Host immune response in children with Down syndrome related to respiratory tract infection

Broers, C.J.M.

2016

document version
Publisher's PDF, also known as Version of record

Chapter 6

Frequency of otitis media, hearing loss and ear, nose and throat surgery in children with Down syndrome

Chantal J.M. Broers
Samantha C.M. Clemens
Reinoud J.B.J. Gemke
Rico N.P.M. Rinkel
A. Marceline van Furth

Submitted for publication

Abstract

Background: Children with Down syndrome are prone to respiratory tract infections, due to altered humoral and cellular immunity and a different anatomy of the respiratory tract. Otitis media is frequently seen in children with Down syndrome.

Methods: The medical records of 204 children with Down syndrome were analysed to determine the frequency of otitis media and associated ear, nose and throat surgery, as well as hearing loss.

Results: One or more episodes of otitis media were reported in 117 out of the 204 children (57%) examined in our study. It appeared to be especially common among the younger age groups. In our study group, 121 of the 204 children (59%) underwent ear, nose and throat surgery; of that group of 121, 90 children (74%) were operated more than once. Ninety-six of the 204 children (47%) underwent placement of ventilation tubes, with posterior otorrhea in 43 children (45%). In this study, 23% of the children suffered from hearing loss.

Conclusions: Otitis media and ear, nose and throat surgery are common in our group of children with Down syndrome. The frequency of post-tympanostomy otorrhea is high.

Introduction

Down syndrome (DS) is one of the most common chromosomal disorders among children, with an estimated prevalence of 16 per 10,000 live births in the Netherlands.[1] Aside from mental retardation, congenital malformations of the heart and the gastro-intestinal system, children with DS are also prone to respiratory tract infections, such as otitis media (OM), tonsillitis, laryngitis, bronchitis, bronchiolitis and pneumonia. This increased frequency of respiratory tract infections is due to three causes: anatomical variants of the respiratory tract, a neurological deficit and an altered immune system.[2] OM in DS may be caused by mid-face hypoplasia, with abnormalities between the middle ear and nasopharynx, where the Eustachian tubes end.[3] Children with DS also have functional abnormalities of the upper respiratory tract: dysfunction of the Eustachian tube, resulting in middle ear fluid accumulation, and consequently, in chronic otitis media (COM).[3,4] Manifestations of neurological deficits in children with DS include general hypotonia, which may decrease functioning of the tensor veli palatini muscles, resulting in diminished functioning of the Eustachian tube and, therefore, in an accumulation of fluid in the middle ear and/or COM.[4] OM is a common health problem in children with DS.[3,5-10] It has been reported that, on average, DS children suffer prolonged periods of illness and need additional treatment more frequently than do children without DS to overcome the same infections.[11] OM is one of the most common infections among children and, therefore, one of the most frequent diagnoses in primary – as well as in hospital – care.[12] OM can occur in acute and chronic states. It is important to distinguish between acute otitis media (AOM), otitis media with effusion (OME) and chronic otitis media (COM), as they call for different therapeutic strategies.[13] AOM is a middle ear inflammation with congestion of middle ear fluid and symptoms of upper airway infection. OME may or may not result from AOM when pus in the middle ear changes to a more serous fluid, a condition also called glue ear. COM is a chronic inflammation of the middle ear with otorrhea lasting at least 2 weeks and featuring spontaneous perforation of the ear drum, or requiring a ventilation tube. Therapeutic strategies for AOM include antibiotics, and in cases of recurrent AOM, adenoidectomy and insertion of ventilation tubes. In COM, topical antibiotics are used. One of the results of recurrent/chronic otitis media is conductive hearing loss, which may impede speech development. Another consequence is cholesteatoma.[14,15] Both are more common in children with DS.

The aim of our study is to determine the frequency of OM, ear, nose and throat (ENT) surgery and hearing loss in children with DS.

Materials and methods

Since 2003, Dutch paediatricians have been required to register children with DS in a national database: the Dutch National Registry. We contacted the parents of 400 children with DS who are registered in this database for their permission to include their children in our study. We also asked these parents for permission to obtain medical data about their children's health from their general practitioners (GP), paediatricians and ENT surgeons. We recorded the following data: age, gender, the results of chromosome analyses, frequency and type of OM as listed in the children's medical records; ENT surgery and the occurrence of hearing loss, if any, from 0 to18 years of age. To conduct this study, we also obtained permission from the Medical Ethical Committee of the VU University Medical Center. All the data obtained were compiled in a database. The medical data were reviewed by three of the authors (SC, CB and RR). A descriptive analysis of frequencies was also performed.

Results

The parents of 212 (52%) children with DS gave us written permission to obtain a copy of their children's medical files from their GPs, paediatricians and/or ENT surgeons. In total, 162 (76%) of these children were registered as patients in the DS outpatient clinic of the Department of Pediatrics at the VU University Medical Center. Ultimately, we were able to obtain medical data for 204 of the 212 children for whom we had parental consent for inclusion in this study. The average age (± standard deviation) of the children in the study group was 11.8 (± 6.0) years; range: 3–30 years and 56% (n=115) were male. Trisomy 21 was found in 197 patients (97%), translocation in 4 patients (2%) and mosaic trisomy 21 in 3 patients (1%). Of the 204 patients with DS, 117 (57%) had had one or more episodes of OM between 0–18 years. As shown in Table 6.1, a total of 536 episodes of OM were reported in this group. The frequency of otitis media is presented according to age. Of these episodes, 31% was diagnosed by the GP, and 69% by a specialist (ENT surgeon, or paediatrician). The children participating in this study can be divided into the following age groups: 85 patients (42%) were aged 3–8; 47 patients (23%) were aged 9–12; 46 patients (22%) were aged 13–18 and 26 patients (13%) were aged 19–33. Figure 6.1 presents the distribution of the type of OM per age group: OM (not otherwise specified), AOM, OME, COM and otorrhoea. Of the 204 children for whom we obtained medical data about ENT surgery, 121 (59 %) had had at least one ENT surgery sometime between early infancy and 18 years of age. In total, 96 of the 204 children (47%) had undergone – mainly bilateral – placement of ventilation

Table 6.1 Frequency of otitis media according to age

Age (years)	Number of children with otitis media episodes ≥1	Number of episodes of otitis media	Number of children participating in this study	% of children with otitis media episodes ≥1
0	19	26	204	9.3
1	30	45	204	14.7
2	49	83	204	24.0
3	46	61	204	22.5
4	28	44	204	13.7
5	46	61	204	22.5
6	33	41	200	16.5
7	31	53	195	15.9
8	25	32	161	15.5
9	17	23	144	11.8
10	13	18	119	10.9
11	8	14	106	7.5
12	8	9	110	7.3
13	5	5	81	6.2
14	8	8	72	11.1
15	3	3	65	4.6
16	5	6	52	9.6
17	2	3	42	4.8
18	1	1	41	2.4
Total		536		

tubes on 196 occasions. Of these 96 children, 43 (45%) developed otorrhea at least once within one year of undergoing treatment with ventilation tubes. In the total group of 204 patients, we encountered 60 adenotomies in 55 children, 8 tonsillectomies in 8 children and 38 adenotonsillectomies in 38 children. One child among the entire group of 204 (0.5%) had undergone surgery at age 9 because of cholesteatoma.

In all, 47 (23%) of the 204 children were reported to have hearing loss. A variety of audiometric test methods were used, according to the age and developmental level of each individual child. Table 6.2 presents the frequency, type and severity of hearing loss in these patients, as well as the results of their 69 most recent hearing tests. Twenty of these 47 patients showed some type of moderate or severe hearing loss in the most recent hearing test. Sixteen of the 204 children (8%) received hearing aids, at an average age of 8 years (range 3–18 years). The main reason for hearing aids was the presence of moderate conductive hearing loss or moderate to severe mixed hearing loss.

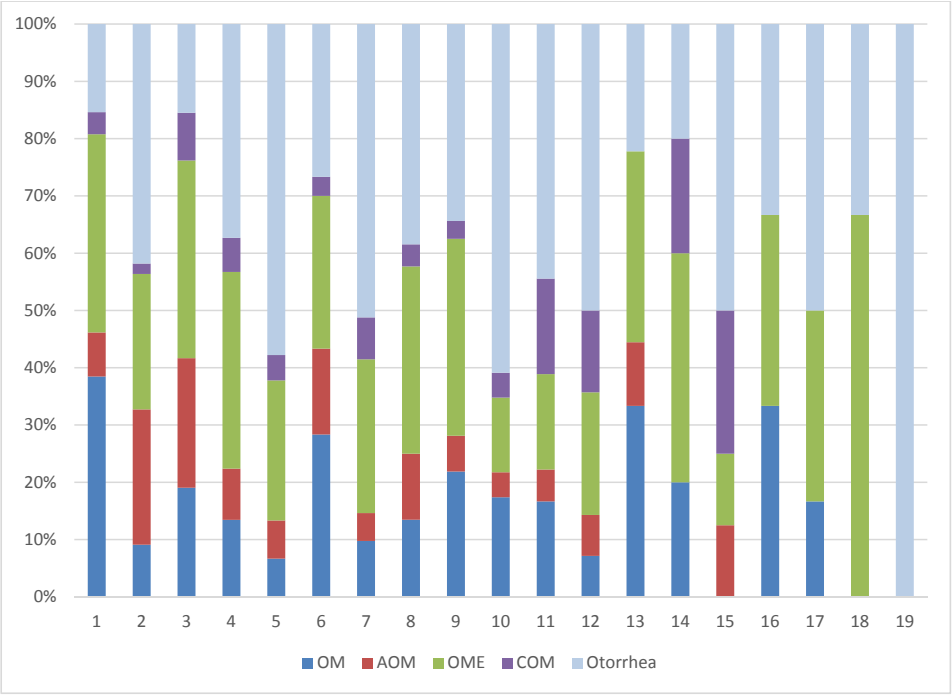

Figure 6.1 Distribution of the type of OM per age group from 0–18 years.

Table 6.2 Results of 69 hearing tests in 47 patients with hearing loss

	Conductive hearing loss	Perceptive hearing loss	Mixed hearing loss
Normal hearing - light hearing loss (0–30 dB)	33	3	1
Moderate hearing loss (30–60 dB)	22	0	4
Severe hearing loss (>60 dB)	2	1	3

Discussion

OM is a very common disorder in young children.[16] In fact, 75% of all individuals will suffer at least one episode of AOM at some point in their lives, with a peak in the 6–18 month age group.[17] In western countries, 80% of all children suffer at least one episode of AOM before the age of three.[18] In the literature, we encountered several reports on the high frequency of OM, especially OME, in children with DS.[5,8,9,19-21] OME is more common in DS because of

Eustachian tube dysfunction.[3,6] In our study, we observed that OM in DS is most common in the 1–8 age group. However, the actual numbers may be underestimated, as our study is based on recorded medical data and it is entirely possible that not all the episodes of OM in children are recognized or presented to a physician. OME can occur at all ages. Moreover, the number of OME cases may be underestimated since the diagnoses of OM (not otherwise specified) probably include cases of OME. In the literature, we found several reports noting that tympanostomy for OME is not as effective in children with DS as it is in healthy children with a high frequency of tympanostomy tube otorrhea.[21] For children without DS, tympanostomy tube otorrhea has been reported for anywhere from 26 to 83%.[22-24] In our study, the frequency of otorrhea following the placement of ventilation tubes in children with DS was 45%, a figure higher than the 24% reported by Barr et al.[19] This raises the question of whether tympanostomy for OME in children with DS is the best choice, or whether they might benefit more from hearing aids.

ENT surgery was frequently reported in our study group: 59% of the children (121/204) had undergone ENT surgery, 74% of whom (90/121) had had more than one ENT surgery, mainly the insertion of ventilation tubes. This is high compared to a study in a Danish birth cohort of 95,095 children, in which 26% of children underwent placement of ventilation tubes.[25]

In our study, we encountered one child (0.5%) among our 204 DS subjects who had been diagnosed with cholesteatoma. This is a high percentage compared to the general paediatric population, in which the incidence rate of cholesteatoma is reported as 3–6 cases per 100,000 individuals.[26] This confirms the data in the literature, which suggests that children with DS have an increased incidence of cholesteatoma, although exact numbers are not known.[27,28]

In our study group, 4 children with reported moderate to severe hearing loss did not use hearing aids. The reason for this is unclear from the data in the medical records. This is a point of interest in the management of hearing loss in children with DS.

In this study, we present the frequency of OM in a large group of children with DS. OM is common, especially in the younger age groups, as is ENT surgery. The strength of our study is the large study group it examines. One weakness, however, is the lack of a control group and the fact that the frequency of OM may be underestimated, as physicians are not always consulted to confirm diagnoses of OM. Moreover, OME may be asymptomatic and, therefore, not registered in medical records. Future prospective case-controlled studies are necessary to assess the frequency of OM and hearing loss in children with DS and to evaluate the efficacy of intervention strategies on both the recurrence rate of OM and on hearing loss.

Conclusions

In our study group of 204 children with DS, OM is a common disorder. Fifty-nine percent of the children underwent ENT surgery; of that group, 74% had been operated more than once. We also observed that 45% had otorrhea subsequent to ventilation tube insertion. Hearing loss was found in 23%.

References

1. Weijerman ME, de Winter JP. Clinical practice. The care of children with Down syndrome. Eur J Pediatr 2010;169:1445-52.
2. Bloemers BL, Broers CJ, Bont L, Weijerman ME, Gemke RJ, van Furth AM. Increased risk of respiratory tract infections in children with Down syndrome: the consequence of an altered immune system. Microbes Infect 2010;12:799-808.
3. Shott SR. Down syndrome: common otolaryngologic manifestations. Am J Med Genet Part C Semin Med Genet 2006;142C:131-40.
4. Strome M. Down's syndrome: a modern a modern otorhinolaryngological perspective. Laryngoscope 1981;91:1581-94. Part C semin Med Genet 2006;15:131-40.
5. Satwant S, Subramaniam KN, Prepageran N, Raman R, Jalaludin MA. Otological disorders in Down's Syndrome. Med J Malaysia 2002;57:278-82.
6. Venail F, Gardiner Q, Mondain M. ENT and speech disorders in children with Down's syndrome: an overview of pathophysiology, clinical features, treatments, and current management. Clin Pediatr (Phila) 2004;43:783-91.
7. Pandit C, Fitzgerald DA. Respiratory problems in children with Down syndrome. J Paediatr Child Health 2012;48:E147-52.
8. Morales-Angulo C, Gallo-Terán J, Azuara N, Rama Quintela J. Otorhinolaryngological manifestations in patients with Down syndrome. Acta Otorrinolaringol 2006;57:262-5.
9. Selikowitz M. Health problems and health checks in school-aged children with Down syndrome. J Paediatr Child Health 1992;28:383-6.
10. Turner S, Sloper P, Cunningham C, Knussen C. Health problems in children with Down's syndrome. Child Care Health Dev 1990;16:83-97.
11. Ram G, Chinen J. Infections and immunodeficiency in Down syndrome. Clin Exp Immunol 2011;164:9-16.
12. CBO Richtlijn Otitis media bij kinderen in de tweede lijn, juni 2012. Nederlandse Vereniging voor KNO-heelkunde en Heelkunde van het Hoofd-Halsgebied.
13. Faden H, Duffy L, Boeve M. Otitis media: back to basics. Pediatr Infect Dis J 1998;17:1105-12.
14. Een update van de multidisciplinaire richtlijn voor de medische begeleiding van kinderen met Down syndroom, december 2011. Werkgroep Down syndroom sectie EAA van de NVK. Onder redactie van Borstlap R, van Gameren-Oosterom HBM, Lincke C, Weijerman ME, van Wouwe JP.
15. Shott SR, Joseph A, Heithaus D. Hearing loss in children with Down syndrome. Int J Pediatr Otorhinolaryngol 2001;61:199-205.
16. Rovers MM, Schilder AG, Zielhuis GA, Rosenfeld RM. Otitis media. Lancet 2004;363:465-73.

17. Klein JO. The burden of otitis media. Vaccine 2001;19: S2-S8.

18. Daly KA, Hoffman HJ, Kvaerner KJ, Kvestad E, Casselbrant ML, Homoe P, Rovers MM. Epidemiology, natural history, and risk factors: panel report from the Ninth International Research Conference on Otitis Media. Int J Pediatr Otorhinolaryngol 2010;74:231-40.

19. Barr E, Dungworth J, Hunter K, McFarlane M, Kubba H. The prevalence of ear, nose and throat disorders in preschool children with Down's syndrome in Glasgow. Scott Med J 2011;56:98-103.

20. Austeng ME, Akre H, Øverland B, Abdelnoor M, Falkenberg E-S, Kværner KJ. Otitis media with effusion in children with in Down syndrome. Int J Pediatr Otorhinolaryngol 2013; 77:1329-32.

21. Iino Y, Imamura Y, Harigai S, Tanaka Y. Efficacy of tympanostomy tube insertion for otitis media with effusion in children with Down syndrome. Int J Pediatr Otorhinolaryngol 1999;49:143-9.

22. Kay DJ, Nelson M, Rosenfeld RM. Meta-analysis of tympanostomy tube sequelae. Otolaryngol Head Neck Surg 2001;124:374-80.

23. Ah-Tye C, Paradise JL, Colborn DK. Otorrhea in young children after tympanostomy-tube placement for persistent middle-ear effusion: prevalence, incidence and duration. Pediatrics 2001;107:1251-8.

24. van Dongen TMA, van der Heijden GJMG, Freling HG, Venekamp RP, Schilder AGM. Parent-reported otorrhea in children with tympanostomy tubes: incidence and predictors. PloS ONE.2013; 8(7): e69062. doi:10.1371/journal.pone.0069062.

25. Todberg T, Koch A, Andersson M, Olsen SF, Lous J, Homøe P. Incidence of otitis media in a contemporary Danish National Birth Cohort. PLoS ONE.2014; 9(12): e111732. doi: 10.1371/journal.pone. 0111732.

26. Shohet JA, de Jong AL. The management of pediatric cholesteatoma. Otolaryngol Clin North Am 2002; 35:841-51.

27. Pappas DG, Flexer C, Shackelford L. Otological and habilitative management of children with Down syndrome. Laryngoscope 1994; 104: 1065-70.

28. Bacciu A, Pasanisi E, Vincenti V, Giordano D, Caruso A, Lauda L, Bacciu S. Surgical treatment of middle ear cholesteatoma in children with Down syndrome. Otol Neurotol 2005; 26: 1007-10.