

The safety and efficacy of propofol as a replacement for amobarbital in intracarotid Wada testing of presurgical patients with epilepsy

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ABSTRACT

Objective: The intracarotid sodium amytal procedure (the “Wada test”) has for many years been the gold standard for language and memory lateralization and remains an important part of presurgical analysis for patients with medically intractable seizures. Due to shortages in the key sedative (amobarbital), neuropsychologists have turned to alternatives such as propofol. Our aim was to investigate the safety and efficacy of propofol relative to amobarbital in the Wada test.

Methods: We performed a retrospective review of the 97 Wada procedures performed at University of Iowa Hospitals and Clinics from 2007 through mid-2015.

Results: Propofol produced similar lateralization rates as amobarbital for both language and memory. Similar rates of patients in each group went on to have the resection surgery. With regard to safety, there were no differences found in average rate or severity of adverse effects. None of the demographic characteristics reviewed were predictive of increased risk for either drug.

Significance: These findings support previous studies indicating that propofol is as safe and efficacious as amobarbital, and can continue to be used in Wada procedures with confidence.

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1. Literature review

The intracarotid sodium amytal (amobarbital) procedure (more commonly known as the Wada test) has for many years been administered to patients as the gold standard for language and memory lateralization [1]. It remains an important part of presurgical analysis, particularly for resection candidates with medically intractable seizures. Despite attempts by newer, less invasive technologies such as fMRI to replace it, the Wada test remains a mainstay of many centers' presurgical workups thanks to its known validity and reliability, particularly in patients with incomplete or atypical language lateralization [2,3]. Additionally, it is likely to remain important for patients who cannot easily undergo a conscious fMRI, such as children and people with metal implants.

Due to a recent worldwide shortage of amobarbital, the original Wada anesthetic, physicians have been investigating alternatives. Among the most used of these is propofol, although etomidate, methohexital, and pentobarbital have also shown promise [4]. The suitability of propofol for injection was initially demonstrated in a few case studies. The first resulted in no adverse events and successful lateralization of speech in a 43 year old male [5]. In the second, both language and memory

lateralization were successfully determined in a 26 year old female [6]. The success of these encounters led to several more systematic reviews.

A 2004 study found similar rates of successful lateralization of both memory and language between propofol and amobarbital. Some unusual side effects were noted for propofol (laughing, head, and eye version), but they resolved quickly and did not impact completion of the test [7]. Several small studies came to similar conclusions, even when used in pediatric populations [8–10]. The largest study to date included 129 procedures and found no difference in lateralization success, but was notable for lower rate of serious adverse events relative to previous studies [11]. Another smaller study came to a similar conclusion, with the caveat that propofol might not be appropriate for patients with low blood pressure due to its vasodilator effects [12].

An adverse event (AE) grading system was devised by Mikuini (2005) to evaluate more precisely the side effect profile of propofol relative to amytal in Wada testing. Of the patients injected with propofol, one-third experienced some sort of AE, although all but one were still able to complete the assessment. Age was found to be positively correlated with risk of experiencing any adverse event, while age, higher doses, and preexisting arteriovenous malformations were all risk factors for a more serious event. Low grade, less serious events were found to be similar between propofol and amobarbital, but more serious grade 3 events were five times higher for propofol when compared with past studies with amobarbital [13]. Unfortunately, there were no direct

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Table 1
Demographic information.

	Range	Mean	Median	SD
<i>a.) Participants in the propofol group</i>				
Age (years)	7–67	38	38	15
BMI (kg/m ²)	18.6–48.2	30.0	29.0	7.1
Systolic BP (mm Hg)	88–174	127	127	19
Diastolic BP	46–98	72	70	11
Formal edu. (years)	2–18	12	12	3
<i>b.) Patients in the sodium amytal group</i>				
Age (years)	10–74	36	35	16
BMI (kg/m ²)	18.7–42.5	29.2	27.7	6.3
Systolic BP (mm Hg)	96–158	128	125	15
Diastolic BP	55–95	74	74	8
Formal edu. (years)	5–19	13	12	2

statistical comparisons between propofol and amobarbital within the study, creating concern for confounders which may impact the results.

One possible concern is the association of propofol with seizure-like phenomena (SLP) in both patients with epilepsy and with no epilepsy when used as a general anesthetic [14]. This may raise concerns about its use in the context of the Wada test, although it has not been a complication noted by previous or subsequent studies.

The current study had several goals: first, to evaluate propofol for use in the intracarotid Wada test with a larger sample size than most prior studies; second, to further establish the efficacy and especially safety of propofol through direct comparison to amobarbital; and last, to determine if particular demographic characteristics make some patients better candidates for the test using these anesthetics. It will serve both as an attempt to verify and clarify findings in previous studies as well as to elaborate on inconsistencies surrounding rates and severities of AEs.

2. Method

2.1. Participants and exclusion criteria

Data were collected from the medical records of 97 patients with medically intractable epilepsy of any etiology who were undergoing presurgical work up for focal cortical resection at University of Iowa Hospitals and Clinics between 2007 and 2015. Of those patients, 49 underwent the procedure with amobarbital (2011 and earlier) and 48 with propofol (2011 and later). Patients were excluded from certain analyses if their records were missing details about the variable being evaluated. Only 4 patients were unable to complete testing (2 per

group) due to age or early drug clearance. No patients were excluded from all parts of the study.

2.2. Clinical protocol

A femoral catheter was inserted into the thigh on the epileptogenic side and threaded up to the ipsilateral internal carotid artery for injection of the anesthetic. Concurrent angiography was performed to establish nonanastomosing arteries, alongside EEG for evidence of sedation. The raw data for these were not available in the medical record, only confirmation of their clinical use. The modal initial injection was either 14 mg propofol (post-2011) or 125 mg sodium amytal (2011 and earlier). Contralateral grip strength was sequentially assessed as a percent of a preinjection baseline at the start, midpoint, and end of memory item presentation to estimate clinical sedation.

During sedation, all patients underwent a neuropsychological assessment administered by a board-certified neuropsychologist. Comprehension was determined by asking the patient to follow three simple instructions. Repetition ability was established using a four word sentence. Naming and memory were tested by presenting images and corresponding sentences involving the key term. For example, a picture of a clock would be shown, and the patient asked to name the object. They would then be aurally presented a related sentence to remember, e.g., “The clock is loud.” Time since injection was recorded alongside each of 10 stimuli. Following completion of stimulus presentation, patients were asked to report how they were feeling.

After recovery, memory for events was rated good, marginal, or poor based on patient descriptions of what happened after getting the injection. They were then asked to freely recall as many of the presented stimuli as they could. Following this, verbal recognition was tested by asking the patient to identify which of five listed possibilities was the one presented during the test. This was repeated for all 10 stimuli. For verbal recognition, patients were told, “I told you something about the _____. What did I tell you about the _____?” for all stimuli. Lastly, visual recognition was tested by showing the patient 5 possible pictures of each stimuli (1 stimuli, 4 foils) and asked to point to the specific picture they were shown.

Following a brief turnover period (about 37 min, on average), the contralateral hemisphere was injected, typically with the same amount of sedative, and the testing repeated. A few patients were not able to complete the full battery because they were too young to maintain attention or because their drug effect wore off too quickly. In these cases, the available scores were taken as a proportion of questions answered and retained in analyses.

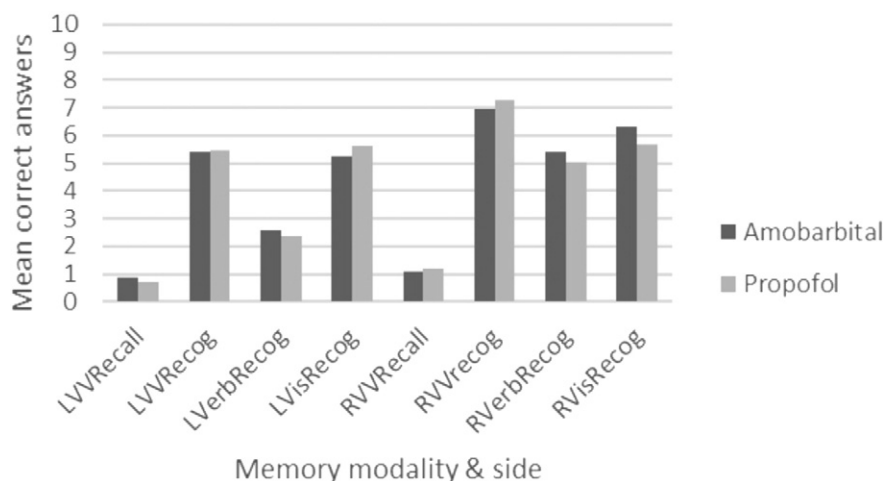


Fig. 1. Between-group comparison of mean memory performance during Wada test.

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