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An audit of UK audiological practice in specialist paediatric oncology centres regarding hearing assessment of children at risk of ototoxicity due to chemotherapy

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Main Article

Ms E Brown takes responsibility for the integrity of the content of the paper

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Abstract

Objective. Platinum-based chemotherapy drugs are associated with substantial ototoxicity. The hearing of children treated with these drugs should be closely monitored.

Method. A questionnaire was sent out to the 19 audiology departments associated with national paediatric cancer specialist centres in the UK looking at current practice in ototoxicity monitoring.

Results. Responses were received from 17 of 19 centres (89 per cent). All offered some form of audiometric monitoring service. Extended high-frequency testing (9–20 kHz) was only utilised by 7 services (29 per cent). A majority of respondents were reluctant to consider self-test devices in paediatric ototoxicity monitoring ($n = 9$; 53 per cent). Provision of long-term audiological follow up is sporadic with only 4 (23 per cent) respondents keeping all children with normal hearing under review once treatment is completed.

Conclusion. While some good practice in paediatric ototoxicity was identified, opportunities exist to improve clinical practice and protocols, promote multidisciplinary team working and to utilise technologies such as extended high frequency and self-test audiometry.

Introduction

Improvements in therapy and supportive care for children diagnosed with cancer have increased the overall 5-year survival rate from 45 per cent for patients diagnosed in the mid-1970s to more than 80 per cent in 2010.[1] However, because of the increased survival rates and the ototoxic nature of some of the drugs used for chemotherapy, more children are living with late effects of their cancer treatment. The platinum-based chemotherapy drugs cisplatin and, to a lesser extent, carboplatin can cause hearing loss in children as in adults. Up to 67 per cent of children treated with cisplatin develop permanent bilateral hearing loss.[2] A recent study looking at hearing loss and quality of life in survivors of paediatric central nervous system tumours found that hearing loss was also associated with impaired physical well-being.[3]

Estimates of the prevalence of hearing loss in children and young people following ototoxic medication are greatly variable and are dependent on how hearing loss is graded and classified. A study that investigated the incidence of hearing loss in a group of 23 survivors of childhood cancer treated with cisplatin reported that 52 per cent of this group had bilateral high-frequency hearing loss on audiometry.[4] Whereas a different study reported an incidence of bilateral hearing loss that was observed in 73 per cent of a group of 33 children treated with cisplatin.[5]

Previous research has demonstrated that children younger than 5 years at the time of their cancer treatment are 21 times more likely to acquire moderately severe high-frequency hearing loss than patients aged 15 to 20 years.[5] The impact of ototoxic hearing loss in young children is further increased as a result of developmental effects of hearing on speech and language acquisition. High-frequency hearing loss can have a significant effect on a child's speech and language development, particularly high-frequency fricative sounds, which are needed for speech clarity and discrimination.[7] It is therefore essential to monitor the hearing of all children who are treated with ototoxic chemotherapy agents.

Measurable loss of inner ear function can occur following just one cycle of cisplatin infusion.[8] It is therefore necessary to obtain a baseline hearing assessment before chemotherapy starts and to start monitoring after the first cycle of chemotherapy. Early identification of any change in hearing function would allow oncologists to make timely decisions over future ototoxic treatment doses, enabling them to limit the amount of damage done to the auditory system when treatment change is an option. This would also allow for the possibility of early intervention to actively manage any hearing deficit that is discovered. Early intervention for congenital sensory neural hearing loss with hearing aids or cochlear implant is associated with higher language scores in children.[9] It

would therefore be reasonable to assume that early intervention would be advantageous in this population also.

Even when hearing loss is detected in the post-chemotherapy paediatric population, the uptake of using amplification is poor; it has been found that 38 per cent of adult survivors of childhood non-central nervous system (CNS) solid tumours and CNS tumours who received ototoxic cancer-directed therapies during childhood were found to have serious hearing loss that equated to a need for a hearing aid. However, only one-third of survivors used some type of hearing intervention. Furthermore among survivors of non-CNS tumours who were found to have serious hearing loss, 41 per cent (95 per cent confidence interval (CI), 30–52 per cent) reported a perceived negative impact of cancer on their education or vocation compared with 29 per cent (95 per cent CI, 21–38 per cent) of survivors without serious hearing loss.[10] This would suggest that there is a need to engage people with the use of hearing technology and to identify and treat any hearing loss in this group. There is also the need for further research to investigate why this group are not engaging with intervention for their hearing loss.

Previous research has highlighted that children exposed to ototoxic medication are also at a higher risk of developing tinnitus, both during and after their treatment. A systematic review reported a tinnitus incidence rate in the population of up to 15.9 per thousand people during childhood cancer treatment.[11] The number of children being referred for help with tinnitus is reported as being low in the general population.[12] This would suggest that children may not express that they are experiencing any issues in the way an adult may. Within the general population there is evidence to suggest that parents are often unaware that their child is experiencing tinnitus.[13] This highlights the need to ask children about their experience. The British Society of Audiology Tinnitus in Children Practice Guidelines 2015[14] states that it should be routine to ask all children seen for audiological assessment whether they hear noises in their ears or head. Tinnitus in children can cause significant distress and lead to problems with sleeping, concentration and listening difficulties. It is also known that tinnitus can be escalated in times of stress and anxiety.[15] It is therefore advisable that regard is given to identifying tinnitus in childhood cancer patients exposed to ototoxic medication during their treatment.

All children and young people in England diagnosed with cancer are referred to one of the 19 paediatric oncology treatment centres. The NHS England service specification document states that each child with suspected cancer should be referred to one of these Principle Treatment Centres, which must make the diagnosis and direct the provision of treatment.[16]

Good practice guidance recommends effective monitoring of hearing during ototoxic chemotherapy treatment. The American Academy of Audiology Position Statement and Clinical Practice Guidelines 2009[17] discusses the merits of different test procedures, but the conclusion is that 'the audiologist bears the primary role in the design and development of ototoxicity monitoring programs'. The International Late Effects of Childhood Cancer Guideline Harmonization Group suggest that conventional pure tone audiometry be used to assess children more than six years old and that children less than six years should be referred to an audiologist for more extensive testing, and it was recommended that healthcare providers should be aware of the risk of tinnitus in this population.[18] There is currently no UK national guideline regarding what monitoring of children at risk of ototoxicity is needed or how this monitoring should take place. However, there is survey evidence to suggest that the practice is not currently widespread.[19] This being the case, there is a risk that survivors of childhood and adolescent cancer are also potentially struggling with speech development and within the educational system because of undiagnosed and untreated hearing loss or tinnitus.

The objective of this study was to investigate current practice in the paediatric audiology departments associated with the 19 UK regional specialist paediatric oncology centres. Information gleaned can potentially be utilised in the development of a common paediatric ototoxicity monitoring protocol.

Materials and methods

A web-based questionnaire was circulated to the 19 audiology departments associated with principal treatment centres for diagnosing and treating cancer in children and young people. The questionnaire was distributed via the JISC Online Surveys (Bristol, UK) platform.

A link to the survey was emailed to a named person within the audiology department wherever possible, but in some cases a generic departmental email address was used. The questionnaire was live online for a period of four weeks. The survey questions can be seen in Appendix 1.

Results

All the respondents who participated were UK based, and all described themselves as audiologists or clinical scientists. All the respondents reported themselves as being mid-career (12 per cent; $n = 2$) or experienced clinicians (88 per cent; $n = 15$).

All respondents reported that their department offered some form of hearing screening service to children exposed to ototoxic drugs as part of their chemotherapy treatment regime. A dedicated team of audiologists was allocated to see these children in 29 per cent ($n = 5$) of the audiology services who responded, and 71 per cent ($n = 12$) of departments saw the children within general paediatric audiology clinics and did not have a dedicated team for this group of children.

The responses showed that 76 per cent ($n = 13$) of services had a dedicated person or email address that could be contacted to arrange hearing assessment appointments. The respondents reported that for 94 per cent ($n = 16$) of the services it was the consultant oncologist or other member of the oncology team who discussed the impact that ototoxic medication might have on the child. Responses also showed that in 82 per cent ($n = 14$) of services the impact of ototoxicity was also discussed with the child or family by the audiological clinicians involved in the child's hearing assessment. In all cases, either the consultant in charge of the child's care or another member of the oncology team was making the decisions about when and how often children's hearing was to be reviewed.

Details of current practice in audiology departments attached to regional oncology treatment centres surrounding the use of extended high-frequency testing (i.e. beyond 8 kHz) in the monitoring of children's hearing are shown in Table 1.

There was a further free-text question to establish which extended high frequencies were being tested. It became clear that extended high frequencies should have been more clearly defined in the questionnaire because 4 of the respondents

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Table 1. Percentages of departments using extended high-frequency testing

Parameter	Respondents (% (*n*))
Attempt EHF testing on all age groups	29.4 (5)
Attempt EHF testing on children who can carry out performance testing	5.9 (1)
Attempt EHF testing on children who can carry out audiometry	5.9 (1)
Do not carry out any EHF testing	58.8 (10)

EHF = extended high frequency

Table 2. Reasons for not carrying out EHF testing

Reason	Respondents (% (*n*))
Not required by oncology team	33 (2)
Concerns about normative data	16.6 (1)
Patients unable to tolerate extended test time	16.6 (1)
Protocols only indicate changes in treatment for frequencies up to 8 kHz	16.6 (1)
Never thought about testing EHFs	16.6 (1)

EHF = extended high frequency

answered that they tested 6 or 8 kHz or both when asked which extended high frequencies were tested. The 24 per cent ($n = 4$) of respondents who tested at frequencies higher than 8 kHz all tested different frequencies, a different number of frequencies and a different combination of frequencies when carrying out extended high-frequency testing. There was no uniformity of practice or agreement between respondents in this area. Respondents reported that they tested '12 and 16 kHz', '9, 10, 11, 12, 14, 16, 18 and 20 kHz', '10 and 12 kHz' and 'earphone testing up to 6 and 8 kHz, distortion product oto-acoustic emissions (DPOAE) up to 10 kHz'.

When looking at why respondents were not carrying out extended high-frequency testing, 25 per cent of respondents reported that they did not carry out extended high-frequency testing because of lack of suitable equipment, and 16 per cent felt that extended high-frequency testing was not needed for this population. A further 58 per cent of respondents had another reason for not carrying out extended high-frequency testing. Reasons given are detailed in Table 2.

It has been recommended[20] that all children should undergo a baseline hearing test prior to commencing ototoxic chemotherapy as cisplatin can cause marked hearing loss following a single administration. Of the departments who responded to this survey, 94 per cent ($n = 16$) reported that the children they see do always get a pre-treatment hearing assessment. Only one department reported that a pre-treatment hearing assessment is often, but not always carried out.

The American Speech-Language-Hearing Association recommend in their guidelines for management of patients receiving ototoxic drugs that hearing assessment should be carried out shortly after every cycle of chemotherapy[17] to detect hearing loss as soon as possible.[21] Participants were asked about who decided about when ongoing hearing assessments were needed. Most often it was the oncology team who dictated when ongoing assessment was indicated. This was the case for 94 per cent ($n = 16$) of respondents. Only 6 per cent ($n = 1$) of respondents saw children for review following a pathway designed by the audiology team.

Ototoxicity because of cisplatin affects high-frequency hearing in the first instance. This might suggest that any hearing assessment for this group of children should focus on testing these frequencies first. To ensure that testing is done in the most time efficient order, a dedicated protocol could be useful to ensure the most effective sequence of testing is employed. Of the respondents completing the survey, 71 per cent ($n = 12$) of departments have a dedicated testing protocol or pathway for use with this group of children, whereas 29 per cent ($n = 5$) of departments do not have any dedicated protocols.

Cisplatin-based chemotherapy can lead to substantial hearing loss.[22] Respondents were asked if they were detecting cases of ototoxic induced hearing loss. It was found that all respondents reported that their departments had needed to make intervention (such as fitting hearing aids) to manage hearing loss caused by ototoxic medication. When asked to quantify how regularly intervention was needed for hearing loss as a result of ototoxicity in childhood cancer patients, 82 per cent ($n = 14$) of respondents reported that intervention was sometimes needed, 12 per cent ($n = 2$) of respondents reported that intervention was often needed and 6 per cent ($n = 1$) felt that intervention was frequently needed in this group of children. No respondent reported intervention as a rare or never event.

There is less literature surrounding the prevalence of tinnitus in children exposed to ototoxic medication, but it is felt that tinnitus is an issue for some of these children.[11] Some respondents (18 per cent; $n = 3$) were not asking children about tinnitus. Of the 82 per cent ($n = 14$) of respondents who were asking about tinnitus, 71 per cent ($n = 10$) reported that these children sometimes or often reported tinnitus, and 29 per cent ($n = 4$) found that children were rarely reporting experiences of tinnitus as a result of their treatment.

Respondents were questioned as to whether they were asking about balance issues in these children, and 24 per cent ($n = 4$) did not ask about balance issues with this client group. Of the 76 per cent ($n = 13$) of respondents who did ask about balance, 38.5 per cent ($n = 5$) reported that balance was sometimes an issue for the children that they saw, whereas 61.5 per cent ($n = 8$) reported that balance was rarely an issue.

In some cases, hearing can deteriorate after treatment is complete.[23] However, of the respondents that completed the survey, only 23 per cent ($n = 4$) of departments always keep children under review if they have normal hearing once their treatment is finished, 59 per cent ($n = 10$) sometimes keep children with normal hearing under review once their treatment is completed, and 18 per cent ($n = 3$) of departments did not offer any follow up if hearing is normal on completion of treatment.

Respondents to the survey were asked about the possibility of the use of some form of self-testing device to screen the hearing of these children, and results show that respondents were quite hesitant about the use of such technology as detailed in Table 3.

Reasons given for hesitation about using a self-test technology were: concerns about reliability of test results; the need to 'train' children to test behaviourally and reliably before treatment starts (because the child is well and not so concerned about medical professionals or hospitals at this stage); concerns about what a self-test device would involve; the need

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Table 3. Willingness to use automated hearing screening devices

Parameter	Respondents (% (*n*))
Would be happy to use with pre-treatment children	6 (1)
Would be happy to use with children during treatment	18 (3)
Would only be happy to use with older children	23 (4)
Would not be happy to use a self-test device	53 (9)

for face-to-face appointments allowing for counselling and checking of other symptoms (e.g. tinnitus); concerns that a self-check device may lead to increased anxiety if over used; thoughts that self-testing may be useful after counselling or the post-treatment regime is completed (i.e. for long-term follow up); and (according to one respondent) a feeling that as they were providing full-testing and had established pathways there was no need for a self-test device.

Discussion

Some form of ototoxicity monitoring is being offered at all the paediatric oncology specialist centres that responded to the survey. The hearing assessment is offered within the general paediatric audiology service 30 per cent of the time and not by a dedicated team. If the service was offered by a dedicated team this may potentially result in a better quality assessment for the children involved.

Childhood cancer is relatively rare. The rate at which new cases develop among children (incidence) is 15.3 per 100 000 per year, which corresponds roughly to 1 in 6500 children and adolescents under age 20.[24] Having advice from a dedicated audiologist or team of audiologists would ensure that parents and children receive the best advice and testing for their particular need. Advice could be more tailored to the particular situation and treatment regimen based on the audiologist's experience. There is a concern that if children are just referred in by a generic pathway they may not be allocated to an appropriate hearing assessment clinic at the appropriate time, leading to delays in assessment and reporting of results. A dedicated team within the audiology department would have increased awareness of who the oncology team are and how to communicate results quickly and efficiently to them.

Continuity of care from a dedicated audiology team would offer a more family-friendly, child-centred approach for these vulnerable children and their families. From clinical experience, as a child progresses through treatment and sees the same audiologist for hearing assessment they engage more in testing and are more willing to communicate with the audiologist at each subsequent visit.

Improving inter-professional links with the oncology team could lead to better quality care and more timely hearing assessment intervals. Opportunities exist for the oncology and audiology teams to work closely together to formulate the best management plan for each individual child and family.

From the survey results it seems that the implications of exposure to ototoxic medications are being discussed by both oncologists and audiologists. It would be of interest to know the quality of the information that is being provided to both parents and children. If ototoxicity is being discussed by both the audiologist and the oncologist, there is a need to ensure that both are giving good quality, concordant and accurate information.

It is known that cisplatin and other ototoxic medication given during chemotherapy can cause irreversible hearing loss, typically in the high-frequency (4 to 8 kHz) and very high-frequency (9 to 20 kHz) ranges. The hearing loss often worsens, affecting progressively lower frequencies in a cumulative, dose-dependent fashion.[22,23] It is therefore important, in any surveillance programme, that testing in children should focus on testing high frequencies first.[25] This approach may differ from the testing sequence employed within the general paediatric audiology population. Audiology departments may benefit from using specific protocols for this client group. Testing children using the guidance of generic service protocols and pathways was the case for 29 per cent ($n = 5$) of respondents. This could lead to a missed opportunity for gathering information about a child's high-frequency hearing. Oncologists generally use ototoxicity grading scales to quantify hearing loss, so any testing undertaken needs to be tailored so that it provides the information that is most useful to the oncologist and is in concordance with what information is needed to grade the hearing levels recorded.

A review paper reported that a weakness of ototoxicity grading scales is a lack of sensitivity to small adverse changes in hearing thresholds, a lack of extended high-frequency audiometry (more than 8 kHz) and lack of indication of which changes are likely to be clinically significant for communication and quality of life.[26] Despite evidence to suggest that extended high-frequency audiometry can pick up the effects of ototoxicity sooner than audiometry carried out up to 8 kHz, few centres are carrying out extended high-frequency testing. Until more data is gathered around these extended high-frequency results, grading scales and treatment decisions cannot be based on extended high-frequency testing. Further evidence is needed to confirm or deny the use of extended high-frequency testing in clinic with this client group.

A further reason to explore extended high-frequency testing is the emergence of evidence to suggest that extended high-frequencies have an effect on how well people can hear in background noise. One study found that extended high frequency hearing loss correlated with self-reported difficulty hearing in noise in adults.[27] Children are often in challenging listening environments with high levels of background noise, for example in the classroom, or on a noisy ward. It might therefore be advantageous to know about any extended high-frequency hearing loss that may affect ability to follow conversation and to complete learning in challenging listening situations.

The follow up regime for this group is different to that used for children in the standard paediatric audiology clinic. Follow up might be much more long term for these patients. There is evidence that ototoxicity can occur a considerable time after treatment is finished. A study looked at 59 children who received cisplatin and had sufficient data to determine the presence of late onset hearing loss, where late onset hearing loss was defined as a significant change in hearing thresholds 6 months past the last cisplatin therapy. Of the 59 patients evaluated, 51 per cent exhibited late onset hearing loss.[4] In view of this, it would seem appropriate to keep a regular review on children's hearing even after the completion of treatment. To ensure this takes place in a timely fashion, a dedicated protocol and pathway would need to be in place.

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Evidence is sparse detailing the prevalence of tinnitus in children exposed to ototoxic medication. It has been found that childhood cancer survivors exposed to platinum drugs had an increased risk of tinnitus occurring five years or more after diagnosis.[28] It is difficult to assess the prevalence of tinnitus in this paediatric population as there is a lack of an objective measurement to detect or quantify tinnitus. Any judgments are based on the child's ability to communicate that they are experiencing tinnitus. It is therefore important that every child who is developmentally able to respond to the question is asked about their experience of tinnitus. Twenty-eight per cent ($n = 3$) of survey respondents are not asking children about tinnitus at all. Of the respondents that do ask about tinnitus, all report that they have come across children who are experiencing tinnitus following exposure to ototoxic drugs. This would further confirm that it is important to be asking the question.

Sparse evidence is available with regard to the prevalence of vestibular or balance issues following chemotherapy. An investigation carried out using questionnaires and modified balance tests on a group of children recovering from cancer treatment found vestibular screening failures were observed in up to 60 per cent of participants. It would therefore seem appropriate to ask about any concerns regarding balance in this group.[29] The respondents to the survey who ask about balance are finding reports of children who are having issues in this area, and so it would confirm that this is a question that needs to be asked and investigated.

There have been studies looking at the use of automated computer-based hearing-screening devices to screen children's hearing in school.[30] There could be potential merit in or benefit from using this type of self-test technology with children exposed to ototoxic medication in order to screen children quickly with a minimum of disruption. Respondents to the survey were markedly hesitant about the use of a self-test type technique. Concerns focused on the reliability of self-test techniques and the lack of availability of anyone to discuss the results. Concern was raised that a self-test would miss the opportunity to ask about tinnitus and balance issues. The use of automated, portable systems in ototoxicity monitoring would allow for the possibility of other healthcare workers to be trained to administer a limited monitoring protocol under the supervision of an audiologist.[31] These devices could also allow for the patient to test himself or herself with results sent to the audiologist for interpretation. This is an area that would merit further investigation.

One area of audiological practice that was not investigated in detail in the present study was that of the use of otoacoustic emission (OAE) testing. Otoacoustic emission testing may be of particular value when a child is uncooperative or otherwise unable to perform behavioural audiometry; however, we note that OAE testing is not advocated as a routine stand-alone procedure in any of the existing protocols for paediatric ototoxicity monitoring. The role of OAEs in test protocols for the identification and monitoring of paediatric ototoxicity associated with platinum-based chemotherapy for cancer is a topic for future research.

Conclusion

Although paediatric ototoxicity monitoring is taking place in specialist centres, there is an opportunity to improve interprofessional relationships between the oncology and audiology teams to implement best practice.

Extended high-frequency testing is rarely performed and the use of this could be improved. The use of tablet based self-assessment tools could be of benefit to increase ease of access to hearing screening.

There is a need to promote greater awareness of the possibility of tinnitus and balance issues in this group and consideration of how any issues identified are going to be managed.

- Regular hearing monitoring is essential for children exposed to ototoxic chemotherapy drugs
- Current practice is not uniform, with differences in testing methods and long-term follow up
- There is a need to increase awareness of tinnitus and balance issues in this group of children
- Technological innovations such as extended high-frequency testing and tablet based self-test audiometry devices are barely used at present, and some reluctance is evident

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Appendix 1. Questionnaire

1. Where do you currently practice?
   UK
   Other

2. What is your profession?
   Audiologist
   ENT specialist
   Audio-vestibular physician
   Clinical scientist
   Other

3. At what stage of your career are you?
   Trainee
   Newly qualified
   Mid-career
   Experienced clinician

4. Do you currently offer a hearing screening service to children exposed to ototoxic medication as part of their cancer treatment regime?
   Yes, dedicated team within the paediatric audiology department provide this
   Yes, children are seen within the general paediatric Audiology service
   No this service is not currently offered
   Other service

5. Do you have a designated person that the oncology team can contact to arrange hearing assessments?
   Yes dedicated audiologist
   Yes dedicated member of admin team
   No dedicated person
   Other

6. Who discusses the impact that ototoxic medication might have with the child and or parent? Please select all that apply
   Consultant overseeing the child's care
   Other member of the oncology team
   Audio-vestibular physician
   ENT consultant
   Audiologist
   Other

7. Who decides when hearing is assessed and what subsequent testing is needed for each child?
   Audiologist
   Consultant in charge of child's care
   Other member of oncology team
   Do not know
   Other

8. Do you carry out any extended high frequency (EHF) testing with these children?
   Attempt EHF testing on all age groups
   Attempt EHF on children who can carry out performance testing
   Attempt EHF testing on children who can carry out audiometry
   Do not carry out any EHF testing

9. If you do not carry out EHF testing why is this?
   Equipment to test EHF is not available within the department
   Concerns about calibration for EHF
   Do not feel EHF testing is needed for this population
   Other

10. If you carry out EHF testing which frequencies do you test?

11. Do paediatric oncology patients get a pre-treatment hearing assessment?
   Yes, always
   Often
   Sometimes
   Never

12. Do you see paediatric oncology patients exposed to ototoxic medication for a regular hearing review?
   Yes, following pathway designed by oncology team
   Yes, following pathway designed by audiology team
   Yes, but not following any particular pathway/guideline
   No follow up offered

13. Do you have testing protocols and pathways dedicated to this group of children?
   Yes
   No

14. How would you feel about using some sort of self-test hearing screening device with this population?
   Would be happy to use with pre-treatment children
   Would be happy to use with children during treatment
   Would only be happy to use with older children
   Would not be happy to use a self-test device

15. Based on the children you see, how often is intervention needed for hearing loss following ototoxic medication?
   Frequently
   Often
   Sometimes
   Rarely
   Never

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16. In your experience, how often is tinnitus reported in this group of children?
    Always
    Usually
    Sometimes
    Rarely
    Never
    We do not ask about tinnitus
17. In your experience, how often is balance reported as an issue in this group of children?
    Always
    Usually
    Sometimes
    Rarely
    Never
    We do not ask about balance
18. Do you continue to review children who have normal hearing after their treatment is finished?
    Yes, always
    Sometimes
    No

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