Aetiological investigations into sensorineural hearing loss in adults.

Produced by the British Association of Audiovestibular Physicians

(BAAP)
2015

INDEX

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Summary

The aim of these guidelines is to have an evidence based approach to the investigation of the cause of sensorineural hearing loss in adults. These guidelines are for use in the United Kingdom but could be applied worldwide depending on local availability of clinical expertise, test facilities and resources.

Investigations to consider include

1) History

2) Clinical Examination findings

3) Family Audiograms

4) Ophthalmology Assessment

5) Genetic Tests

6) MRI/CT scans

7) Renal Ultrasound

8) Haematological/Biochemical and Immunological Tests

9) Metabolic/Serological Tests

10) ECG

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Aims

The aim of these guidelines is to have an evidence based approach to the investigation of the cause of hearing loss in adults (over 18). Guidelines are "systematically developed statements to assist decisions about appropriate care for specific clinical circumstances based on systematic reviews of research literature" (1 -3). These guidelines were produced in line with procedure detailed in the BAAP manual for producing guidelines (4).

These guidelines are for use in the United Kingdom but could be applied worldwide depending on local availability of clinical expertise, test facilities and resources. The intended users of these guidelines are all health practitioners involved in the management of hearing impaired adults. The guidelines:

- Provide up to date advice on effective clinical practice
- Support staff in improving and benchmarking Audiovestibular Medicine services
- Identify audit measures for performance and review
- Promote patient safety and implementation of clinical governance

These guidelines are evidence-based and link their concluding recommendations to the evidence base identified through the literature search (5). They are not intended to restrict clinical freedom but practitioners are expected to use the recommendations as a basis for their practice. Areas lacking in evidence may form a basis for future research.

Why investigate hearing loss?

There are several reasons why it is important to investigate hearing loss:

1. To try and answer questions like "Why have I got a hearing loss?"
2. To identify and treat associated medical conditions such as 8th nerve tumours, autoimmune disorders, neurological disorders, metabolic disease, co existing haematological disorders, vestibular hypofunction etc
3. The results of investigations can assist the individual in making decisions about the most appropriate communication mode including assistive listening devices and counselling on auditory implants
4. To help with general counselling on hearing loss and genetic counselling
5. The information from investigation of hearing loss informs epidemiological research, improves understanding of adult hearing loss and is also likely to be helpful in the future in correlating outcome of interventions such as auditory implants with aetiology.

Search Methodology

The literature search covered databases including PubMed, Medline, Embase, AMED, BNI, CINAHL, HMIC, PsycINFO and Cochrane Library Database. The keywords detailed in Appendix 2 were used. The search was carried out by the librarians at Portsmouth Hospitals NHS Trust (Appendix 5). All relevant articles including randomised control trials, systematic reviews, meta-analyses, observational studies, case reports and expert opinion were reviewed.

Some review articles were referenced but not included to support recommendations in the guidelines. Case reports and series were included as there was paucity of references with level of evidence 1 and 2. Articles not available in English or only available in abstract forms were excluded. Relevant guidelines and standards from other national and international organisations were included in this review.

The literature search covered a period from January 1980 to April 2014. The abstracts of the list of articles obtained following the literature review were scanned to produce a list of articles relevant to the guideline. This was done by all members of the guideline group. Full texts of all these relevant articles were obtained with the help of the librarian. Members of the guideline group reviewed the full texts of the articles. The articles (Appendix 1: References) relevant to the guideline were graded for evidence level as below.

Keywords (Appendix 2)

The keywords were guided by questions using the PICOT format:

- **P**opulation to which the question applies
- **I**ntervention (e.g. or diagnostic test, exposure etc.) being considered in relation to this population
- **C**omparison(s) to be made between those receiving the intervention and those who do not receive the intervention
- **O**utcome(s) i.e. any effect caused by the intervention
- **T**imeframe (optional)

Grade of evidence and recommendation

The evidence from the full text articles was graded according to the Scottish intercollegiate Guideline Network [SIGN] grading system as follows (6):

Level of evidence	Definition
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of Bias
2++	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

The strength of recommendations in this guideline is based on the SIGN grading of evidence as follows (6)

A This recommendation is based on evidence rated as 1 + + or 1 + directly applicable to the target population and demonstrating overall consistency of results

B This recommendation is based on evidence rated as 2 + + or based on extrapolated evidence from studies rated as 1 + + or 1 + directly applicable to the target population and demonstrating overall consistency of results

C This recommendation is based on evidence rated as 2 + or based on extrapolated evidence from studies rated as 2 + + directly applicable to the target population and demonstrating overall consistency of results

D This recommendation is based on evidence rated as level 3 or 4 or based on extrapolated evidence from studies rated as 2 +

Guidelines for Good Practice

These guidelines apply to all permanent sensorineural hearing losses whether unilateral or bilateral, with or without additional symptoms. Age related hearing loss is the commonest cause of hearing loss in adults over the age of 50 (7). If additional or another aetiology is suspected then further aetiological investigations need to be arranged. However for adults less than the age of 50, investigations to determine aetiology is advised for all if the aetiology is not known or not been investigated before.

1) History: (8-23) Recommendation - D except Noise, Recommendation - B

Detailed history of:

- onset of symptoms, progression, fluctuation or changes with adverse events
- pregnancy, delivery and postnatal period if congenital hearing loss suspected
- symptoms of systemic or autoimmune disease eg: skin rash, unexplained fever, arthropathy, recurrent miscarriages, red and dry eyes
- any associated vestibular symptoms and/or tinnitus
- history of visual loss such as night blindness

History of exposure to risk factors e.g.

- noise (occupational, recreational or social)
- ototoxic medications/ radiation
- head injury/barotrauma
- outer and/or middle ear disease
- meningitis (bacterial or carcinomatous)
- bacterial and viral illness
- vascular risk factors (medical eg: diabetes, hypercholesterolaemia, hypertension; lifestyle eg: smoking)

Family history:

- hearing loss or risk factors associated with hearing loss in first and second degree relatives. Eg: pigmentary changes in skin, hair or eyes
- history of consanguinity and ethnic origin
- history of autoimmune disease/thyroid disease

2) Clinical Examination and Audiological Assessment: (11,24,25) Recommendation - D

- Ear examination in all individuals. Examination of the head and neck for dysmorphic features. Nose and throat examination if indicated.

- Examination of the skin for birthmarks and diseases of the skin

- Neurological, Vestibular and cardiovascular examination if indicated. Consider vestibular examination in cases of unilateral or asymmetrical hearing loss in order to decide whether imaging is required in borderline cases.

- Hearing loss confirmed by Pure tone Audiometry

- Consider Vestibular investigations where vestibular symptoms are present or if hearing loss is congenital profound or if hearing loss is due to meningitis. Also if syndromes especially known to be associated with vestibular defects are suspected (Usher, Jervel Lange Nielsen, Autoimmune inner ear disease).

- Consider Tympanometry, Speech Audiometry, OAEs, Stapedial reflexes and ABRs to determine site of loss if indicated.

3) Family audiograms: (26,27) Recommendation - D

It is also advisable for parents, children and siblings to have an audiogram if genetic aetiology is suspected or aetiology is not certain. Hearing loss in these audiograms could confirm a genetic aetiology or normal audiograms could suggest a de novo pathogenic mutation.

4) Ophthalmological assessment: (28,37) Recommendation - D

Assessment of visual acuity and fundoscopy if impairment is suspected. (The greater the hearing loss the greater the need to assess visual function to help with rehabilitation especially if there is a dual sensory impairment). Auditory neuropathy patients may also require visual evoked potentials to rule out optic neuropathy.

5) Investigations

a) Genetic tests: (29-37) Recommendation - C

Consent should be sought for the test, storage of the sample if further testing is required in the future and for anonymised research and for sharing the results with other family members and professionals. It should be explained, that genetic testing can take a long time. See guidelines for consent for genetic testing (38).

The following should be considered:

- GJB2 and GJB6 deletion analysis (Encoding Connexin 26 and Connexin 30): for all bilateral congenital or early onset non-syndromic sensorineural hearing loss

- SLC26A4 gene (encoding Pendrin): when imaging shows large vestibular aqueduct (LVA) and/or if there is a goitre

- m.1555A>G mutation: if there is a history of aminoglycoside exposure, progressive hearing loss, unexplained high frequency loss or family history of mitochondrial inheritance.

- OTOF gene (encoding Otoferlin) for Auditory Neuropathy Spectrum Disorder and EYA1, SIX1 and SIX6 gene (causing BOR) if there are bilateral preauricular ear pits.

 ***Further genetic testing*:**

Consider referral to Clinical Geneticist especially if

- a syndrome is suspected,
- patient has multiple system involvement or multiple anomalies
- opinion required on interpretation of genetic mutation testing
- after completion of investigations if a genetic disorder is diagnosed or suspected but no cause has been identified.

Note: More widespread genetic testing for hearing loss is now available with the advent of Next Generation (Massively Parallel) sequencing where large numbers of genes can be sequenced rapidly and cost-effectively. In the case of non-syndromic hearing loss many genes can be tested simultaneously, without regard to phenotype but this can make interpretation of multiple novel or rare genetic variants more difficult initially. Guidelines for further genetic testing are likely to evolve over the next few years. Testing for syndromic forms of hearing loss is also more widely available.

b) MRI of internal auditory meatus and/or CT Scan of petrous temporal bone: (39-43) Recommendation - C

Consider MRI for asymmetrical hearing loss, symmetrical fluctuating, sudden or rapidly progressive hearing loss at a rate that would be quicker than expected due to ageing, persistent unilateral tinnitus (longer than 6 months) or to check for inner ear malformations if congenital loss is suspected with no previous imaging.

MRI IAMs is the preferred modality of imaging for sensorineural hearing loss. However if MRI is not possible, consider a CT scan +/- contrast. CT scan is primarily indicated for studying middle ear and labyrinthine integrity.

Both MRI and CT should be done in all post-meningitic (bacterial) hearing loss as urgent cochlear implantation may be necessary before cochlear ossification occurs.

c) Renal ultrasound: (32,33,44) Recommendation - D

 If patient has pre-auricular pits or sinuses, deformity of ear, branchial cleft or cysts

 Mondini defect or LVA on imaging

 If there is a possible congenital conductive component not previously identified

d) Haematology, Biochemistry and Immunology: (13,21,22,24,32,33,45-50) Recommendation - D

Consider the following:

Thyroid Function tests :

 if there is family history of thyroid disease

 if clinical symptoms or signs of thyroid disease like goitre present

 if there is LVA or Mondini deformity of cochlea

Full Blood Count, Glucose, Lipid Profile, Urea and Electrolytes:

- If vascular/renal risk factors prominent in history.

Autoimmune tests:

- if there is systemic involvement like fever, joint symptoms, skin rash, ocular inflammation, cutaneous lesions, polymyalgia, maturity onset asthma or persistent upper airway symptoms.
- if there is unexplained hematuria including microscopic hematuria, recurrent miscarriage or pulmonary infiltrates
- if there is unexplained progressive hearing loss

Consider the following autoimmune tests

ANA, ANCA, AECA, Antiphospholipid, Anticardiolipin, Rheumatoid factor, Antithyroid antibodies, Anti Ds DNA and others as required. Anti 30, 42 and 68kDa antibody if possible.

e) Metabolic/Serological Screen on blood and urine: **(51- 57)**
Recommendation - D except HIV: Recommendation - B

- Syphilis serology if suspected or cause remains unknown (Recommendation D)
- Other tests where clinically indicated such as screening for Borrelia, toxoplasmosis or metabolic disorders other than Diabetes/Thyroid disease (Recommendation D).
- HIV serology if suspected or cause remains unknown (Recommendation B)

f) ECG: (58,59) Recommendation - D

- ECG for QTc-interval if hearing loss is congenital and profound with associated balance problems and/or syncopal episodes (Refer also to BAAP guidelines for investigation of hearing loss in children)

Appendix 1- References

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Appendix 2- Keywords and Audit Measures

The following keywords were used for the literature searches:

aetiological test/aetiology	Alport syndrome	autoimmune/immunological
blood test	biochemistry	BOR
Cardiovascular disease	chromosomal analysis	clinical examination
diabeties	smoking	head injury
ECG/electrocardiogram	kidney disease	full blood count
genetic /hereditary	Borrelia	haematology
herpes	history	HIV/Human Immunodeficiency Virus
Hyperlipidemia	Jervell Lange Nielsen syndrome/long QT	kidney /renal function/U & E/urea electrolytes
kidney /renal ultrasound	liver function	measles
meningitis	trauma	ototoxicity/ototoxic drug
metabolic screen	mitochondrial mutation	MRI
mumps	anaemia	hypertension
ophthalmology/eye	QTc interval	Otoferlin
permanent conductive hearing loss	Pendred syndrome /Pendrin	parent/sibling/family audiogram
Rubella	Sensorineural hearing loss	Serology
syndrome	syphilis	thyroid function test
thyroid disease	connexin/GJB	CT
toxoplasma	Usher	varicella
vestibular	Infections	Vascular

Proforma of the BAAP national audit can be used to benchmark practice

Appendix 3 – Abbreviations

ABR	Auditory Brainstem Response
AECA	Anti endothelial Cell antibody
ANA	Antinuclear antibody
ANCA	Anti neutrophil cytoplasmic antibody
BAAP	British Association of Audiovestibular Physicians
BOR	Branchio oto renal syndrome
CT	Computed tomography
Ds DNA	Double stranded DNA
ECG	Electrocardiogram
HIV	Human Immunodeficiency Virus
IAM	Internal Auditory Meatus
LVA	Large Vestibular Aqueduct
MRI	Magnetic resonance imaging
OAE	Oto Acoustic Emissions
RCT	Randomised Controlled Trial

Appendix 4- Future Research

The evidence to support aetiological investigations is thin. Areas of research that could help to support evidence include

1. Yield of aetiological battery and individual aetiological tests with various degrees and types of hearing loss like severe to profound/moderate/mild/unilateral loss.

2. Yield of history and clinical examination using a prospective study

3. Systematic review of studies on aetiological investigations

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