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Effect of cortical cooling on interictal epileptiform activities

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ABSTRACT

Objective: To determine if applying chilled solution to exposed cerebral cortex can reduce interictal epileptiform activities in patients during surgery.
Methods: Electrocorticography was used to record the epileptiform activity of 12 patients (ages 18–53) undergoing cortical mapping and resection surgery. Interictal spikes were counted at baseline and compared with spikes after applying room temperature and chilled Lactated Ringer's or normal saline solution.
Results: Cortical irrigation with 150-cm^3, chilled (4 °C) normal saline solution reduced the mean number of interictal spikes from 11.46 to 4.87 spikes per minute ($p = 0.04$). There was no significant reduction in the epileptic spike frequency when room temperature normal saline was used.
Conclusion: The application of chilled solution directly to the cortex can reduce interictal epileptiform activities, suggesting that seizure potential can be suppressed to avoid evoked seizures during intraoperative surgery.

1. Introduction

Surgical resection is a procedure used to reduce seizure frequency in patients with refractory epilepsy. During surgery, direct cortical stimulation mapping is used to identify and preserve functional neural tissue. Unfortunately, up to 5% of patients experience intraoperative seizures during such mapping.[1] The conventional treatment of intraoperative seizures with intravenous antiepileptic medications can complicate mapping by increasing postictal sedation and patient lethargy. Several researchers have suggested brain cooling as a possible alternative method of suppressing epileptiform activity, thus controlling seizures during surgical resection.[2]

Relatively little research in brain cooling has been done in human subjects. One such study demonstrated that cold Lactated Ringer's (LR) solution can successfully treat seizures during intraoperative brain mapping.[3] Other studies have shown success with the use of brain cooling in animal models. A study on fetal sheep found that cerebral cooling did not prevent delayed seizures but suppressed a rise in cortical impedance.[4] In cats, global hypothermia decreased the amplitude and frequency of epileptic spikes in the hippocampus.[5] Focal cooling of the hippocampal region in rats abolished the production of epileptiform discharges.[6,7] Another study in rats found that brain cooling rapidly terminated neocortical seizures.[8]

The rapid and reliable termination of seizures by cooling could profoundly improve intraoperative brain mapping procedures, but this technique has yet to be researched adequately. This pilot study prospectively analyzed the ability of cold saline irrigation to reduce the frequency of intraoperative epileptic discharge (measured by electrocorticographic (ECoG) spike frequency) thereby decreasing cortical irritability and seizure potential during cortical mapping. Additionally, this pilot study attempted to quantify the effect of cold irrigation on cortical interictal epileptiform activity.

2. Methods

2.1. Participants

Patients scheduled to undergo cortical mapping and resection surgery for refractory seizures were asked to participate in the study. Patients who met inclusion criteria were 18 years or older, had intractable focal epilepsy requiring surgical brain resection, were already scheduled for surgery, and were capable of providing informed consent for the study procedure. All study participants provided informed consent prior to surgery. The research protocol was approved by the Institutional Review Board at Via Christi Regional Medical Center.

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2.2. Procedure and data collection

All patients were anesthetized by way of fentanyl, propofol, or isoflurane, the standard anesthetic agents used for epilepsy surgical mapping. Electrocorticography was performed using a 132-channel Nicolet portable BMSI recording system. Brain mapping was performed using an Ojemann cortical stimulator with a monopolar probe.

ECoG activity was measured with a 1 in. × 4 in. subdural strip applied to the lateral anterior temporal lobe of each patient. Appropriate placement was determined by confirmation of epileptiform discharge on baseline readings, and positions were not changed prior to counting the spikes. The study hypothesis was that cold saline applied directly to the cortex reduces interictal epileptiform activity.

Two minutes of baseline cortical activity was measured for each patient. Recording was collected by the Nicolet portable unit. One hundred fifty cm^3 of room temperature (18 °C) normal saline (NS) was applied directly to the cortex for 30 s followed by 2 min of ECoG recording. Then, 150 cm^3 of chilled (4 °C) NS was applied to the cortex for 30 s followed by 10 min of ECoG recording. The number of baseline interictal spikes was compared to the number occurring during application of room temperature and chilled solution. All data were collected prior to any cortical stimulation and mapping of seizure focus. The cortical temperature was not measured due to the invasiveness involved. ECoG analyses and counting of spike frequency were first undertaken by two blinded researchers and were later confirmed by an epileptologist. Because all patients were asleep under general anesthesia, data could not be gathered to compare those who were awake with those who were anesthetized.

2.3. Statistical analyses

The frequency of epileptic spike activity at baseline was compared with the spike frequency after applying first room temperature solution and then chilled solution. A standard statistical program (SPSS) was used to conduct one-way ANOVAs on the data. The Tukey post hoc test was selected due to its conservative nature.

3. Results

Twelve patients met the study's inclusion criteria. Interictal spike frequencies for all 12 patients are summarized in Table 1. The patient population consisted of eight females and four males with a mean age of 36 years (range: 18–53).

Irrigation with 150-cm^3, chilled NS solution decreased the absolute baseline spike frequency in eleven of twelve patients. The mean number of spikes per minute for baseline was 11.46, compared to 9.29 for room temperature NS and 4.87 for chilled NS (4 °C) (Fig. 1). The reduction in epileptic discharges was statistically significant when 150-cm^3, chilled 4 °C NS was used compared to the same volume of room temperature solution, $t(2) = 3.377$, $p = 0.040$, $\eta^2 = 0.17$. The most substantial decrease in spike frequency occurred during the first 2 min after application of chilled solution. The number of spikes reduced from 11.46 spikes per minute at baseline to 4.70 spikes per minute during the second minute, and averaged 4.60 spikes per minute for the remainder of the 10-min recording.

Table 1
Interictal spike frequency for all patients at baseline, after room temperature irrigation, and after chilled solution irrigation of intraoperative cortex[a]

Patient number	Baseline average (spikes/min)	Room temperature average (spikes/min)	Chilled solution average (spikes/min)
Patient #1	30.0	20.5	2.3
Patient #2	11.0	15.5	10.6
Patient #3	25.0	13.0	4.7
Patient #4	18.0	15.5	11.0
Patient #5	11.5	6.5	3.7
Patient #6	1.5	8.0	3.0
Patient #7	6.5	7.5	5.1
Patient #8	4.0	2.5	1.6
Patient #9	4.5	4.0	1.2
Patient #10	10.0	4.5	3.2
Patient #11	5.5	3.0	4.3
Patient #12	10.0	11.0	7.7
Group mean (S.D.)	11.46 (8.727)	9.29 (5.790)	4.87 (3.265)
p value*	Not applicable	0.682	0.040

[a] Irrigation amounts for Patients #1–#12: 150 cm^3 NS.
* p value test results compared to baseline average.

4. Discussion

This preliminary study indicates that irrigation with 150-cm^3, chilled NS solution irrigation significantly reduced baseline seizure discharge frequency. These results correlate with animal and other research showing that cortical hypothermia decreases the electrical transmission activity of the brain.[7,9] In turn, this reduces the potential to have seizures, and possibly aborts seizures intraoperatively. In this experiment, chilled solution was irrigated directly on the cortex in the absence of seizures; however, it is highly assumptive to suggest that decreased spike frequency would yield a decrease in ictal patterns. Further research with cortical irrigation during intraoperative seizure activity would clarify the potential to abort seizures once they occur.

It is not known whether amounts greater than 150 cm^3 would further suppress more epileptic discharge. While actual cortical temperature measurements were not obtained, it would appear that greater amounts of irrigation solution provided better surface area for cooling effects to cause the reduction seen during the procedure. The cooling solution temperature was chosen at 4 °C based on available storage for the saline solution during the experiment, as well as past research performed by Sartorius and Berger.[3] One study suggests that the temperature for terminating normal cortical activity may be higher than the temperature needed for terminating seizures.[10] Another study reported that cooling to 20 °C can reduce successive seizure activity and severity.[11] Further research is necessary to evaluate optimal cooling temperatures of the cortex to maximize the effects of interictal discharge suppression.

Normal saline solution was used for patients irrigated with 150-cm^3 solution. LR solution can also be used, as in the case reported by Sartorius and Berger.[3] Further research is necessary to explore which solution is more effective in reducing intraoperative, interictal epileptic discharge. While statistical significance was obtained to show the effects of chilled solution on discharge frequency, this study included a small sample size. Nonetheless, the moderate effect sizes, not influenced by sample size, demonstrate a sizable correlation between irrigation amounts and ECoG spikes, and a notable difference between room temperature and chilled normal saline.

4.1. Limitations

Interictal activity may not predict true ictal activity; as such, these results may or may not have clinical relevance. However, given the volume of cortical surgery and its inherent mapping combined with the known effect of irrigation on true intraopera-

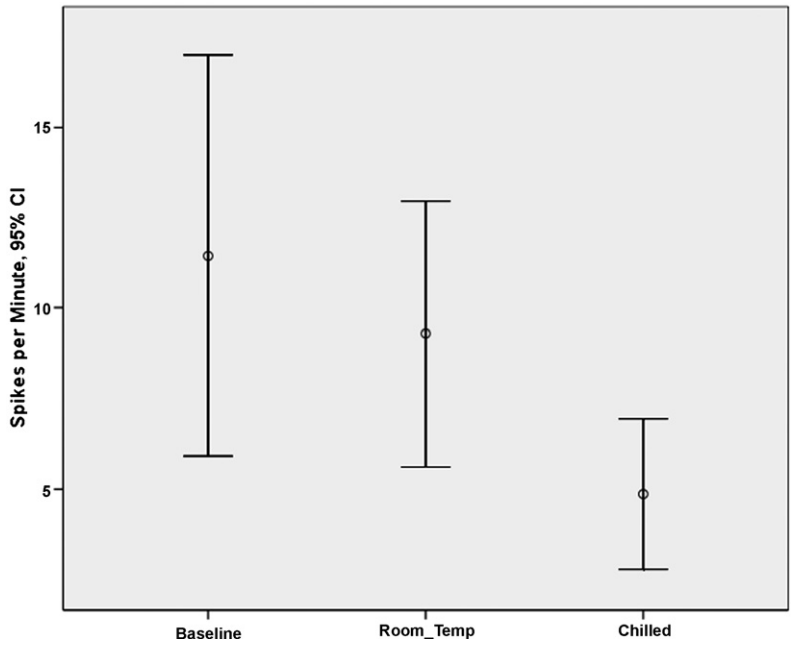

Fig. 1. Epileptic spikes per minute at baseline, after applying 150-cm^3, room temperature NS, and after 150-cm^3, chilled 4 °C.

tive ictal events, surely iced saline has been used to abort or limit intraoperative ictal events.

5. Conclusions

Applying 4 °C chilled solution directly to the cortex reduced interictal epileptiform discharges by 57% from baseline. This suggests seizure potential can be suppressed to avoid evoked seizures during intraoperative surgery. However, the fact that cooling can decrease spike frequency does not necessarily imply that seizures can be aborted altogether. The decrease in spike frequency was most significant during the first 2 min after application. Applying room temperature solution did not show a statistically significant reduction in epileptic discharges.

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