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Long term electroencephalography in preterm neonates: Safety and quality of electrode types

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Abstract

Objectives: The objective of this study was to compare gold cup and hydrogel electrodes for frequency of electrode replacement, longevity of the original electrodes after initial placement, recording quality, and skin safety issues in long-term EEG studies in preterm neonates.

Methods: We performed a prospective trial with newborns born at 23 weeks and 30 weeks of gestational age (GA). Two mirror image EEG electrode arrays were utilized on consecutive subjects, where gold cup electrodes alternated with hydrogel electrodes.

Results: Our sample included 50 neonates with mean GA of 27 (± 1) weeks. The mean recording time was 84 (± 15) hours. No difference was present in the frequency of replacement of either type across the total recording time ($p = 0.8$). We collected the time at which electrodes were first replaced, and found that hydrogel electrodes showed a longer uninterrupted recording time of 28(± 2) hours vs. 20(± 2) hours for gold cup electrodes ($p = 0.01$). Recording quality was similar in either type ($p = 0.2$). None of the patients experienced significant skin irritation from a discrete electrode.

Conclusion: Long-term EEG studies can be performed with either gold cup or hydrogel electrodes, validating the safety and quality of both electrode types.

Significance: Hydrogel electrodes are a reasonable alternative for use in long-term EEG studies in preterm neonates.

Keywords

Electroencephalography; Gold cup Hydrogel; Electrode; Safety; Quality

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Conflict of interest

The authors have no potential conflicts of interest to disclose.

1. Introduction

Seizures in preterm neonates have been reported with an incidence ranging between 3.9% and 48% (Hellstrom-Westas et al., 1985; Scher et al., 1993; Vesoulis et al., 2014; Lloyd et al., 2017). Seizure incidence varies with the EEG modality utilized-amplitude-integrated EEG (aEEG) versus conventional EEG. Early life seizures in sick premature neonates portend both poor short and long term outcomes. Seizures in extremely low birth weight neonates were associated with short term morbidities such as severe intraventricular hemorrhage, sepsis, meningitis and cystic periventricular leukomalacia (Davis et al., 2010). Long-term adverse outcomes (cerebral palsy, developmental delay and epilepsy) were reported in preterm neonates with confirmed neonatal status epilepticus (Scher et al., 1993; Pisani et al., 2016), and decreased language performance at 2 years of age was noted in patients with seizures detected in the first three days of life (Vesoulis et al., 2014). To better define the prevalence and significance of seizures in this population, long-term conventional EEG recording in preterm neonates is gaining widespread interest and increasingly being clinically utilized.

Full montage EEG (full scalp coverage) has significant advantages over amplitude-integrated EEG. aEEG is a bedside neuromonitoring tool that records EEG signal using one or two channels placed in the centro-parietal areas of the newborn's head (Toet and Lemmers, 2002). aEEG was found to have lower sensitivity and specificity in seizure detection, in newborns (Hellstrom-Westas, 1992; Toet et al., 2002; Rennie et al., 2004; Shah et al., 2008). The time-compressed nature of aEEG tracings and the centro-parietal location of the electrodes, may lead to reduced detection of seizures with low amplitude, brief duration (Hellstrom-Westas, 1992) and focal seizures distant from the aEEG electrodes (Rakshasbhuvankar et al., 2015).

The use of full montage EEG electrode array on a preterm neonate can be challenging due to the small head size and the vulnerability of the premature skin. Additionally, for long term EEG studies, the integrity of the skin must be balanced against EEG recording quality. At our institution, we currently utilize gold cup electrodes for all clinical studies. With application of gold cup electrodes, first a gentle cleansing gel is used to remove debris from the skin, and conductive paste and paper tape are used to fix the electrodes in place. Collodion, used to glue down the gold cup electrodes in most long-term EEG studies, is not used in the preterm population due to the fragility of the preterm scalp, which limits the stability of the gold cup electrodes, especially in a humidified and warm environment such as in an incubator.

The skin of extremely low birth weight preterm neonates is not fully developed compared to term newborns with an immature stratum corneum, which poses problems in the care of the preterm skin. The stratum corneum which is the outermost layer of the epidermis develops in the third trimester of pregnancy, and is responsible for protection against microorganisms, reducing transepidermal water loss and minimizing absorption of toxins from topical products (Ness et al., 2013). Unfortunately, the preterm skin lacks this protective layer, making it fragile and easily damaged. The removal of tape or adhesive dressings can be harmful to the preterm skin due to weak epidermal-dermal junctions, and decreased elastic

fibrils (Ness et al., 2013). This is why it is recommended to decrease the use of adhesives in this population, and to replace with hydrogel electrodes when available (Lund et al., 2001).

Hydrogel electrodes have been shown to be an adequate alternative to gold cup and subdermal needles in aEEG recordings when used with adequate skin preparation (Foreman et al., 2011). They have the advantage of increased adhesion to the preterm skin, especially in a humidified environment, and they have a flat surface, decreasing pressure points on the skin when the neonate's head lies on electrodes and wires. In addition, hydrogel electrodes are sterile and disposable, but not reusable.

While evaluating the frequency of seizures in the preterm population, we hypothesized that hydrogel electrodes can be used instead of the gold cup electrodes for full EEG recordings and they are non-inferior compared with gold cup electrodes in the recording quality and maintenance with better skin tolerance. Our objectives were to compare the recording safety and quality between the gold cup and hydrogel electrodes using a study design that directly compares the two electrode types in each neonate.

2. Methods

2.1. Study population

All newborns born at 23 weeks and 30 weeks of gestational age and admitted to the neonatal intensive care unit of Saint Louis Children's Hospital, were eligible if the following inclusion criteria were met: 1-aged less than 24 h of age, and 2-no known congenital anomalies or genetic syndromes were identified. These neonates were not recruited for neurological risk or clinical indications, rather this population reflects the typical preterm NICU population. Parents of eligible neonates were approached for written informed consent. The study was conducted with the approval of Washington University Human Research Protection Office.

2.2. Electrode placement

Two mirror image EEG electrode (montages) arrays providing full scalp coverage with standard gold cup electrodes (F-E5GH48, Grass-Telefactor, Inc., West Warwick, RI, USA) alternating with hydrogel electrodes (Natus Medical Inc, San Carlos, CA, USA) and the two arrays were used alternately on consecutive subjects. The usage of both types of electrodes on each subject allowed us to test each type over the largest number of gestational ages (head sizes, and shapes), scalp types (presence of hair) and incubator environments, and allowed us to directly compare the performance of each electrode type in the same subject. Alternating electrode placements are shown in Figs. 1A and 1B.

EEG electrodes were placed according to the following protocol:

1. Using a cotton swab, we gently cleaned the skin with the Nuprep gel (Nuprep is a cleansing gel that effectively cleans the surface of the skin in order to achieve a better impedance).
2. We applied the hydrogel or gold cup electrodes using the International 10–20 system modified for neonates, according to the American Clinical

Neurophysiology Society's guidelines (Shellhaas et al., 2011). The gold cup electrodes require a conductive paste applied to the skin (Ten20 Conductive Paste), and fixed using a paper tape (Hypafix). Due to the fragility of the premature skin, collodion and cloth tape were not used. Hydrogel electrodes are applied directly to the skin, and the adhesive nature of the gel helps affix them to the skin.

3. The electrodes were then connected to the EEG machine (CNS Monitor, Moberg Research Inc., Ambler, PA), and recordings were continued for up to the first 96 h of life. The EEG recording system tracks real time impedance values at 1 Hz. The study team monitored the recordings during the day, and an EEG tech telemetry team monitored the impedance trends of the studies at nights and on weekends, and serviced electrodes with poor recording quality.

We collected the frequency of electrode replacement per day and the type of the electrode and its position on a log sheet. Electrode replacement was dictated mainly by the poor recording quality (determined by an impedance value greater than 20 K Ω) recorded on the EEG machine or if the electrode detached from the scalp. We accepted higher impedances than are typically used in clinical EEG (greater than 5 K Ω) due to good EEG signal and desire to reduce electrode manipulation in this population.

Skin examination was performed at least two times per day to evaluate for irritation and the results were recorded on a separate log sheet (Lund and Osborne, 2004).

2.3. Statistical analysis

Frequency of electrode replacement by type (hydrogel vs. gold cup) over the course of the recording was compared using the Wilcoxon signed-rank test. Frequency of electrode replacement by position over the course of the recording was compared using the Mann-Whitney test. Frequency of replacement of electrodes was normalized to a 96-h interval in order to correct for the slightly varying study lengths. We then compared the frequency of replacement among different electrode positions by electrode type using the Kruskal-Wallis test.

Recording quality of the two electrode types was compared by computing the mean impedance values of each recording during the portion of time where the recording quality was considered acceptable (impedance value of <20 K Ω). We compared the values of the mean impedances using an independent samples *t*-test.

To study the longevity of each electrode type after initial placement, we used a custom analysis program written in MATLAB (The Math Works, Natick, MA) which scanned the impedance time series for those electrodes that were replaced and noted the time at which each electrode recording reached an impedance >20 K Ω . We then created Kaplan-Meier survival curves comparing the survival of the hydrogel and gold cup electrodes after initial application.

3. Results

3.1. Study population

Our study included 50 neonates with mean gestational age (GA) of 27 (± 1) weeks. Mean birthweight was 1100 (± 260) grams. Twenty-six subjects were females (52%) and 26 (52%) subjects were African-American. Four neonates expired during their hospital stay. One of the subjects died within the first 24 h before any electrodes were applied. Death was attributed to extreme prematurity, severe IUGR and respiratory distress. Two other patients expired due to necrotizing enterocolitis at two weeks of age. One other patient was born at 24 weeks GA, and expired at 5 days of age due to suspected sepsis.

The mean recording time of the EEG-video study was 84 (± 15) hours, and the age at EEG study start was 20 (± 9) hours.

3.2. Frequency of replacement of the hydrogel and gold cup electrodes

Frequency of electrode replacement was not different across all subjects with either electrode type ($Z = 0.7$, $p = 0.5$, $r = 0.06$). We compared hydrogel and gold cup electrodes in terms of frequency of replacement at each of the 11 electrode positions. No significant differences between the two electrode types at any specific electrode position were present (Table 1).

Frequency of replacement of the hydrogel electrodes ($\chi^2 = 64$, $p < 0.001$) and gold cup electrodes ($\chi^2 = 59$, $p < 0.001$) was significantly affected by electrode positions. Most of the differences observed were driven mainly by the Cz (central vertex) electrode position that most frequently needed replacement with both electrode types. Fig. 2 depicts the boxplots corresponding to the frequency of replacement of hydrogel and gold cup electrodes at the eleven positions of the electrode array.

3.3. Recording quality

No difference in the recording quality between the two electrode types was noted in the study. The mean impedance of hydrogel electrodes during acceptable recording periods was 3.8 ± 3.2 vs. 3.5 ± 2.7 for gold cup electrodes ($p = 0.2$).

3.4. Longevity analysis

46% of the gold cup electrodes and 41% of the hydrogel electrodes did not need replacement throughout the entire recording period ($\chi^2 = 1.4$, $p = 0.2$). We collected the time to first replacement for each electrode after initial application. Among the electrodes that were replaced, the mean uninterrupted recording time for the gold cup electrodes was 20 (± 2) hours vs. 28 (± 2) hours for the hydrogel electrodes ($p = 0.01$). Kaplan–Meier curves show the difference in longevity between each type, and this difference is significant as shown in Fig. 3 (Tarone-Ware test $p = 0.03$).

3.5. Safety/skin integrity and irritation

None of the patients experienced significant skin irritation from a discrete electrode that required intervention or discontinuation of the EEG monitoring. One patient developed signs

of mild irritation over the whole scalp (involving both electrode types) and monitoring was discontinued after 48 h. Differences were not noted between the two electrode types, demonstrating that successful long term EEG studies can be performed safely on preterm neonates with fastidious attention to skin preparation and integrity under study conditions.

4. Discussion

Our study was a prospective trial and the first to directly compare the safety and quality of hydrogel and gold cup electrodes for recording long term conventional EEG in preterm neonates.

We performed 50 EEG studies in a group of preterm neonates evaluating hydrogel and gold cup electrodes in terms of skin irritation and safety of either type in continuous EEG studies. No adverse effects were noted with either type, demonstrating that hydrogel electrodes can be used safely as an alternative to gold cup electrodes. Additionally, hydrogel electrodes are non-inferior to gold cup electrodes in terms of frequency of replacement. Recording quality is similar between the two electrode types, with comparable impedance values. Though both electrode types typically required replacement of only half the electrodes throughout multiday EEG studies, hydrogel electrodes showed a longer uninterrupted recording time than gold cup electrodes after initial placement.

Hydrogel electrodes have been widely used for EEG studies for more than a decade, yet hydrogel electrodes have not been widely adopted for full montage EEG studies. The use of the disposable, flat surface electrodes for full EEG recordings was recommended by few authors (Lloyd et al., 2015), stating that in their experience, impedance rarely increased and electrodes were only occasionally replaced. Their study, however, did not include direct comparison with gold cup electrodes. Other electrode types have been used for neonatal EEG studies. A recent study compared wet and dry sensors in EEG recordings of newborns born at 35–42 weeks postmenstrual age (Fridman et al., 2016). The authors found a good correlation between dry and wet signal recordings in power spectral density curves, and similar interpretation of EEG background and seizure patterns. This study is similar to ours in terms of investigating the value of an alternative modality that can be quick and easy to apply in conventional EEG recordings.

Our study had few limitations. The lack of available personnel to continuously monitor the studies affected the promptness with which electrodes were replaced when the recordings got corrupted. This is why the longevity analysis in our study offers a better understanding of electrode survival. Additionally, electrodes were affected in rare cases by the performance of head ultrasound and intubation, a reflection of the realities of a busy clinical environment. The use of both electrode types in each subject and in the alternating fashion, hindered comparison of time needed to apply each electrode type alone, but we noticed that gold cup electrodes required more skin preparation and handling before application than hydrogel electrodes. Study procedure may have included more patient surveillance than in clinical EEG routine necessary for insuring patient safety under study protocols, not reflecting true real life usage under clinical conditions, but our data did not suggest significant differences

in electrode safety between electrode types, despite concerns over the higher profile and the use of paper tape when using the gold cup electrodes.

The strengths of our study included the prospective nature of the study design which consisted of the use of gold cup and hydrogel electrodes in long-term EEG among preterm neonates in the neonatal intensive care unit. Preterm neonates are a challenging study population, especially in the first few days of life. Despite the fragility of their skin, we were able to perform long term EEG-video studies without adverse events. We used hydrogel and gold cup electrodes in the same subjects, to reduce the effects of hair and skin maturity on the maintenance of either electrode type. The dual array that we used in our montage contributed to altering the electrode positions in either type and therefore evaluating selective vulnerability of each electrode type in different head positions.

Finally, we conclude that both electrodes types are safe for preterm EEG studies and overall had similar quality.

Gold cup electrodes are the standard in many neonatal units across the world. They are widely available and reusable between patients. Our study showed that they are equally safe and effective compared to hydrogel electrodes. Despite concerns over laying on electrode edges and wires, in this comprehensive trial, the gold cup electrodes performed well. EEG labs tend to use gold cup electrodes because they can be used on multiple patients, making them perhaps more cost effective but at the same time increasing cross patient risks. It takes longer to prepare the skin with gold cup electrodes, and the lack of use of collodion which is undesirable in preterm neonates may compromise the stability of the electrode.

Given the findings of electrical and logistical equivalence, the advantageous properties of hydrogel electrodes, namely sterility and single-use, argue for a favorable alternative replacement of gold cup electrodes. With the lack of hair on the preterm scalp, the hydrogel electrodes allow easy application with perhaps less skin preparation and scalp manipulation with tape and paste, and less prominent edges compared to gold cup electrodes. Most importantly, the initial electrode life for hydrogel electrodes was longer than that of gold cup electrodes (28 h vs 20 h), which makes them beneficial for overnight or 24 h studies that are increasingly performed for brain surveillance of our youngest patients.

5. Conclusions

Full montage EEG studies were well tolerated in preterm neonates with either electrode type. Hydrogel electrodes are a reasonable alternative to gold cup electrodes for long-term EEG monitoring in preterm neonates. The hydrogel electrodes showed no serious adverse skin irritation along with easy application and appropriate longevity showing acceptable impedances throughout EEG monitoring. All of these factors make hydrogel electrodes a more than acceptable alternative compared to standard gold cup electrodes in preterm neonates who are candidates for long-term EEG monitoring.

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HIGHLIGHTS

- Hydrogel and gold cup electrodes can be used safely in long-term EEG studies in preterm neonates.
- Hydrogel electrodes are non-inferior to gold cup electrodes in terms of replacement frequency and recording quality.
- Hydrogel electrodes showed a longer uninterrupted recording time than gold cup electrodes.

Fig. 1A.

Full head EEG electrode array. Gold cup electrodes alternate with hydrogel electrodes in two consecutive neonates.

Fig. 1B.

The top panel depicts the Moberg machine displaying full EEG recording, and the bottom panel depicts the impedance values corresponding to each position of the 10–20 International System

Fig. 2. Boxplots corresponding to the frequency of replacement of hydrogel and gold cup electrodes in the eleven positions of the electrode array.

Fig. 3.

Plot for the longevity curves for each electrode type. Among the electrodes that were replaced, the initial hydrogel electrodes recordings were longer than those of gold cup electrodes (Tarone-Ware test: $\chi^2 = 4.6$, $p = 0.03$).

Frequency of replacement of hydrogel and gold cup electrodes in the different positions of the array. Values are reported as medians and range. Mann-Whitney tests were performed to compare the frequency of replacement between the two types in the different positions

Table 1

Electrode position	Frequency of replacement Median (range)	Mann-Whitney U	Z-scores	p-value
Fp1	H: 1.0 (0-7.8) G: 0 (0-3.1)	217	-1.5	0.1
Fp2	H: 0 (0-3.2) G: 0 (0-3.2)	249	-1.0	0.3
T3	H: 0 (0-1.4) G: 0 (0-2.1)	227	-1.8	0.08
T4	H: 0 (0-1.1) G: 0 (0-1.4)	276	-0.4	0.7
C3	H: 0 (0-6.8) G: 0 (0-6.9)	282	-0.1	0.9
C4	H: 1.0 (0-4.2) G: 0 (0-3.2)	218	-1.5	0.1
Cz	H: 2.4 (0-7.2) G: 0 (0-8.2)	275	-0.2	0.8
O1	H: 0 (0-2.8) G: 0 (0-2.1)	270	-0.4	0.6
O2	H: 0 (0-1.4) G: 0 (0-2.1)	274	-0.4	0.5
Reference	H: 0 (0-2.8) G: 0 (0-2.8)	264	-0.6	0.5
Ground	H: 0 (0-5.7) G: 0 (0-4.0)	277	-0.2	0.8