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Short communication

Language assessment in Wada test: Comparison of methohexital and amobarbital

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ABSTRACT

Introduction: Methohexital has replaced amobarbital during Wada testing at many centers. The objective of our study was to compare the use of methohexital and amobarbital during Wada testing regarding language and memory lateralization quotients as well as speech arrest times.
Methods: A chart review of 582 consecutive patients undergoing 1041 Wada-procedures was performed (left = 60, right = 63, bilateral = 459). Language lateralization was calculated based on duration of speech arrest using a laterality index, defined as $(L - R)/(L + R)$. Memory lateralization was expressed as percentage of retained objects and laterality quotient.
Results: Language and memory lateralization revealed a similar distribution with amobarbital and methohexital. Speech arrest after left and right-sided injection was significantly longer in the amobarbital group as compared to the methohexital group. Language lateralization did not differ in the two groups. Percentage of retained memory items was higher in the methohexital group and there were fewer presented test items in the methohexital group.
Discussion: Language and memory testing during the Wada test can successfully be performed with methohexital instead of amobarbital. The shorter half-life of methohexital allows repeated injections and shorter interhemispheric testing intervals, but also shortens the testing window.

1. Introduction

Since the 1940s, intracarotid amobarbital injection has been used in the presurgical language assessment of epilepsy patients.[1] Memory testing during the Wada test was added by Milner et al. in 1962.[2] During a recent shortage amobarbital was replaced by methohexital. Only limited information is available on methohexital as an anesthetic in the Wada test.[3–7] The objective of our study was to test methohexital as an anesthetic agent in the Wada test and to compare methohexital and amobarbital regarding language and memory lateralization quotients as well as speech arrest times during the Wada test.

2. Methods

A retrospective chart review of 582 consecutive Wada tests carried out at the Cleveland Clinic between 1997 and 2003 was performed. All patients (294 males) were included. A total of 1041 injections (left = 60; right = 63, bilateral = 459) were analyzed. Mean age was 32 years ranging from 5 to 84 years. Patients underwent left ($n = 60$), right ($n = 63$), or bilateral ($n = 459$) internal carotid artery catheterization and injection.

Amobarbital was used from 1997 until March 2001. After that date amobarbital was difficult to obtain and it was replaced by methohexital. Angiography was performed and all patients were monitored with simultaneous EEG recording according to the 10–20 system. An epileptologist was present during the procedure.

Methohexital (133 patients; 3–10 mg) or amobarbital (449 patients; 75–250 mg) was injected (Table 1). Amobarbital (usually 100 mg) was given as a single injection over 3–5 s (handpush). Methohexital (usually 3 mg) was given over 3–5 s intravenously (handpush). In case of incomplete hemiparesis after initial injection an additional dose of Methohexital (2 mg) or Amobarbital (25 mg) was given. Rarely an additional dose was given 30 s later. Effective injection was demonstrated by

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[1] We commemorate Dr. Dudley S. Dinner who passed away during the completion of the manuscript.

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Table 1
Patient descriptives and demographics.

	Amobarbital	Methohexital	All
Demographics			
Patients	449	133	582
Mean age in years (range)	31.96 (6–75)	32.7 (5–84)	32.1 (5–84)
Males	230	64	294
Procedures	804	237	1041
Bilateral procedures	355	104	459
Left-sided procedures only	44	16	60
Right-sided procedures only	50	13	63
Barbiturate dose			
Average dose in all right-sided procedures in mg (range)	108 (75–175)	5 (3–7)	–
Average dose in all left-sided procedures in mg (range)	115 (75–325)	5 (3–10)	–
Type of MRI lesion			
MCD	43 (10%)	14 (10%)	57 (10%)
Hippocampal atrophy/MTS	137 (30%)	33 (25%)	170 (29%)
Tumor	103 (23%)	36 (27%)	139 (23%)
AVM/cavernous angioma	20 (4%)	4 (3%)	24 (5%)
Encephalomalcia/trauma	37 (8%)	12 (9%)	49 (9%)
Other MRI lesions	26 (6%)	8 (6%)	33 (6%)
No lesion/normal	83 (19%)	27 (20%)	110 (18%)
Sum	449 (77%)	133 (23%)	582
Lateralization of MRI lesions (n = 472)			
Lesion left	174 (48%)	65 (61%)	239 (50%)
Lesion right	163 (44%)	29 (28%)	192 (41%)
Lesion bilateral	29 (8%)	12 (11%)	41 (9%)
Sum	366 (77%)	106 (23%)	472

MCD—malformation of cortical development; MTS—mesial temporal sclerosis; AVM—arteriovenous malformation; TS—tuberous sclerosis; SWS—Sturge–Weber syndrome.

contralateral hemiparesis. Interval between hemispheric injections was 30–45 min between amobarbital doses and 15–30 min between methohexital doses.

Language testing included counting, repetition, spontaneous speech, object naming, and reading words. Absolute duration (in s) of speech arrest (return to normal speech) after right and left injection was documented. Language lateralization was calculated in bilaterally injected patients based on the laterality index (LI) defined as (Left speech arrest time − Right speech arrest time)/(Left speech arrest time + Right speech arrest time), cutoff >0.5 (left) or <−0.5 (right).[8] Patients with a laterality index of 0.5 to −0.5 were considered bilateral dependent. Patients with no speech arrest after right and left injection were considered bilateral independent.[8,9]

The memory test paradigm consisted of presentation of 9–20 words and objects. Number of items was determined by duration of hemiparesis. Presented items included function words and object words as well as designs and pictures. Fifteen to 30 min after resolution of the hemiparesis, memory was tested using a selection paradigm. The patient was presented with four different choices and had to select the correct picture or word. The percentage of retained objects was calculated as a separate ratio (number of retained items/number of presented items) for each hemisphere. Memory lateralization was determined by the larger percentage of retained objects and words in patients with bilateral injections. Additional details on Wada test methodology have been described elsewhere.[10]

Statistical testing was performed with SPSS 10.0 (Chicago, IL, USA). For all statistical comparisons, a significance level of 0.05 was accepted.

3. Results

3.1. Demographics

Patient descriptives and intracranial lesions did not differ between both compared patient populations (Table 1).

3.2. Methohexital

Details on speech arrest times are listed in Table 1. Language lateralization in patients with bilateral methohexital injections was left in 76%, right in 5.9%, bilateral dependent in 16.3% and bilateral independent in 1.9% (Table 2). Memory lateralization was predominantly left in 60.6%, bilateral in 16.3%, and predominantly right in 23.1% (Table 2).

3.3. Amobarbital

Language lateralization in patients with bilateral injections was left in 79.7%, right in 5.9%, bilateral dependent in 13% and bilateral independent in 1.4% (Table 2). Memory lateralization was predominantly left 60.8%, predominantly right in 30.7% and bilateral in 8.5% (Table 2).

3.4. Comparison between amobarbital and methohexital

Speech arrest after left and right-sided injection was significantly longer in the amobarbital group as compared to the methohexital group ($p < 0.05$ left; $p < 0.01$ right). Language lateralization did not differ in the two groups. Also, the two groups did not differ in terms of memory lateralization quotients, although an increased number of patients with bilateral memory representation was seen in the methohexital group (Table 2). The percentage of retained objects after methohexital was significantly higher than after amobarbital ($p < 0.0001$). During methohexital testing fewer items (objects and words) for memory testing were presented as compared to amobarbital ($p < 0.0001$).

3.5. Language lateralization in patients with bilateral injections

3.5.1. Left-sided language

In patients with left-sided language lateralization after amobarbital injection median left-sided speech arrest time was 142 s and median right-sided speech arrest duration was 0 s. In

Table 2
Language and memory lateralization results.

	Amobarbital	Methohexital
Speech arrest times		
Median speech arrest in all left-sided injections in s (range)**	130 (0–723)	5 (3–7)
Median speech arrest in all right-sided injections in s (range)*	8 (0–526)	5 (3–10)
Language lateralization results in patients with bilateral injections		
Language left	283 (79.7%)	79 (76%)
Language bilateral dependent	46 (13%)	17 (16.3%)
Language bilateral independent	5 (1.4%)	2 (1.9%)
Language right	21 (5.9%)	6 (5.9%)
Sum	355	104
Objects presented during memory testing		
Median objects presented left injection***	16	12
Median objects presented right injection***	16	10
Median objects retained left injection	8	8
Median objects retained right injection	10	10
Memory lateralization results in patients with bilateral injections		
Memory left	216 (60.8%)	63 (60.6%)
Memory bilateral	30 (8.5%)	17 (16.3%)
Memory right	109 (30.7%)	24 (23.1%)
Sum	355	104

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

patients with left-sided language lateralization after methohexital injection median left-sided speech arrest time was 121 s and median right-sided speech arrest time was 5 s. Differences between amobarbital and methohexital were significant after left and right injection ($p < 0.05$).

3.5.2. Right-sided language

In patients with right-sided language after amobarbital injection median left-sided speech arrest duration was 2 s and median right-sided speech arrest duration was 156 s. In six patients with right-sided language lateralization after methohexital injection median left-sided speech arrest was 19 s and median right-sided speech arrest was 159 s. Results were not significant ($n = 21$).

3.5.3. Bilateral language

In patients with bilateral dependent language lateralization after amobarbital injection, median left-sided speech arrest time was 87 s and median right-sided speech arrest time 93 s. In patients with bilateral dependent language lateralization after methohexital injection, median speech arrest time on the left was 52 s and median right-sided speech arrest time on the right was 47 s. Differences between amobarbital and methohexital were not significant. In seven patients with bilateral independent language, all values were by definition zero.

4. Discussion

Language testing during the Wada test can be successfully performed with methohexital instead of amobarbital. Both anesthetics appear equal in their ability to evaluate language and memory lateralization. Speech arrest with amobarbital is significantly longer than with methohexital. Methohexital has a shorter half-life (1–2 h) than amobarbital (10–40 h) allowing dose titration. Shorter recovery after injection of methohexital allows more efficient bilateral hemispheric testing. Fast recovery may require a modified memory testing protocol with fewer test items given the shorter testing interval.

Advantages of methohexital include the shorter duration of the anesthesia due to its' shorter half-life and therefore faster testing intervals and less likelihood of involvement of the contralateral hemisphere.[4] Lesser degree of encephalopathy may also be one explanation for the higher number of absolute retained memory items in our series. Shorter testing times may allow more efficient testing. In our series, speech arrest duration after methohexital was significantly shorter. Additionally, recovery intervals could be shortened by 15–30 min between injections. However, shorter testing time may also limit time for memory testing. In our series significantly fewer memory test items could be presented. It is possible that the increased percentage of retained items was related to a shorter sedation effect and hence to the fact that the patients were able to memorize objects better. Alternatively, this could also be related to a smaller number of objects presented, which may affect recall after the test. Additionally, shorter testing periods and reduction in the number of presented objects may further impact the already limited reliability of Wada memory testing.[11] Speech arrest cut-offs and duration of hemiparesis differ with methohexital as compared to amobarbital. However, results appear reproducible and allow for meaningful comparisons between both hemispheres.

Methohexital is the only barbiturate with epileptogenic properties.[12] Several patients with seizures after methohexital injection have been described[13–15] and patients undergoing Wada testing are more prone to develop seizures after methohexital injection as compared to injection of amobarbital.[16] After injection of amobarbital, 0.7% had a seizure and 4.1% had a seizure after methohexital injection.[16]

Results of the study need to be interpreted within the retrospective study design setting. Only epilepsy surgery patients at a tertiary epilepsy center were included. Additional limitations include reliance on duration of speech arrest only as a means of lateralizing language, the variable number of presented objects due to differences in hemiparesis duration and additional potential variations in the protocol hampering reliability and validity.[11,17] Furthermore, we compared two different patient populations with varying drug doses instead of comparing test data in the same patient population. However, a prospective trial design with two injections in the same patient might be difficult due to ethical consideration because of possible complications during the Wada test such as carotid artery dissections and strokes.[18,19]

5. Conclusion

Methohexital can be used as an anesthetic agent in Wada testing. There seems to be no difference between amobarbital and methohexital in the determination of language and memory lateralization. The shorter half-life of methohexital allows repeated injections and shorter testing interval. A trade off is a shortened length of the memory testing window and possible induction of seizures. At Cleveland Clinic, it was decided to continue testing with methohexital, although overall Wada test numbers are declining. Despite methodological limitations including calculation of comparable memory scores, shorter sedation effect with methohexital, epileptogenic properties of methohexital and potential procedural variability our data provides further clinical data on the comparison between methohexital and amobarbital. Prospective studies involving comparison of methohexital and amobarbital and possibly propofol[20,21] or etomidate[22] in Wada testing, as well as other less invasive lateralization techniques may help in the future to define the ideal agent, test paradigm and protocol for selected patients.[17]

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