothbrushing would be a strong factor causing NCCL in thalidomide embryopathy subjects, the majority of whom had malformations of the upper limbs. Erosion is a more plausible causing factor.

The prevalence of autism in Swedish persons with thalidomide embryopathy has been observed to be 4–5% [3]; in the present group it was 10%. This is much higher than in the general population [28].

This study presents oral findings in a group of middle-aged individuals suffering from thalidomide embryopathy. To our knowledge, no such studies in adults with this diagnosis have been published. The participants comprise less than a third of those with this diagnosis who lived in Sweden in October 2005 (Figure 1). The reasons for lack of participation in the study are not fully known. However, through their organization, almost a quarter of the subjects had declared that they did not want to participate in any more studies because of the extensive and repeated examinations they had undergone earlier. Almost as many answered negatively to the letter of invitation and an even larger group never answered the letter. It can be assumed that the reasons were similar, i.e. disinterest in participating in more examinations. It was not possible to evaluate how representative the investigated subjects were of the total group. However, the frequency of ophthalmological diagnoses in a previous study of 84 of the Swedish group of thalidomide embryopathy subjects did not differ significantly from those in the present group of 31 subjects ([2]; see also Strömland 2008 personal communication). Three persons with autism or autistic traits were observed and that is comparable to the 4 patients reported in the study of 100 Swedes with thalidomide embryopathy presented in 1994 [3]. This suggests that the small group examined may be considered representative of the larger group studied previously [2]. Even though the small number of participants is a limitation of the study, the results are of interest since there do not seem to be any published odontological data on adults with thalidomide embryopathy.

Conclusions

The 31 examined subjects with thalidomide embryopathy, aged 45–49 years, had a generally well-functioning masticatory system without great deviations in normal anatomy or function. Caries and periodontal

conditions were acceptable, but on average slightly worse than in current Swedish population samples of the same age. Tooth wear was on average more extensive than in comparable age groups, which was considered to be related to dental erosion associated, among other things, with a high prevalence of regurgitation and to a lesser extent to the use of their teeth as tools.

Acknowledgments

We thank all participants in the Swedish comprehensive thalidomide embryopathy study for support and pleasant collaboration: Professor Kerstin Strömmland (Göteborg), Professor Marilyn Miller (Chicago, USA), Professor Christopher Gillberg (Göteborg), Dr Shadi Afrin Ghasemi (Göteborg), Dr Aina Danielsson (Göteborg), Dr Elisabeth Wentz (Göteborg), Dr Maria Johansson (Göteborg), Speech pathologist Lotta Sjögren (Göteborg), Dr Jan Andersson-Norinder (Göteborg), Mrs Kerstin Lamberg (Göteborg), and Mrs Lisbeth Heijl and Mrs Linda Gustavsson (Göteborg).

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

- [1] Schmidt M, Salzano FM. Clinical studies on teenage Brazilian victims of thalidomide. *Braz J Med Biol Res* 1983;16:105–9.
- [2] Strömmland K, Miller MT. Thalidomide embryopathy: revisited 27 years later. *Acta Ophthalmol (Copenh)* 1993; 71:238–45.
- [3] Strömmland K, Nordin V, Miller M, Akerström B, Gillberg C. Autism in thalidomide embryopathy: a population study. *Dev Med Child Neurol* 1994;36:351–6.
- [4] Schuler-Faccini L, Soares RC, de Sousa AC, Maximino C, Luna E, Schwartz IV, et al. New cases of thalidomide embryopathy in Brazil. *Birth Defects Res A Clin Mol Teratol* 2007;79:671–2.
- [5] Axrup K, D'Avignon M, Hellgren K, Henrikson C-O, Juhlin I-M, Larsson KS, et al. Children with thalidomide embryopathy: odontological observations and aspects. *Acta Odontol Scand* 1966;24:3–21.
- [6] Stahl A. Clinical, orthodontic and radiological findings in the jaws and face of children with dysmelia associated with thalidomide-embryopathy. *Int Dent J* 1968;18:631–8.
- [7] Helkimo M. Studies on function and dysfunction of the masticatory system. II. Index for anamnestic and clinical dysfunction and occlusal state. *Swed Dent J* 1974;67: 101–21.
- [8] WHO: Oral Health Surveys – Basic Methods, 4th edn. Geneva: World Health Organization; 1997. p. 36–8.
- [9] Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999; 4:1–6.
- [10] Hugoson A, Bergendal T, Ekfeldt A, Helkimo M. Prevalence and severity of incisal and occlusal tooth wear in an adult Swedish population. *Acta Odontol Scand* 1988;46:255–65.
- [11] Ekfeldt A, Hugoson A, Bergendal T, Helkimo M. An individual tooth wear index and an analysis of factors correlated to incisal and occlusal wear in an adult Swedish population. *Acta Odontol Scand* 1990;48:343–9.
- [12] Strömmland K, Philipson E, Andersson Grönlund M. Offspring of male and female parents with thalidomide embryopathy: birth defects and functional anomalies. *Teratology* 2002;66:115–21.
- [13] Bernhardt O, Gesch D, Splieth C, Schwahn C, Mack F, Kocher T, et al. Risk factors for high occlusal wear scores in a population-based sample: results of the Study of Health in Pomerania (SHIP). *Int J Prosthodont* 2004;17:333–9.
- [14] Thilander B, Myrberg N. The prevalence of malocclusion in Swedish schoolchildren. *Scand J Dent Res* 1973;81:12–20.
- [15] Bergendal B. When should we extract deciduous teeth and place implants in young individuals with tooth agenesis? *J Oral Rehabil* 2008;35 Suppl 1:55–63.
- [16] Agerberg G. Maximal mandibular movements in young men and women. *Swed Dent J* 1974;81–100.
- [17] Salonen L, Helldén L, Carlsson GE. Prevalence of signs and symptoms of dysfunction in the masticatory system: an epidemiological study in an adult Swedish population. *J Craniomandib Disord* 1990;4:241–50.
- [18] Magnusson T, Egermark I, Carlsson GE. A prospective investigation over two decades on signs and symptoms of temporomandibular disorders and associated variables. A final summary. *Acta Odontol Scand* 2005;63:99–109.
- [19] Carlsson GE. Epidemiology and treatment need for temporomandibular disorders. *J Orofac Pain* 1999;13:232–7.
- [20] Johansson A, Unell L, Carlsson GE, Söderfeldt B, Halling A. Gender differences in symptoms related to temporomandibular disorders in a population of 50-year-old subjects. *J Orofac Pain* 2003;17:29–35.
- [21] Johansson A, Unell L, Carlsson GE, Söderfeldt B, Halling A. Risk factors associated with symptoms of temporomandibular disorders in a population of 50- and 60-year-old subjects. *J Oral Rehabil* 2006;33:473–81.
- [22] Hugoson A, Koch G, Göthberg C, Nydell Helkimo A, Lundin S-Å, Norderyd O, et al. Oral health of individuals aged 3–80 years in Jönköping, Sweden during 30 years (1973–2003). *Swed Dent J* 2005;29:139–55.
- [23] Dahl BL, Carlsson GE, Ekfeldt A. Occlusal wear of teeth and restorative materials. A review of classification, etiology, mechanisms of wear, and some aspects of restorative procedures. *Acta Odontol Scand* 1993;51:299–11.
- [24] Johansson A, Johansson A-K, Omar R, Carlsson GE. Rehabilitation of the worn dentition. *J Oral Rehabil* 2008; 35:548–66.
- [25] Johansson A-K, Lingström P, Birkhed D. Comparison of factors potentially related to the occurrence of dental erosion in high- and low-erosion groups. *Eur J Oral Sci* 2002;110: 204–11.
- [26] Ten Cate JM, Imfeld T. Dental erosion. Summary. *Eur J Oral Sci* 1996;104:241–4.
- [27] Khan F, Young WG, Shahabi S, Daley TJ. Dental cervical lesions associated with occlusal erosion and attrition. *Aust Dent J* 1999;44:176–86.
- [28] Rodier P. The early origins of autism. *Sci Am* 2000;282: 56–63.