NHS England

Evidence Review:

Auditory brainstem implantation for prelingual profoundly deaf children.

June 2015

NHS England

Evidence Review:
Auditory brainstem implantation for prelingual profoundly deaf children.

First published: June 2015

Updated: (only if this is applicable)

Prepared by [Insert CRG name]

Contents

1. Introduction

The majority of profoundly deaf people will be suitable for auditory rehabilitation with a cochlear implant (CI). The device works by means of an electrode array surgically implanted into the cochlea that then electrically stimulates the cochlear nerve directly as it enters the cochlea. This process relies on two essential criteria: it must be possible to surgically implant the electrode array into the cochlea in order to bring it into contact with the cochlear nerve and the nerve itself must be functionally intact. For this reason there are both absolute and relative contraindications to CI. Congenital causes include dysplasia of the cochlear nerve (cochlear nerve deficiency (CND)) and severe cochlear malformations. Acquired causes include injury or scarring to the cochlea or nerve from meningitis, severe inflammatory conditions, trauma or tumours.

An auditory brainstem implant (ABI) is a device that is identical to a CI except that the stimulating electrode array is designed to be surgically implanted on to the surface of the brainstem to provide direct electrical stimulation of the cochlear nucleus and subsequent central auditory pathways. A microphone and sound processor unit worn on the side of the head transmits to the internal receiver-stimulator package in exactly the same way as with a CI. The resulting electrical stimulation of the cochlear nucleus may provide auditory sensation but does not restore normal hearing. The ABI is the only option for auditory rehabilitation when a profoundly deaf person cannot benefit from a CI in either ear for the reasons described above.

Evidence from cochlear implantation has demonstrated that a person with profound prelingual deafness can only benefit from auditory rehabilitation within the first years of life. Auditory plasticity, the ability of the brain to make sense of sound, is gradually lost if no auditory sensation takes place.

Expertise is required to insert the ABI, to tune it electronically after insertion, and to train the patient (and family) in its use. It is expected that only experienced centres will achieve good results.

The commonest indication for an ABI is tumours secondary to neurofibromatosis type 2 (NF2). These tumours develop gradually so patients are always postlingually deafened, the earliest the ABI is likely to be required being about 12 years of age. Other acquired causes leading to postlingual deafness are very rare. The second commonest indication is in young children with either congenital causes or meningitis leading to prelingual deafness. The assessment process and outcomes are different in this situation than with postlingual deafness. This evidence review is therefore restricted to ABI indications which result in prelingual profound deafness only.

It has been estimated that 2/100 000 population or 2% of prelingual profoundly deaf children may be a candidate for an ABI[13]. The fact that to date (June 2015) only 10 prelingually deafened children from the UK have received an ABI demonstrates that many parents choose not to undergo this option. It is estimated that the need is one or two patients per annum from England.

2. Research Questions

The research question is the effectiveness and cost-effectiveness of ABI in non NF2 patients.

Population: Prelingual profoundly deaf children unable to gain adequate benefit from conventional well-fitted hearing aids or cochlear implants due to damage to or congenital abnormalities of the auditory nerves or the cochlea, treated in the recent era (since 2000).

Intervention: auditory brainstem implant

Comparator: conventional standard of care

Outcome: quality of life, long term hearing outcome, adverse events in patients.

3. Methodology

A Medline search was undertaken using the following query dated 4th June 2015:

auditory brainstem implant* [tiab]

OR

ABI [tiab]) AND (deaf/ OR deaf [tiab] OR hearing impairment/ OR hearing loss/)

OR

Auditory brain stem implantation [mh]

OR

Auditory brain stem implants [mh]

This produced 301 articles which were then examined by title and abstract. Articles were only further included if they contained details of paediatric patients receiving an ABI. This produced 30 articles. These articles were examined in full. Review of the introduction, discussion and references of these did not produce any further articles of relevance. Articles were then only included if they had clear details of prelingual deaf patients having an ABI with results of either adverse surgical events or

postoperative outcomes. Reviews and diagnostic articles were excluded. Multiple articles from the same centre were excluded unless they provided different information. This produced 12 articles which are detailed below in Table 1.

Table1: Scottish Intercollegiate Guideline Network (SIGN) levels of evidence

Level of evidence	Type of evidence
1++	High quality meta-analyses, systematic reviews of RCTs (including cluster RCTs), or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–*	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of, or individual high quality non-randomised intervention studies (controlled non-randomised trial, controlled before-and-after, interrupted time series), comparative cohort and correlation studies with a very low risk of confounding, bias or chance
2+	Well conducted, non-randomised intervention studies (controlled non-randomised trial, controlled before-and-after, interrupted time series), comparative cohort and correlation studies with a low risk of confounding, bias or chance
2–*	Non-randomised intervention studies (controlled non-randomised trial, controlled before-and-after, interrupted time series), comparative cohort and correlation studies with a high risk of confounding, bias or chance
3	Non-analytical studies (eg case reports, case series)
4	Expert opinion, formal consensus
*Studies with a level of evidence (–) should not be used as basis for making recommendations. *Source*: adapted from SIGN (2001).	

Table 2: Scottish Intercollegiate Guideline Network (SIGN) Grades of Evidence

Grades of recommendations
Grade 'A'   At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population ***or***   A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results.
Grade 'B'   A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results ***or***   Extrapolated evidence from studies rated as 1++ or 1+
Grade 'C'   A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results ***or***   Extrapolated evidence from studies rated as 2++
Grade 'D'   Evidence level 3 or 4 ***or***   Extrapolated evidence from studies rated as 2+

Source: Adapted from the Scottish Intercollegiate Guidelines Network (SIGN), 2001

4. Results

There was only one controlled study that compared auditory outcomes of ABI with CI in children with cochlear nerve deficiency (CND)[5]. This centre (Verona, Italy) has far more experience than any other centre with paediatric ABI. The study demonstrated much improved hearing with an ABI in a subgroup of children who had normal cognition, concluding the ABI should be the first choice for auditory rehabilitation in children with CND. There is a significant possibility of bias in this study as the populations were small and no detail was provided for why children were selected for CI. CND is a heterogenous diagnosis where some children may benefit from CI but most will not and the selection process is critical in recognizing the small proportion who might obtain reasonable outcomes. For this reason this study has been graded as "2-"; it is not possible at present to say that ABI should be the first line treatment for CND prior to CI.

Other studies are case series or reports. The larger of these have been graded as "2++" as, assuming children are only considered for ABI after CI has been excluded as a possible option, then the only comparator is for no audition at all.

The centre in Verona have also published their overall results with ABI in 59 prelingually deaf children[3], including follow up up to 12 years. The results have been independently verified by an international expert from the United States so the level of potential bias is very low. This paper demonstrated outcomes were variable although all children gained some audition. Only univariate analysis was carried out but this demonstrated a highly significant predictive effect of associated cognitive disorders on auditory outcome. Age appeared to have a significant effect but it must be noted that the children with cognitive disorders were older than those with normal cognition. Likewise diagnostic category appeared to have an effect but categories either had very small numbers or included those children with cognitive disorders while others did not. Overall 90% of children with normal cognition were able to recognize environmental sounds, 62% gained speech understanding of common phrases without lip reading and 21% could use the telephone with a familiar speaker.

All the other series combined accounted for 46 prelingually deafened children receiving an ABI[1,2,4,6,7,8,10,12]. Follow up was less than 4 years in all studies, the majority less than 2 years, so only short term outcomes could be assessed. These studies reported higher rates of children gaining no benefit from the ABI (7 of 46 children). Most centres reported very few children achieving any speech discrimination. The main exception was Sennoroglu et al[12] who described 36% gained speech understanding of common phrases without lip reading and 18% could use the telephone with a familiar speaker after 15 months of follow up.

Various studies reported surgical outcomes with adverse events occurring in 18 of 71 children[1,4,6,7,9,10,11,12]. One child suffered an intracerebellar bleed that required return to theatre and an extended stay in intensive care. This child recovered fully. One child suffered meningitis 2 years after the surgery. It is not clear whether the ABI was directly related to this as children with congenital inner ear malformations have a higher risk of meningitis anyway. One child had temporary swallowing and voice difficulties that did not require treatment. One child had a postoperative seizure. Six children had cerebrospinal fluid (CSF) leaks that required reoperation and one child had a CSF leak that was managed with a lumbar drain. Six children

had subcutaneous CSF collections that resolved without further treatment. One child had a minor wound infection that required antibiotics.

The effect of ABI on quality of life or long-term educational achievements was not reported in any paper. No papers reported cost effectiveness.

Table 3

Clinical Effectiveness and / or safety					
Level of Evidence	**Study design & Intervention**	**Outcome measure(s)**	**Results**	**Reference**	**Comments**
3	Design: Case report Intervention: ABI	Adverse events Auditory perception	No adverse events. Environmental awareness at 3 months follow up.	1	Feasability study that is part of the on-going FDA approved study into use of ABI in prelingual deafness.
3	Design: Case series 5 children Intervention: ABI	Auditory perception	4 out of 5 gained environmental awareness	2	Study mainly looking at use of cortical evoked potentials to aid programming. Short follow up.
2++	Study design: Case series of 59 children (excluding 5 postlingually deafened older children). Up to 12 years of follow up. Differentiation between those with cognitive disorders and those with normal cognition. Intervention: ABI	Auditory perception	All children had auditory sensation. Children with cognitive disorders: 9/30 (30%)able to recognize environmental sounds 1/30 (3%)achieved basic speech discrimination Children with normal cognition (all aged <5 years at implantation): 26/29 (90%) able to recognize environmental sounds 18/29 (62%) achieved basic speech discrimination 6/29 (21%) could use the telephone with a familiar speaker	3	Currently by far the largest series and with the longest follow up. The results have been independently ratified by an international expert.

Clinical Effectiveness and / or safety					
Level of Evidence	**Study design & Intervention**	**Outcome measure(s)**	**Results**	**Reference**	**Comments**
3	Design: Case series 4 children Intervention: ABI	Adverse events Auditory perception	2 children had subcutaneous cerebrospinal fluid (CSF) collection – no treatment required. 1 no auditory perception 1 Environmental awareness only 2 children able to recognize environmental sounds	4	
2-	Design: Non-randomised case control study comparing 20 age matched children with prelingual deafness secondary to cochlear nerve deficiency in each group. Intervention: ABI or CI	Auditory perception	2/20 children with CI gained environmental sound recognition. No child with a CI obtained any speech perception. Children with an ABI and normal cognition and normal cochlea all obtained speech discrimination.	5	This study is included, despite the ABI population being part of reference 3 detailed above, as it gives a comparator with CI results. Results with CI in CND are very dependent on the nerve anatomy and function so there is a great potential for bias in this study depending on how they selected these children.
2++	Design: Case series 12 children Intervention: ABI	Adverse events Auditory perception	4/12 had CSF leaks that required reoperation 5/12 no auditory perception. 3/12 environmental awareness only 2/12 able to recognize environmental sounds 1/12 basic speech discrimination Top 3 users all had no cognitive problems.	6	

Clinical Effectiveness and / or safety					
Level of Evidence	**Study design & Intervention**	**Outcome measure(s)**	**Results**	**Reference**	**Comments**
3	Design: Case series of children with cochlear aplasia: 4 had CI and 1 had ABI. Intervention: ABI and CI	Adverse events Auditory perception	No adverse events Child with ABI obtained minimal speech discrimination. Children with CI gained: 2/4 minimal speech discrimination. 1/4 basic speech discrimination 1/4 could use the telephone with a familiar speaker	7	This study demonstrated that CI function may be possible even if the cochlea appears to be absent as the vestibule may contain auditory fibres.
3	Design: Case series 4 children Intervention: ABI	Auditory perception	3/4 environmental awareness only 1/4 basic speech discrimination	8	
3	Design: Case series 3 children Intervention: ABI	Adverse events	No adverse events	9	

Clinical Effectiveness and / or safety					
Level of Evidence	**Study design & Intervention**	**Outcome measure(s)**	**Results**	**Reference**	**Comments**
3	Design: Case series 8 prelingually deafened patients (excluding 3 who were postlingually deafened) including 3 who were aged 6, 9 and 18 years at implantation Intervention: ABI	Adverse events Auditory perception	2 CSF leaks: 1 required reoperation and 1 managed conservatively with lumbar drain. 1 postoperative seizure. All had some audition but 2 had less than 3 months follow up. 1 child < 3yrs age with normal cognition had gained minimal speech discrimination after 15 months follow up. 2 children with cognitive disorders achieved environmental awareness and discrimination respectively. Children aged 6 and 9 years at implantation gained minimal speech discrimination. Patient aged 18 year at implantation gained environmental discrimination.	10	
2++	Design: Case series 31 children (some older); mean age 6 years. Intervention: ABI	Adverse events	1 had intracerebellar bleed requiring return to theatre but had full recovery. 1 had meningitis after 2 years: unclear whether this was directly related to ABI as congenital inner ear malformations can also predispose to meningitis. No CSF leaks but 4 had CSF subcutaneous collection requiring no treatment. 1 minor wound infection treated with antibiotics. 1 had temporary swallowing difficulties and dysphonia.	11	Paper also reviewed literature for complications of microvascular decompression, a very similar operation performed on adults and estimated complication rates were likely to be similar: 1% chance of cerebellar damage from stroke or bleeding; 1% chance of meningitis

Clinical Effectiveness and / or safety					
Level of Evidence	**Study design & Intervention**	**Outcome measure(s)**	**Results**	**Reference**	**Comments**
2++	Design: Case series 11 children Intervention: ABI	Adverse events Auditory perception	1 CSF leak required reoperation 5/11 environmental awareness only 2/11 able to recognize environmental sounds 2/11 achieved basic speech discrimination 2/11 could use the telephone with a familiar speaker	12	

Table 4

Cost-effectiveness					
Level of Evidence	**Study design & Intervention**	**Outcome measure(s)**	**Results**	**Reference**	**Comments**
	No studies identified				

5. Summary of Evidence

The published evidence consists of one controlled study (with a high risk of bias and therefore no recommendation is given for this paper) and case series. The larger of these series (those with more than 10 children) have been graded as 2++ as the only comparator for auditory outcomes is inevitably no hearing. The recommendations are therefore Grade B.

No review was conducted regarding ABI candidacy. It is assumed that expert Cochlear Implant centres will assess the child's suitability for cochlear implantation and only refer for an ABI if the child is deemed unsuitable or has been implanted and not gained benefit.

The ABI is able to provide significant auditory benefit in some children including speech understanding without lip reading. It is likely that others will gain either very little or no benefit. Children with significant cognitive disorders seem to gain no more than environmental sound recognition. Although it is likely that auditory plasticity (ie. the age at implantation) will have a significant effect, the maximum age at implantation was not clear from the evidence. Extrapolation from cochlear implant evidence would suggest that the earlier a child is implanted, the more likely they are to benefit and that children should not be implanted over the age of 5 years if they have had no hearing.

The procedure has a risk profile that seems similar to other skull base procedures such as microvascular decompression surgery. This includes a 1-2% risk of intracranial bleeding, stroke or meningitis, a 1-2% risk to surrounding cranial nerves (particularly the facial, glossopharyngeal and vagal) and a 10-15% risk of CSF leak (of whom half may require reoperation). Long term adverse events, in particular those of revision surgery to replace a failed ABI, cannot be assessed.

No paper reported on bilateral ABI implantation.

No papers were identified evaluating cost effectiveness.

References

1. Puram SV, Tward AD, Jung DH, Dilger AE, Herrmann BS, Duhaime AC, Barker FG 2nd, Lee DJ. Auditory brainstem implantation in a 16-month-old boy with cochlear hypoplasia. Otol Neurotol. 2015 Apr;36(4):618-24.
2. He S, Teagle HF, Ewend M, Henderson L, Buchman CA. The electrically evoked cortical auditory event-related potential in children with auditory brainstem implants. Ear Hear. 2015 May-Jun;36(3):377-9.
3. Colletti L, Shannon RV, Colletti V. The development of auditory perception in children after auditory brainstem implantation. Audiol Neurootol. 2014;19(6):386-94.
4. Siegbahn M, Lundin K, Olsson GB, Stillesjö F, Kinnefors A, Rask-Andersen H, Nyberg G. Auditory brainstem implants (ABIs)--20 years of clinical experience in Uppsala, Sweden. Acta Otolaryngol. 2014 Oct;134(10):1052-
5. Colletti L, Colletti G, Mandalà M, Colletti V. The Therapeutic Dilemma of Cochlear Nerve Deficiency: Cochlear or Brainstem Implantation?Otolaryngol Head Neck Surg. 2014 Apr 23;151(2):308-314.
6. Bayazit YA, Kosaner J, Cinar BC, Atac A, Tutar H, Gunduz B, Altinyay S, Gokdogan C, Ant A, Ozdek A, Goksu N. Methods and preliminary outcomes of pediatric auditory brainstem implantation. Ann Otol Rhinol Laryngol. 2014 Aug;123(8):529-36.
7. Goffi-Gomez MV, Magalhães AT, Brito Neto R, Tsuji RK, Gomes Mde Q, Bento RF. Auditory brainstem implant outcomes and MAP parameters: report of experiences in adults and children. Int J Pediatr Otorhinolaryngol. 2012 Feb;76(2):257-64.
8. Bento RF, Monteiro TA, Tsuji RK, Gomez MQ, Hausen Pinna M, Goffi-Gomez MV, Brito R. Retrolabyrinthine approach for surgical placement of auditory brainstem implants in children.Acta Otolaryngol. 2012 May;132(5):462-6.
9. Choi JY, Song MH, Jeon JH, Lee WS, Chang JW. Early surgical results of auditory brainstem implantation in nontumor patients.Laryngoscope. 2011 Dec;121(12):2610-8.
10. 8 children: All some audition; 2 children only 1 month FU; 1 child <3 years age cognition OK – CAP 4 after 15/12; 2 children poor cognition – CAP 1 and 3 after 24/12; 18yrs age – CAP 3; 9 yrs age – CAP 4; 6 yrs age – CAP 4.
11. Colletti V, Shannon RV, Carner M, Veronese S, Colletti L. Complications in auditory brainstem implant surgery in adults and children. Otol Neurotol. 2010 Jun;31(4):558-64.
12. Sennaroglu L, Ziyal I, Atas A, Sennaroglu G, Yucel E, Sevinc S, Ekin MC, Sarac S, Atay G, Ozgen B, Ozcan OE, Belgin E, Colletti V, Turan E. Preliminary results of auditory brainstem implantation in prelingually deaf children with inner ear malformations including severe stenosis of the cochlear aperture and aplasia of the cochlear nerve. Otol Neurotol. 2009 Sep;30(6):708-15.

13. Kaplan AB, Kozin ED, Puram SV, Owoc MS, Shah PV, Hight AE, Sethi RK, Remenschneider AK, Lee DJ. Auditory brainstem implant candidacy in the United States in children 0-17 years old. Int J Pediatr Otorhinolaryngol. 2015 Mar;79(3):310-5.

Appendices
Appendix 1 - Search strategy

Question(s)

Identify all aspects of the topic that need to be explored in order to develop a policy

- Is the intervention in tariff?
- Is it, or can it be, adequately covered by the appropriate detail in the service specification?
- Is it very low volume or does it have a low number of requests, such as less than 10 per year? If it is low volume then it may not merit a clinical commissioning policy or may be deferred to the next round of policy reviews.
- Does it appear too difficult to establish an evidence base or find suitable evidence to support a new clinical commissioning policy? If there is such limited evidence that it will not be possible to answer the review question then it will not be possible to generate a clinical commissioning policy.
- Is it a clinical area included within the scope? If not, then a clinical commissioning policy may not be suitable for this

Search strategy *Indicate all terms used in the search*

P – Patients / Population Which patients or populations of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?	Prelingual or perilingual profoundly deaf children unable to benefit from hearing aids or cochlear implants. Subgroups: • Cochlear nerve deficiency (agenesis / hypoplasia / aplasia) • Cochlear dysplasia / inner ear malformation • Cochlear obliteration (meningitis / trauma)
I – Intervention Which intervention, treatment or approach should be used?	ABI
C – Comparison What is/are the main alternative/s to compare with the intervention being considered?	Cochlear implantation Sign language and lip reading.
O – Outcomes What is really important for the patient? Which outcomes should be considered? Examples include intermediate or short-term outcomes; mortality; morbidity and quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission; return to work, physical and social functioning, resource use.	*Critical to decision-making:* Non-auditory outcomes: • Mortality rates. • Morbidity rates including intracranial complications (stroke, meningitis and bleeding), nerve damage (facial palsy and voice and swallowing problems), CSF leak and device infection. • Proportion of users.

	• Quality of life measures. Auditory outcomes: • category of auditory performance. • speech intelligibility rating, • language development. • educational placements/attainment • communication strategies. *Important to decision-making:*
Assumptions / limits applied to search English language	

Appendix 2- Version Control Sheet

Version	Section/Para/Appendix	Version/Description of Amendments	Date	Author/Amended by
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				