NICE advice

CerebAir for continuous EEG monitoring in intensive care

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Summary

- The **technology** described in this briefing is CerebAir. It is used for continuous electroencephalogram (EEG) monitoring of people who are critically ill in intensive care.
- The **innovative aspects** are that it is a wireless headset with pre-positioned electrodes, which is designed to be quicker and easier to apply than conventional continuous EEG. Specialist training is not needed to apply the headset and data can be reviewed by neurophysiologists remotely.
- The intended **place in the clinical pathway** would be as an alternative to conventional continuous EEG in people who are critically ill in intensive care.

- The **main points from the evidence** summarised in this briefing are from 3 studies (1 retrospective and 2 prospective single-centre observational studies) including 157 adults in intensive care. They show that CerebAir is quicker to apply than conventional EEG and has good sensitivity and specificity for detecting abnormal EEG activity. Skin redness may happen with longer monitoring periods (over 15 hours) but is likely to resolve without needing medical treatment.
- **Key uncertainties** around the evidence or technology are that all studies had small sample sizes and no study examined the effect on clinical outcomes or treatment decision making.
- **Experts advised** that the technology has potential to decrease time to diagnosis, prognosis, and treatment, and reduce secondary brain injuries. However, using CerebAir may increase the number of continuous EEG recordings being made and the time demands on neurophysiologists to interpret the data. The device may cause minor local skin injury and it is unclear if the device can be used on people after surgery on the skull.
- The **cost** of purchasing CerebAir is £20,000 to £30,000 depending on the hardware configuration. There are additional consumable costs for the pre-gelled electrodes that cost £89 per use. The cost of purchasing a standard portable EEG machine (including laptop, associated software and video camera) is estimated to be between £10,000 and £20,000. These costs do not include the cost of EEG interpretation. All costs exclude VAT.

The technology

CerebAir (Nihon Kohden) is a wireless headset for continuous electroencephalography (EEG) monitoring of people who are critically ill in intensive care. It is a telemetry EEG amplifier comprising of 8 pre-gelled disposable electrodes pre-positioned on an adjustable headset. The EEG data recorded using the device is sent by Bluetooth to a local storage device (PC or other) and can be viewed remotely by a specialist within the hospital or offsite (depending on IT policy).

Innovations

The pre-positioned EEG electrodes are designed to improve speed and ease of electrode placement compared with conventional 10–20 EEG systems. It is also designed to remove

the need for specialist training in EEG electrode placement. Data is transmitted wirelessly and can be viewed remotely so the patient does not have cables surrounding them. The company states that CerebAir's ease of application and wireless data transmission can help decrease time to diagnosis and decision support for people who are critically ill.

Current care pathway

In intensive care units, EEG can be used to diagnose status epilepticus and suspected ongoing seizures, and to assess brain function in people with unexplained and persistent unconsciousness. A standard EEG is a 20- to 30-minute EEG recording. It consists of 21 electrodes that are attached to the person's scalp and connected by wires to an EEG recording machine. Some EEGs use caps or nets to hold the electrodes. Electrode locations and names follow the International 10–20 system. An EEG is usually done by a clinical neurophysiologist. When continuous EEG monitoring is used it most commonly consists of 4 to 8 electrodes and not the full 10–20 configuration. One of the experts noted that episodic EEG recordings are widely used in the NHS but not universally available, and that access to neurophysiology services across the UK can differ depending on the region. They also said that access to continuous EEG is more limited than access to standard 20- to 30-minute EEG recordings.

The following publications have been identified as relevant to this care pathway:

- European Society of Intensive Medicine consensus statement on the use of EEG monitoring in critically ill patients (2013). The consensus recommends EEG in generalised convulsive status epilepticus and to rule out nonconvulsive seizures for people with brain injuries and people who are in a coma in intensive care without primary brain injury who have unexplained and persistent altered consciousness.
- The Critical Care Continuous EEG Task Force of the American Clinical Neurophysiology Society consensus statement on continuous EEG in critically ill adults and children (2015). It recommends critical care continuous EEG for diagnosing nonconvulsive seizures, nonconvulsive status epilepticus and other paroxysmal events, and for assessing the efficacy of therapy for seizures and status epilepticus. It also recommends considering critical care continuous EEG for identifying ischemia in people at high risk of cerebral ischemia; for assessing the level of consciousness in people having intravenous sedation or pharmacologically induced coma; and for prognosis in people after cardiac arrest.

- The Neurocritical Care Society and the European Society of Intensive Care Medicine consensus recommendations on multimodality monitoring in neurocritical care (2014). It suggests continuous EEG monitoring as the preferred method over routine EEG monitoring whenever feasible for people in a coma in intensive care without an acute primary brain condition and with unexplained impairment of mental status or unexplained neurological deficits to exclude nonconvulsive seizures.
- Kubota et al. (2018) Continuous EEG monitoring in ICU. A review article on continuous EEG monitoring in intensive care.

Population, setting and intended user

According to Egawa et al. (2020), nonconvulsive status epilepticus (NCSE) occurs in 8% to 20% of people in intensive care. People diagnosed with seizures in intensive care are more likely to have worse outcomes such as increased mortality and longer length of hospital stay. More than half of people diagnosed with nonconvulsive seizures (NCS) and NCSE in intensive care will go on to experience recurrent seizures after being discharged from hospital (Punia et al. 2015). Because of the high morbidity and mortality associated with NCS and NCSE, timely diagnostic testing and treating the underlying cause is important.

The device is intended to detect abnormal EEG patterns and seizure activity in people admitted to intensive care with suspected or known seizure activity, traumatic injury, altered or fluctuating consciousness, or post-cardiac arrest. EEG monitoring with CerebAir would be done by the emergency or intensive care team. Data can be reviewed remotely by a neurophysiologist and locally in intensive care. The company states that the technology could also be used in operating theatres but using it in this setting is not the focus of this briefing.

Costs

Technology costs

Purchasing the CerebAir system costs between £20,000 and £30,000 depending on the hardware configuration (for example, laptop or touchscreen monitor). The company states that an installation fee is included in the costs. The system also has consumable costs for the pre-gelled electrodes which are £89 per use. All costs exclude VAT. The technology comes with a 2-year warranty, and the cost of any software updates are covered by the

company. The company states that the expected lifespan of the device is between 7 and 10 years. The costs described for CerebAir do not include the cost of interpreting EEG recordings.

Costs of standard care

The cost per person for conventional EEG monitoring is £219 (NHS reference costs 2019/20, HRG AA33C). Conventional EEG monitoring refers to a standard 20- to 30-minute 10–20 EEG done in an inpatient or outpatient setting. This includes electrode consumables or cleaning, as well as a neurophysiologist's time to get the EEG recording, interpret data and write a report. One of the experts who commented on the briefing noted that there is currently no NHS reference cost for continuous EEG. They estimate that the capital costs of a standard portable 10–20 EEG, laptop and associated software and video camera are between £10,000 and £20,000.

Resource consequences

The company states that CerebAir is currently being used in 4 NHS centres. The technology costs more than standard care but could be resource releasing if adopting the technology leads to shorter hospital stays and improved outcomes for patients through a quicker diagnosis and treatment. The technology may free up neurophysiologists' time because specialist training on electrode placement is not needed to apply the headset. But expert advice is that CerebAir will lead to more continuous EEG recordings being done and will place increased time demands on neurophysiologists who will need to interpret the data. One expert who commented on the briefing also said that some NHS sites may need additional local storage for data. Evidence shows the CerebAir monitoring is quicker to start than conventional EEG but its effect on treatment decisions, clinical outcomes and length of hospital stay has not been explored. The company states that product specific training is included in the purchase price and covers how to apply the headset and how to use the software.

Regulatory information

CerebAir is a CE-marked class IIa medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

No equality issues or considerations were identified.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Three studies were identified by the literature search and are summarised in this briefing. They include a total of 157 people admitted to intensive care, 137 of whom had monitoring with CerebAir.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The evidence base is limited and mainly comes from single-centre observational studies that involve a relatively small number of people. The studies mainly assessed the feasibility of using the technology in an acute setting and its diagnostic accuracy compared with routine electroencephalogram (EEG) only. None of the studies reported about changes in clinical management because of CerebAir monitoring. Two of the 3 studies were prospective in design. None of the studies were done in the UK.

Overall, the evidence base suggests that CerebAir is faster to position than standard EEG techniques and is likely to be feasible in an acute setting. However, clinical expert advice

was that the reduction in the time to apply CerebAir as shown in Caricato et al. (2020) is unlikely to be clinically significant. The technology appears to be reliable in detecting abnormal EEG patterns, with Egawa et al. (2020) reporting a sensitivity and specificity for detecting abnormal EEG patterns of 0.974 and 0.909, respectively. Caricato et al. (2020) reported that more people having monitoring with CerebAir experienced skin redness. No adverse reactions were observed by Egawa et al. (2020) and the remaining study did not report this outcome.

There is limited evidence on CerebAir for continuous EEG monitoring. The evidence base would benefit from further prospective evidence including a larger cohort of patients, ideally done in the UK. Also, future studies evaluating the impact of using the technology on patient outcomes and changes in clinical management would be useful.

Caricato et al. (2020)

Study size, design and location

Single-centre prospective observational study of 40 people with critically neurological illness admitted to either neurointensive care (20 people; study group) or general intensive care (20 people; control group) in Italy.

Intervention and comparator

CerebAir compared with conventional simplified EEG (8-electrodes-EEG positioned by an EEG technician).

Key outcomes

The time needed to apply electrodes was shorter with CerebAir than with the control (6.2 minutes compared with 10.4 minutes, $p<0.001$). Length of monitoring was shorter with CerebAir (57 hours compared with 75 hours, $p<0.001$) but was longer than 24 hours in 43% of people (n=13). CerebAir needed more interventions per person to correct artifacts and get good quality EEG recordings (1.7 compared with 0.5, $p<0.001$). A total of 35 interventions (4 electrode replacements and 31 gel or paste applications) were needed with CerebAir compared with 11 interventions (3 electrode replacements and 8 gel or paste applications) with the control. EEG abnormalities were detected in 14 people in the CerebAir (7 people with epilepsy and 7 without) and control group (5 people with epilepsy and 9 without). EEG recordings led to antiseizure medicines in 10 people in the CerebAir

group compared with 7 cases in the control group. Seventeen people in the CerebAir group experienced skin redness because of pressure lesions. Lesions appeared after a mean time of 15 hours and resolved without further intervention. In 4 people, EEG monitoring was stopped because of more severe pressure lesions. This happened after a mean time of 52 hours.

Strengths and limitations

Study groups were similar in terms of age, gender, diagnosis, length of intensive care stay and likelihood of recovery.

The sample size was small, and the 2 groups were also treated on different intensive care wards (neuro and general). The study was not powered to show differences in detected EEG abnormalities between the 2 groups. No conclusions can be drawn about the accuracy of the technology for seizure diagnosis compared with conventional EEG. The study was done in Italy and may limit the generalisability to the NHS. One of the authors is an associate editor of the journal. The EEG recordings were reviewed by an expert neurologist and not at the bedside by an intensivist.

Egawa et al. (2020)

Study size, design and location

Single-centre prospective observational study of 65 people with altered mental state admitted to neurointensive care between January and December 2017 in Japan.

Intervention and comparator

AE-120A EEG Headset (CerebAir) compared with conventional continuous EEG monitoring, both with a video camera monitoring.

Key outcomes

Of the 65 people who were monitored with CerebAir, 50 (76.9%) were included in the final analyses (median age of 72 years; 66% were male). The sensitivity and specificity of CerebAir for detecting abnormal EEG patterns were 0.974 (95% confidence interval [CI] 0.865 to 0.999) and 0.909 (95% CI 0.587 to 0.998), respectively. The sensitivity and specificity of CerebAir for detecting periodic discharges were 0.824 (95% CI 0.566 to

0.926) and 0.970 (95% CI 0.842 to 0.999), respectively. Thirteen people (26%) were diagnosed with nonconvulsive status epilepticus (NCSE) using CerebAir, and the technology could detect NCSE with a sensitivity and specificity of 0.706 (95% CI 0.440 to 0.897) and 0.970 (95% CI 0.842 to 0.999), respectively. The median time to start monitoring with CerebAir was 57 minutes (ranging from 5 to 142 minutes). No adverse reactions were seen.

Strengths and limitations

EEG recordings were interpreted by 1 neurointensivist as well as a board-certified neurophysiologist.

The study included a relatively small number of people. It was done prospectively at a single centre but retrospectively analysed, which may have introduced potential selection bias. Interventions were not used simultaneously, meaning differences could have been caused by the time interval between recordings and clinical interventions used. The median monitoring time with CerebAir was only 134.5 minutes. A longer monitoring time may have been needed to detect NCSE. The study was done in Japan and may limit the generalisability to the NHS. There is limited information on people with acute brain injury which may be of interest to intensivists working in the NHS.

Meyer et al. (2021)

Study size, design and location

Retrospective single-centre observational study of 52 adults (over 18 years) having treatment in a neurointensive care unit for reduced consciousness after serious neurological or metabolic diseases in Germany.

Intervention and comparator

CerebAir compared with intermittent monitoring with routine 10–20 EEG.

Key outcomes

There were 47 people included in the final per-protocol analysis. Five people did not have routine EEG because of technical issues or medical conditions. The agreement between CerebAir and routine EEG for EEG background activity, epileptiform discharges and seizure

activity was 53% (24 of 45 people; p=0.126), 68% (32 people; p=0.162) and 98% (46 people; p value not stated), respectively. Compared with routine EEG, CerebAir detected the same or additional intensive care-relevant EEG patterns in 89% of people.

Strengths and limitations

Patients' conditions were typical of those in neurointensive care. CerebAir recordings were analysed by physicians blinded to routine EEG results. It was unclear from the study whether physicians were specialist neurophysiologists or intensivists.

Analysis was done per protocol because, out of the 52 people in the study, only 47 people had both interventions. EEG activity may have been affected by adjustments of antiseizure and sedative medicines as well as the time between recordings with the 2 interventions. It was not documented whether using CerebAir led to treatment changes, so the clinical consequence of using the technology is not known. The study was done in Germany and may limit the generalisability to the NHS.

Sustainability

The company says that the main environmental benefit provided by the CerebAir is from reducing travel between hospitals for neurophysiology staff. There is no published evidence to support these sustainability claims.

Recent and ongoing studies

No ongoing or in-development trials were identified by NICE when searching key clinical trial registries. The company states that there are ongoing clinical studies being done at the Queen Elizabeth hospital in Birmingham and the Walton Centre in Liverpool.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All experts were familiar with continuous electroencephalogram (EEG) monitoring or intermittent EEG monitoring in intensive care, and 1 had used CerebAir before.

Level of innovation

Three experts felt that the technology was a minor variation to standard care that is unlikely to alter the procedure's safety and efficacy. Another expert felt that the technology was innovative with uncertain utility. Two experts agreed that CerebAir would be used in addition to existing standard care. One of these experts noted that some patients will also need video telemetry to match up the EEG with clinical findings. The remaining 2 experts said that the technology could replace standard care or a part of standard care. Two of the experts highlighted that alternative technologies are available, including depth of anaesthesia monitors and 3 other technologies similar in function to CerebAir.

Potential patient impact

The potential patient benefits identified by experts include allowing monitoring of patients with, or at risk of, brain injury timely diagnosis of seizures; allowing early treatment; measuring response to therapy; helping to get a prognosis after a cardiac arrest, subarachnoid haemorrhage or traumatic head injury; the ease of application of the technology; and the ability for continuous EEG to be done outside of regular working hours. One of the experts said that people with unexplained coma would benefit most from CerebAir. Two experts said that people with acute brain injury would benefit most. Another expert said that potentially all people with severe brain injuries resulting in reduced or fluctuating level of consciousness could benefit, as well as those at risk of this who need prolonged sedation with or without neuromuscular blockade.

Potential system impact

The main system benefit identified by the experts was a shorter time to diagnosis and prognosis, and a potential reduction in secondary brain injuries. Two experts felt that using CerebAir is likely to cost more than standard care. One of these experts noted that there would be capital and consumable costs, IT costs and costs associated with education and expert interpretation of data. Another expert felt the costs were likely to be similar. This expert highlighted that although applying CerebAir may not need highly trained healthcare professionals, using CerebAir is likely to increase the number of continuous EEG recordings being made. This would result in additional time demands on neurophysiologists to interpret the data. The remaining expert said the resource impact of CerebAir is uncertain because the clinical impact of using the technology is not yet known.

One of the experts stated that the technology would need to be compatible with secure hospital Wi-Fi networks and not be susceptible to background electrical interference.

General comments

One expert said that continuous EEG of any form is rarely used in intensive care in the UK. They said that the main barriers to adoption of continuous EEG include poor technology and ease of use, lack of knowledge around the interpretation of EEG data, cost of technologies and a lack of clear treatment pathways. For CerebAir specifically, this expert said the main barriers to adoption are training, education and expertise among intensive care clinical staff. Another expert said that other factors may influence uptake of the device, in addition to uncertainty around its clinical impact. This includes its MRI compatibility, whether it can be used for people after brain surgery, how it integrates with clinical information systems, as well as data security and storage and potential electrical interference from other medical devices. Three experts felt that the device would only be used in a minority of hospitals but in at least 10 in the UK. One of these experts said that its main use would be in specialist neurosciences intensive care units and that use of the technology in district general hospitals is likely to be very limited without further research. The other expert thought it would be used in most or all district hospitals. Two experts said that the technology may cause minor local skin injury. One expert said that potential electrical interference may alter the diagnostic ability of the technology. Another expert said that clinicians may need to be reassured that use of CerebAir will not interfere with tracheal intubation or that the device could be removed quickly if necessary. One of the experts said that it is not clear whether the device is suitable for people who have had craniectomy (a type of brain surgery in which doctors remove a section of a person's skull). One of the experts noted that results from the CERTA trial showed that continuous EEG monitoring led to increased seizure detection but did not lead to improvements in clinical outcomes compared with intermittent EEG (Rossetti et al. 2020).

Expert commentators

The following clinicians contributed to this briefing:

- Dr Jonathan Ball, consultant in intensive care, St George's University Hospitals NHS Foundation Trust. Did not declare any interests.

- Dr Colin Andrew Eynon, consultant in neurosciences intensive care, University Hospital Southampton NHS Foundation Trust. Did not declare any interests.
- Professor Tonny Veenith, consultant in critical care medicine and neurosciences, University Hospitals Birmingham NHS Foundation Trust. Did not declare any interests.
- Dr Matt Thomas, consultant, intensive care medicine, North Bristol NHS Trust. Did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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