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Bilateral Wada test: Amobarbital or propofol?

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ABSTRACT

Purpose: The Wada test is still the gold standard procedure to predict language and memory deficits before temporal lobe epilepsy surgery. As amobarbital was no longer available, our aim was to validate propofol as an alternative.
Method: We retrospectively studied 47 patients who underwent a bilateral intracarotid procedure, performed with amobarbital (18), or propofol (29), between 2000 and 2010 during the preoperative evaluation of temporal lobe epilepsy.
Results: The number of patients experiencing an adverse event (mostly transient disturbance of consciousness or benign ocular symptoms) during both injections did not differ significantly between amobarbital and propofol. Hemispheric dominance was successfully determined in 96.5% patients with propofol vs. 94.4% with amobarbital for language, and in 72.4% under propofol vs. 77.7% under amobarbital for memory with no significant difference between groups.
Conclusion: Propofol can be used for the Wada test with an efficacy and safety comparable to amobarbital.

1. Introduction

The Wada test traditionally consists of a selective intracarotid injection of a fast acting barbiturate drug, generally sodium amobarbital, which transiently inhibits the ipsilateral cerebral hemisphere, in order to isolate the contralateral hemisphere and assess its activity. The original aim of this intracarotid procedure (ICP) developed by Dr Jung Wada in 1960[1] was to confirm the hemispheric lateralization of speech during preoperative evaluation of some refractory epilepsies in order to predict a risk of aphasic sequela. The test was extended to the study of hemispheric localization of memory functions, especially before considering anterior temporal lobectomy, in order to prevent the risk of global amnesic syndrome as in patient HM.

Nowadays, the traditional Wada test needs to be re-evaluated because amobarbital is no longer available in many countries[3] and other anesthetic drugs with different pharmacokinetic characteristics are currently used.[4]

There is still no consensus on a single substitute for amobarbital. One of the most widely used alternatives is propofol. Bazin and colleagues[5] were the first to describe the use of propofol to perform ICP and propofol ICP has now been reported in several studies,[6–10] where it appears to be as effective and well tolerated as the amobarbital procedure.

In 2004, 12 propofol ICP were compared to 55 amobarbital ICP.[7] ICP was successfully performed for language in 12 patients and for memory in 9 with propofol, in comparison to 52 language lateralization and 41 conclusive memory assessments using amobarbital. Only minor adverse effects (AE) were observed (laughing in one patient, and head and eye version in another).

In 2005 a study evaluated all AE, apart from the well-known cardiovascular effects, induced by intravenous propofol injection[8] during ICP in 58 patients and proposed a classification of AE in three severity grades (see Fig. 1). AE were reported for one third of patients with propofol. Magee et al.[10] recently reported AE in 29.1% of unilateral propofol ICP with no significant differences in number and type of AE compared with amobarbital.

Nevertheless it is difficult to draw definitive conclusions from these studies because of the small number of patients (at most 25 propofol ICP[9]), the heterogeneity of affections (only a specific cohort of epileptic patients[10]) and absence of standardized

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Grade 3	hypotension, hypertension, increased muscle tone with twitching and tonic posture or rhythmic movements, disturbance of consciousness
Grade 2	confusion, head and eye version, involuntary movements, tremor
Grade 1	eye pain, lacrimation , face contortion, headache, laughing, apathy, shivering, sweats, warm feeling

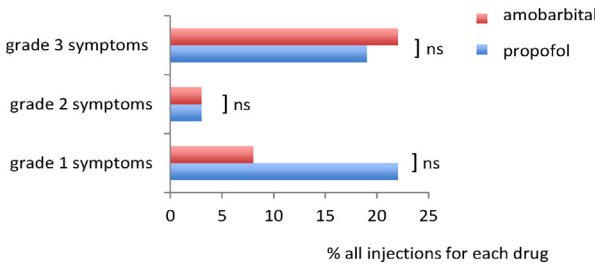

Fig. 1. AE considering all ICP, according to classification adapted from Mikuni et al.[8] ns: non significant. *The following AE were already described in Mikuni et al.'s classification[8]: eye pain, lacrimation, face contortion, shivering laughing and apathy (grade 1), confusion, head and eye version and involuntary movements (grade 2), increased muscle tone with twitching and rhythmic movements or tonic posture (grade 3). We added symptoms not reported in Mikuni's study: headache, sweats and warm feeling (grade 1), tremor (grade 2), disturbance of consciousness, and significant arterial hypotension or hypertension (grade 3). Grade 1 symptoms: we observed no significant difference between amobarbital and propofol during first ($\chi^2_1 = 0.721$, $p = 0.396$), second ($\chi^2_1 = 2.715$, $p = 0.099$) or both injections ($\chi^2_1 = 3.118$, $p = 0.077$). Grade 2 symptoms: we observed no significant difference between amobarbital and propofol during first injections ($\chi^2_1 = 0.033$, $p = 0.855$). No grade 2 symptoms were observed during second injections with either drug. Grade 3 symptoms: we observed no significant difference between amobarbital and propofol during first ($\chi^2_1 = 0.033$, $p = 0.880$), second ($\chi^2_1 = 0.559$, $p = 0.455$) or both injections ($\chi^2_1 = 0.146$, $p = 0.702$).

protocols. Not only do propofol doses vary across centers but also only one unilateral ICP is usually performed, although it has been demonstrated that bilateral ICP has a better prognostic value in predicting both post-operative verbal memory and verbal intelligence quotient.[11]

For all these reasons, standardization and validation of propofol use are needed, especially in bilateral ICP. We sought to contribute to this by retrospectively reviewing the complete series of epileptic adult patients who underwent ICP in our center. Our purpose was to make a detailed comparison of the technical characteristics and tolerance of bilateral ICP with propofol and amobarbital. We are aware that noninvasive techniques are currently being developed with the potential effect of making the Wada test obsolete.[12,13] Despite this context, we are convinced that ICP still has indications and that it is important to discuss which drug to use for the procedure.

2. Method

2.1. Population

We retrospectively reviewed all data from 51 patients (26 women) aged 18–57 years (mean age = 34.6 ± 10), who had undergone an ICP between 2000 and 2010 during preoperative evaluation of refractory epilepsy at the University Hospital of Toulouse, France. All patients had a comprehensive assessment, including neurological examination, neuropsychological testing, routine MRI, surface EEG and video. ICP was carried out as part of the patients' clinical care. Each patient received detailed information about the objectives and course of the procedure, and gave informed consent in the usual way.

We used amobarbital in 18 patients (from 2000 to 2003), then, at the beginning of the shortage of amobarbital in France, methohexital in 3 patients (2003). We very quickly stopped using methohexital because duration of action of the drug was too short, and propofol has been employed since then. Thirty patients have had propofol ICPs since 2004.

2.2. Procedure

Selective catheterization of the internal carotid artery (ICA) was performed by an interventional neuroradiologist (PT or MK), using a transfemoral approach. An angiography of the intracranial circulation was performed before each anesthetic injection to study its distribution territory. Selective ICA anesthesia was performed with the same procedure for both sides in each patient. The cerebral hemisphere to be operated on was first anesthetized. Blood pressure, heart rate and oxygen saturation were monitored non-invasively throughout the procedure. EEG recording (sampled at 256 Hz, bipolar montage, 10 channels, reference between Cz and Pz electrodes), started several minutes before the anesthetic injection and continued several minutes after the return of baseline clinical and EEG signs. It was read on line by an electroencephalographer (MD or LV). Before injection, a baseline state was obtained for EEG, visual fields, hand strength and cognitive functions. Patients were instructed to maintain arms and hands up, and to count aloud. While they counted to ten, the anesthetic solution was slowly injected manually through the catheter directly into the ICA (see Table 2). The injection was stopped when effective anesthesia was confirmed, as soon as hemiparesis was observed. Hand strength, sensitivity, visual field and language were evaluated periodically before the start of the test, after every minute and at the end of the test. A memory retention test was done after recovery had been verified through complete normalization of EEG and a neurological examination. The second hemisphere was evaluated about 30 min after the first.

2.3. Neuropsychological assessment

All patients underwent neuropsychological testing before ICP to determine the appropriate level of difficulty for the items of the test. The dominant hemisphere for language was determined by the onset of language impairment (speech arrest, dysphasia, delay in understanding and producing comprehensible language) after drug injection into one side but not the other. Speech control was defined as bilateral if language impairment occurred after injection of both sides, and was not defined when no language impairment occurred after injection of both sides.

Memory assessment began approximately 1 min after injection, as soon as anesthesia was both effective and allowed sufficient cooperation from the patient. Memory items were presented in three consecutive parts, in the same order in each part and for each patient (who was instructed to repeat, read or name every item and to memorize them) to assess verbal and nonverbal episodic memory: 3 audio presented words, 3 abstract Figure 3 written words, 3 concrete pictures, a sentence, and two real objects. The memory retention test began 5–10 min after clinical examination and EEG had returned to baseline, usually 10–15 min after the injection.

Free recall and recognition memory were tested by using a three-alternative forced-choice task. Total memory score was obtained by adding one point for each item with good retrieval. An asymmetry score was calculated by subtracting the memory score of the pathological hemisphere from the memory score of the contralateral hemisphere. One hemisphere was considered dominant when there was a gap of more than two points between the total memory scores of the two hemispheres.