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Successful Adrenal Vein Sampling Using Dexamethasone Premedication in Patients With Iodine Contrast Media Allergy

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Abstract

Context: Preparation of patients with iodine contrast media (ICM) allergy who require adrenal vein sampling (AVS) to establish source of aldosterone excess of their confirmed primary aldosteronism (PA) is controversial. Usual premedication with high-dose prednisone can interfere with cortisol determinations, possibly altering the aldosterone to cortisol ratios for the identification of lateralized aldosterone excess.

Objective: We aimed to evaluate the efficacy and safety of premedication with high-dose dexamethasone to perform AVS in patients with ICM.

Methods: One hundred and seventy-seven consecutive patients with confirmed PA who underwent bilateral simultaneous basal and post-ACTH bolus AVS at our center between January 2010 and December 2020 were retrospectively analyzed for history of ICM allergy. A total of 7 patients (4%) with previous allergic reactions to ICM were prepared with 3 doses of 7.5 mg dexamethasone premedication rather than the usual 50 mg of prednisone.

Results: No breakthrough allergic reactions were reported in the 7 patients. Despite adequate serum cortisol suppression following dexamethasone, the basal and post-ACTH selectivity index were respectively > 2 and > 5 bilaterally in all patients, confirming adequate cannulation of both adrenal veins. Four patients had lateralized ratios (A/C ratio > 2 basally and > 4 post-ACTH), while 3 had bilateral source during AVS study. In the 3 patients undergoing unilateral adrenalectomy for lateralized source and contralateral suppression and adequate follow-up data, cure of PA was achieved at mean 58 months postoperatively.

Conclusion: AVS using dexamethasone premedication is safe and accurate for diagnosing the source of aldosterone excess in patients with PA and ICM allergy.

Key Words: adrenal vein sampling, dexamethasone, primary aldosteronism, iodine contrast allergy

Abbreviations: ACTH, adrenocorticotropic hormone; APA, aldosterone-producing adenoma; AVS, adrenal vein sampling; BAH, bilateral adrenal hyperplasia; DRC, direct renin concentration; DST, dexamethasone suppression test; GBCM, gadolinium-based contrast media; HPA, hypothalamic-pituitary-adrenal; ICM, iodine contrast media; LR, lateralization ratio; PA, primary aldosteronism; PAC, plasma aldosterone concentration; SI, selectivity index.

Primary aldosteronism (PA) is an increasingly frequent cause of secondary hypertension resulting from primary excess renin-independent aldosterone production; classically subtyped into a unilateral aldosterone-producing adenoma (APA) with suppressed contralateral aldosterone production, and bilateral adrenal hyperplasia (BAH) with distinct therapeutic implications [1-3]. Recently, an increased risk of both cardiovascular and cerebrovascular disease, especially stroke, was reported in PA when compared with essential hypertension [4, 5]. According to PA guidelines [6, 7] all patients with proven lateralized aldosterone production should be offered unilateral adrenalectomy, because it may lower cardiovascular events, compared to medical therapy, especially when renin remains suppressed despite high doses of mineralocorticoid antagonists [8, 9]. The optimal approach to adequately subtype PA into predominantly lateralized or bilateral disease is adrenal venous sampling,

which requires injection of contrast media to identify localization of adrenal veins [6, 7]. Hence, performing AVS in patients with iodine contrast media (ICM) allergy is challenging. Limited options are available for these patients and alternative subtyping techniques have been recently proposed in limited case reports: AVS with the use of either gadolinium-based contrast media (GBCM) for adrenal venography [10-12], or carbon dioxide (CO2) as a substitute for contrast dye [13], and NP59 (radioiodine-labeled cholesterol analogue) adrenal scintigraphy [14]. Each of these alternatives has its own limitations. Nephrogenic systemic fibrosis, a life-threatening, albeit rare side effect, is a potential side effect of GBCM, particularly in patients with advanced chronic kidney disease [15, 16]. The use of CO2 is also associated with technical difficulties because of its buoyancy and there is also the potential risk of air embolism [17]. Finally, adrenal iodocholesterol scintigraphy for PA

had relatively low success rate, as pretreatment with dexamethasone is required to decrease zona fasciculate uptake; in addition, imaging acquisitions are obtained 5 days after radioactive analogue administration, and the procedure is thus a lengthy one [18]. Traditionally, in patients with known or suspected ICM allergy who are undergoing vascular or imaging procedures requiring ICM, oral premedication with glucocorticoids (usually 3 doses of prednisone 50 mg), with or without nonselective antihistaminic drugs, is administered at 13, 7, and 1 hours prior to intervention to lower the likelihood of an allergic reaction [19]. In the case of AVS, this method has long been abandoned because prednisone can interfere with cortisol assays and suppress basal cortisol levels, rendering AVS interpretation difficult [13]. Only 1 case in the literature reported successful AVS with concomitant dexamethasone for ICM allergy [20]. In a recent case report, the authors commented that they used gadolinium since they believed that glucocorticoid pretreatment may alter AVS interpretation and is insufficiently safe to prevent ICM allergy [11]. As we have successfully utilized dexamethasone premedication for performing AVS in patients with ICM allergy in our center over several years, we performed the retrospective analysis of the 7 patients who were studied with this approach.

Methods

The electronic medical records of 177 consecutive patients with confirmed PA, who underwent AVS at our center between January 2010 and December 2020, were retrospectively analyzed. PA was confirmed according to the diagnostic criteria recommended by the Endocrine Society guidelines for the diagnosis and management of PA [6]. A 1-mg overnight dexamethasone suppression test (DST) was performed in 5 patients prior to AVS to rule out cortisol co-secretion, a potential confounder for interpretation of AVS results. Although the remaining 2 patients did not have a DST, their urinary free cortisol measurements were in the normal range before undergoing AVS (data not shown) and their serum cortisol was less than 50 nmol/L after high-dose dexamethasone preparation for AVS.

Only 7 patients (4%) had reported ICM allergy, ranging from diffuse cutaneous reactions in most patients or reported angioedema in only 1. Written informed consent was obtained from all 7 patients to perform the AVS with concomitant use of dexamethasone per our center's protocol: either 6 or 7.5 mg of dexamethasone was taken orally at 6 PM and midnight the night before the procedure and at 6 AM the morning of the procedure; 25 mg of diphenhydramine, a first-generation nonselective antihistamine, was taken along with the 6 AM dose. The AVS procedure at our center was performed by an experienced angioradiologist with a high rate of successful adrenal vein catheterization, via a bilateral femoral venous approach [21]. Blood samples for both aldosterone and cortisol measurements, were collected simultaneously from left and right adrenal veins and the periphery (i.e., the left iliac vein). Two basal time points (T −5 and T 0) were collected, followed by a bolus injection of 250 mcg of adrenocorticotropic hormone (ACTH) 1-24 (Cortrosyn, Organon Canada), with blood samples subsequently drawn at 5-minute intervals (T 5, T 10, and T 15). Venography of bilateral renal and adrenal veins, using intravenous ICM, was conducted at the time of catheter insertion and at the end of the procedure to verify adequate localization of the catheters. Iodixanol 270 mg/mL (Visipaque 270, GE Healthcare), an iso-osmolar iodine contrast medium, was administered as necessary to adequately position the catheter in the adrenal veins (from 20 to 100 mL).

Successful AVS was defined according to the selectivity index (SI), (cortisol adrenal vein/cortisol peripheral vein > 2 without stimulation or > 5 post-ACTH). Lateralized source of aldosterone was confirmed with either a basal lateralization ratio (LR) ≥ 2 or post-ACTH ≥ 4 [21].

Data regarding medical treatment or post-adrenalectomy follow-up was available in 6 out of 7 patients, allowing us to assess biochemical or clinical cure and accuracy of AVS results with concomitant use of dexamethasone. Cure of PA following adequate management was defined as either a clinical cure such as normotension without use of antihypertensive medications after adrenalectomy or unsuppressed direct renin concentration (DRC) (> 10 ng/dL) after adrenalectomy or under treatment with a mineralocorticoid receptor antagonist in patients with a bilateral aldosterone source.

The Centre hospitalier de l'Université de Montréal (CHUM) institutional review board granted permission to analyze and publish these results without written consent from the patients, because of the retrospective and anonymous nature of the study.

Hormone Assays

Several assays were used to measure plasma aldosterone concentration (PAC) during the period of the study, the latest being the DIAsource Aldosterone radioimmunoassay kit (DiaSource Diagnostics, Cat# 5331235, RRID:AB_2916289). Coefficients of variation of all assays were less than 10%. Serum cortisol was measured using the Access Cortisol chemiluminescence enzyme immunoassay kit antibody (Beckman Coulter Cat# 33600, RRID:AB_2802133) with a coefficient of variation < 8%. However, cross-reactivity exists with several exogenous glucocorticoid compounds, dexamethasone having negligible cross-reactivity. Hence, we opted to use dexamethasone in our iodine allergy premedication protocol.

Results

Demographic and baseline characteristics of all 7 patients are shown in Table 1. A descriptive analysis was conducted, with all results for quantitative variables expressed as means ± SD. The mean age at the time of AVS procedure was 55.1 ± 16.8 years. Patients had been hypertensive for a mean of 6.7 ± 5.9 years. Then mean systolic blood pressure on the day of the procedure was 137.4 ± 4.2 mmHg and the mean diastolic blood pressure 77.1 ± 12.9 mmHg. No evidence of cortisol co-secretion was found in any patient, as shown in Table 1. Even though 1 mg DST results were missing for 3 patients, no record of hypercortisolism was found in their electronic medical records. Most patients had at least 2 antihypertensive medications in their drug regimen prior to AVS procedure, none being mineralocorticoid receptor antagonists.

No adverse reactions or complications were reported by any of the 7 patients following AVS performed under dexamethasone and diphenhydramine premedication.

Table 1. Demographic and baseline characteristics of the 7 patients who underwent AVS with dexamethasone premedication

Patients	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Allergy reaction recorded in medical file	N/A	N/A	Angioedema	cutaneous	cutaneous	N/A	cutaneous
Sex	M	M	F	F	M	M	M
Age at time of AVS (years)	65	72	65	29	38	69	48
Hypertension duration (years)	7	2	15	2	3	15	3
Number of antihypertensive medications	2	0	3	2	2	3	3
Potassium (mmol/L)	3.9	4	4.2	4.3	3.8	3.9	4.2
Creatinine (µmol/L)	73	75	79	47	75	98	82
Potassium supplementation (mmol/day)	125	0	40	120	60	20	0
Aldosterone (pmol/L)	2035	352	611	626	1123	942	590
Renin (PRA) (ng/mL/h)	0	0.2	0.19	N/A	N/A	N/A	N/A
Renin (DRC) (ng/dL)	N/A	N/A	N/A	2.49	3	1.7	4
ARR (PRA) (pmol/L/ng/ml/h)	2035	1760	3215	N/A	N/A	N/A	N/A
ARR (DRC) (pmol/L/ng/dL)	N/A	N/A	N/A	251	374	554	147.5
Adrenal imaging	Bilateral adrenal nodules	Left adrenal nodule	Right adrenal nodule	Right adrenal nodule	No adrenal nodules or masses	Right adrenal nodule	Left adrenal nodule
Nodule size (mm)	Small, less than 10 mm	10	17	17	N/A	18	17
DST (nmol/L)	37	8	N/A	N/A	17	37	17

Abbreviations: ARR, aldosterone to renin ratio; AVS, adrenal vein sampling; DRC, direct renin concentration; DST, 1-mg overnight dexamethasone suppression test; N/A, not available; PRA, plasma renin activity.
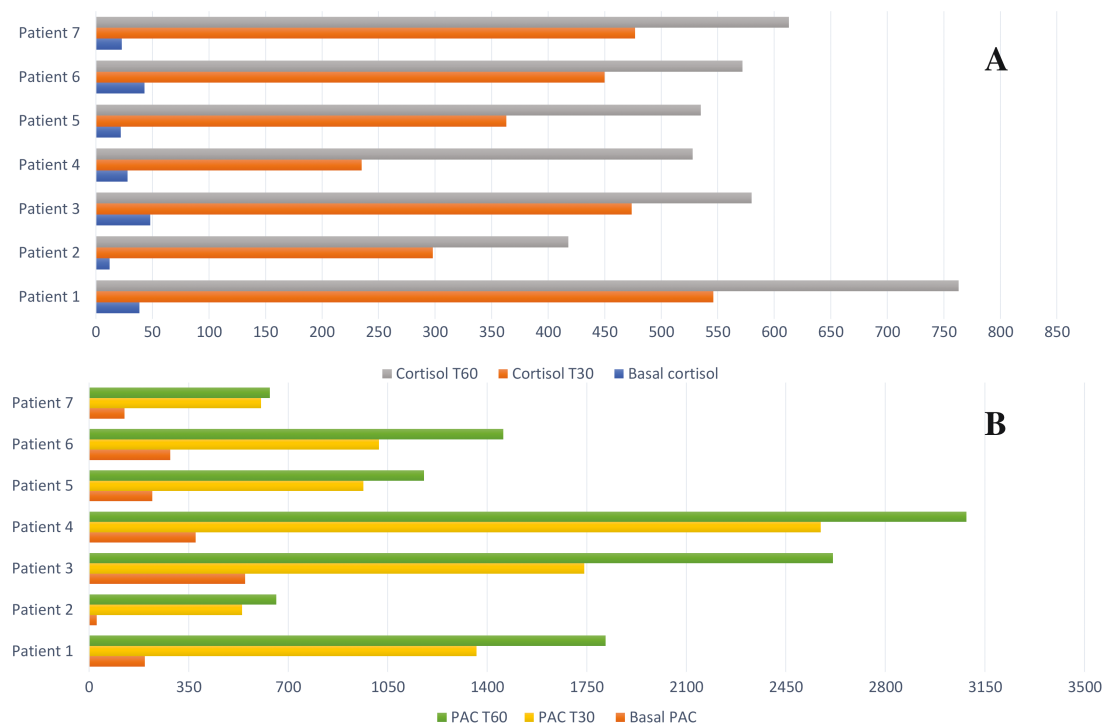
Figure 1. Basal (average of T −5 minutes and T 0 minutes) and post-ACTH (T 30 minutes and T 60 minutes) peripheral cortisol (nmol/L) (1A) and aldosterone (pmol/L) measurements (1B), data following dexamethasone premedication.

Dexamethasone Suppression Effect on AVS

As shown in Fig. 1, all basal peripheral cortisol levels were suppressed, < 50 nmol/L, confirming adequate ACTH suppression and lack of meaningful cortisol co-secretion. In our center, a normal maximal cortisol response to a 250 mcg ACTH stimulation test is above 420 nmol/L. Despite dexamethasone administration, cortisol response to ACTH was adequate, rising above 420 nmol/L at T = 60 minutes for all 7 patients, except 1 who had borderline increase (418 nmol/L), but considered sufficient to allow AVS interpretation.

Basal peripheral PAC was also reduced by dexamethasone administration with values below 300 pmol/L in 5 of 7 patients. Compared with PAC measured during PA diagnosis investigation (ambulatory and 15 minutes in seated posture), basal peripheral values of PAC during AVS (in supine posture) were reduced by an average of 66% ± 30% following dexamethasone premedication. Nevertheless, peripheral PAC also increased following ACTH bolus injection with an average rise of 698.8% ± 644.5% from baseline.

AVS Results

Bilateral AVS selectivity was successful in all 7 patients in spite of dexamethasone suppression, with a mean right SI of 10.3 ± 4.3 and left SI of 7.5 ± 1.64, at baseline, without ACTH stimulation. The mean post-ACTH SI was 181.6 ± 119.2 on the right and 149.1 ± 66.3 on the left.

Table 2 shows the LRs in all patients with subsequent management (medical vs surgical) and clinical or biochemical cure. Follow-up data for a mean of 58 ± 41.4 months was available for 6 patients. Of these 6 patients, 3 had lateralization to the right adrenal gland on AVS, based on both basal and post-ACTH LRs, with contralateral suppression $(PAC_{contralateral\ (CL)}/PAC_{peripheral\ (p)} < 1.5)$ in all 3 patients. Furthermore, these results were confirmed by the finding of an adrenocortical adenoma at histopathology following successful right adrenalectomy in all 3 patients and clinical (n = 3) or biochemical cure (n = 2) at follow-up. Immunohistochemistry of aldosterone synthase expression was not yet available in our center at the time of those adrenalectomies. A representative example of detailed AVS results and interpretation for patient #3 with right lateralization is shown in Fig. 2.

Among the 3 patients with bilateral aldosterone source on AVS, all had adrenal imaging compatible with unilateral disease. Only 1 patient had a normalized DRC > 10 ng/dL with mineralocorticoid receptor antagonists exclusively. However, all 3 had normal blood pressure on relatively low dose spironolactone (25-50 mg daily) in combination with other antihypertensive medications. A detailed representative example of AVS results and interpretation for patient #7 with bilateral aldosterone excess source is shown in Fig. 2.

Discussion

Our results demonstrate that AVS performed under dexamethasone premedication is safe and reliable in subtyping PA and can achieve postoperative cure in lateralized PA. In our cohort of patients, only 4% had a reported ICM allergy, mostly mild or moderate reactions. Battistel et al had previously found that 2.6% of their patients who presented for AVS had a history of severe allergic reaction to contrast dye; they had excluded patients with mild reactions in their cohort, possibly explaining the higher prevalence in our study [13]. ICM is relatively rare, and severe allergic reactions using modern imaging procedures are rare, especially with the wider use of low or iso-osmolar ICM in clinical practice, which can result in less and milder allergic reactions [19, 22-27]. In a large multicenter study, the prevalence of any hypersensitivity

Table 2. AVS results in the 7 patients with subsequent therapy and clinical or biochemical cure

Patients	Lateralization	Basal LR	Post-ACTH LR	PAC_{CL}/PAC_P	Management	Pathology	Initial adrenal imaging	Clinical/biochemical cure post op	Follow-up period (months)
Patient 1	Right lateralization	61.4	45.81	1.36	N/A	N/A	Bilateral adrenal nodules	N/A	N/A
Patient 2	Bilateral source	1.53	1.55	61.61	Spironolactone 25 mg daily	N/A	1 cm left adrenal nodule	Normotension DRC 5 ng/dL	120
Patient 3	Right lateralization	71.18	26.85	1.56	Right adrenalectomy	adenoma 2 cm	1.7 cm right adrenal nodule	Normotension No medication DRC 206 ng/dL	72
Patient 4	Right lateralization	36.35	46.08	1.15	Right adrenalectomy	adenoma 1.3 cm	1.7 cm right adrenal nodule	Normotension No medication	84
Patient 5	Right lateralization	52.34	73.3	0.93	Right adrenalectomy	adenoma 1.1 cm, with surrounding cortical hyperplasia	Normal adrenals on imaging	Normotension No medication DRC 12 ng/dL	15
Patient 6	Bilateral source	1.4	2.11	31.77	Spironolactone 50 mg daily	N/A	1.8 cm right adrenal nodule	Normotension DRC 1.6 ng/dL	40
Patient 7	Bilateral source	1.84	1.53	25.87	Spironolactone 37.5 mg daily	N/A	1.7 cm left adrenal nodule	Normotension DRC 93 ng/dL	17

Abbreviations: DRC, direct renin concentration; LR, lateralization ratio; N/A, not available; PAC_{CL}/PAC_P, plasma aldosterone concentration contralateral/plasma aldosterone concentration peripheral.

reaction to ICM administration was 0.73%, while that of severe reactions was 0.01% [28]. Risk factors for ICM allergy include a history of a prior reaction [22, 25, 28-30], especially a severe one [30], hyperthyroidism [28], other known allergies [25, 28-30], a family history of ICM allergy [28], diabetes [30], and contrast agent dose > 65 g [29]. Premedication with glucocorticoids [31-33] and an antihistamine medication [28] as well as, changing the culprit ICM [28, 30] have been shown to be useful in reducing likelihood of allergic reactions recurrences. Nonetheless, 1 study reported no protective effect of premedication with glucocorticoids [30] and another one showed that the estimated number needed to treat to prevent any type of reaction was 69, while 569 patients would be needed to be premedicated to prevent a serious reaction [33]. Thus, the American College of Radiology (ACR) considers corticosteroid premedication when ICM is absolutely necessary and cannot be substituted by another contrast agent, while stating that efficacy in preventing severe adverse reactions in high-risk patients is not absolute [19].

As such, alternative options are being suggested for patients with PA who have a history of ICM allergy and require AVS to guide therapeutic management, although not all have proven to have a high diagnostic accuracy [10, 11, 13, 14]. Our results show that patients with ICM allergy also benefit from AVS despite premedication with a glucocorticoid. In our center, we used a premedication protocol in line with ACR recommendations to perform AVS in at-risk patients [19], based on oral glucocorticoids given at least 13 hours prior to procedure then again the morning of the procedure with a nonselective antihistamine. We chose the dose of 7.5 mg dexamethasone based on its 25- to 30-fold anti-inflammatory activity compared with hydrocortisone, while prednisone was estimated to have a 4-fold higher anti-inflammatory activity compared to hydrocortisone. During the AVS procedure, the lateralization ratio utilizes the cortisol concentration to correct the differences in blood flow and dilution by renal vein contamination in the left adrenal vein; the ratios of aldosterone/cortisol are compared between each adrenal vein. We opted for dexamethasone as our premedication of choice as it would not interfere with cortisol assays but is expected to suppress hypothalamic-pituitary-adrenal (HPA) axis. In fact, the second-generation competitive chemiluminescent immunoassay used to measure cortisol concentrations in our center, has negligible cross-reactivity with dexamethasone compared to prednisone and cortisone [34]. Dexamethasone is a potent synthetic glucocorticoid capable of suppressing the HPA axis, even in the acute setting [35], as demonstrated by suppressed basal peripheral cortisol levels in all 7 patients who underwent AVS with dexamethasone premedication. Regardless, post-ACTH response was normal for all patients and the SI was not affected by dexamethasone suppression. All 7 patients had selective AVS bilaterally based on basal and post-ACTH SIs. Contrary to our results, Battistel et al, were not able to document adequate adrenal vein catheterization following premedication with steroids in 3 out of 4 patients, nor were they capable of ascertaining aldosterone lateralization [13].

In addition, we noticed that the basal aldosterone concentrations were also reduced following dexamethasone administration by an average of 66% from pre-AVS values, with a significant post-ACTH response averaging a 700% increase from baseline. ACTH bolus has been shown to produce a larger aldosterone increase in patients with PA, regardless of

Patient 3

Time	Right adrenal vein			Left adrenal vein			R/L Ratio	L/R Ratio	Peripheral vein		
	PAC	Cortisol	PAC/C	PAC	Cortisol	PAC/C	PAC/C	PAC/C	PAC	Cortisol	PAC/C
minutes	pmol/L	nmol/L		pmol/L	nmol/L				pmol/L	nmol/L	
"-5	91118	427	213.39	823	279	2.95	72.34	0.01	487	49	9.94
0	97244	387	251.28	872	243	3.59	70.02	0.01	611	47	13.00
+5	200605	9346	21.46	10499	7217	1.45	14.75	0.07	695	80	8.69
+10	373712	13228	28.25	12047	11448	1.05	26.85	0.04	1039	222	4.68
+15	371533	13652	27.21	15033	10279	1.46			1236	309	4.00
+30									1741	474	3.67
+45									2040	528	3.86
+60									2616	580	4.51

R basal SI	8.47	L basal SI	5.43
R ACTH SI	116.83	L ACTH SI	90.21
basal LR	71.18	Basal PAC CL / PAC P	1.56
ACTH LR	26.85		

Patient 7

Time	R adrenal vein			L adrenal vein			R/L Ratio	L/R Ratio	Peripheral vein		
	PAC	Cortisol	PAC/C	PAC	Cortisol	PAC/C	PAC/C	PAC/C	PAC	Cortisol	PAC/C
minutes	pmol/L	nmol/L		pmol/L	nmol/L				pmol/L	nmol/L	
"-5	3720	173	21.50	3220	192	16.77	1.28	0.78	131	22	5.95
0	6197	200	30.99	3204	247	12.97	2.39	0.42	118	24	4.92
+5	47633	20000	2.38	28820	18550	1.55	1.53	0.65	139	77	1.81
+10	49017	22400	2.19	47229	24550	1.92	1.14	0.88	278	255	1.09
+15	58880	24550	2.40	51560	24150	2.13	1.12	0.89	432	333	1.30
+30									605	477	1.27
+45									616	547	1.13
+60									635	613	1.04

R basal SI	8.10	L basal SI	9.51
R ACTH SI	259.74	L ACTH SI	240.91
Basal LR	1.84	Basal PAC CL / PAC P	25.87
ACTH LR	1.53		

C: cortisol; CL: contralateral; L : left; LR: lateralization ratio; P: peripheral vein; PAC: plasma aldosterone concentration; R: right; SI: selectivity index

Figure 2. A representative example of AVS results and interpretation, for patient #3 with right lateralization and patient #7 with bilateral aldosterone source, data following dexamethasone premedication.

etiology, than the normal 2-fold increase seen with normal subjects [36]. The same study demonstrated reduced aldosterone concentrations following 1 mg dexamethasone suppression, most apparent in patients with BAH [36]. Other studies also reported increased aldosterone production in response to ACTH stimulation in PA, although the increase was most significant in APA and unilateral hyperplasia, allowing authors to advocate its use for PA subtyping [37-39]. Analysis of adrenal tissues resected from patients with PA and normal subjects, demonstrated variable increased expression of several G-protein coupled receptors mRNA, including the MC2R, explaining aldosterone's excessive response to ACTH in PA [40]. Therefore, one might expect that dexamethasone premedication would blunt not only the HPA axis but also aldosterone levels; despite this suppression, we were still able to clearly identify the source of aldosterone excess in all 7 patients studied using premedication with dexamethasone. The lower aldosterone concentrations at baseline can also be secondary to the important effect of posture on aldosterone production in PA, as patients undergoing AVS are in a supine position for several minutes prior to the procedure [41]. St-Jean et al have previously demonstrated the renin-independent important increase in aldosterone levels during upright posture in patients with PA either from APA or BAH [36].

When interpreting AVS results, we used the following cutoffs for lateralized PA: LR ≥ 2 or post-ACTH ≥ 4 [21]. In all 3 patients in our cohort that lateralized to the right, both basal and post-ACTH LRs were concordant, despite dexamethasone use. Our group previously demonstrated the importance of basal LRs in the interpretation of AVS results, particularly when basal and post-ACTH ratios are discordant [21, 42]. We also demonstrated that the ratio PAC_{CL}/PAC_p was superior to that of $PAC/C_{CL}/PAC/C_p$ for contralateral suppression assessment [21, 42]. Therefore, we used $PAC_{CL}/PAC_p < 1.5$ to determine contralateral suppression in our patients. Two patients had a ratio < 1.5 and the third was borderline at 1.56; however, all 3 had ratios < 2.15, which was found to be best associated with clinical and biochemical postoperative cure [42]. All 3 patients underwent unilateral right adrenalectomy and had a confirmed pathologic diagnosis of APA with postoperative cure of PA. This supports that the AVS results are accurate and reliable despite dexamethasone use, which is consistent with a recent report by Prins et al [20].

Reference ranges for catecholamine concentrations in adrenal veins were obtained during AVS in patients with cortisol-producing adrenal tumors or PA in 2 different studies [43, 44]. This method was mostly used in cases of adrenal Cushing syndrome secondary to bilateral adrenal masses, where correct catheterization of an adrenal vein was determined based on a difference of 100 pg/mL of plasma epinephrine between the adrenal vein and the peripheral vein [45, 46]. A recent retrospective study of 101 patients undergoing AVS for PA [47] reported that epinephrine measurement during AVS is useful to predict successful cannulation of adrenal veins, especially in patients with unsuccessful cannulation based on the traditional SI. In patients with ICM allergy that are premedicated

with prednisone, a possible alternative for the use of cortisol measurements to correct for blood flow during AVS, is the use of catecholamine measurement. However, glucocorticoids can increase epinephrine secretion and their half-lives may be too short compared to that of cortisol resulting in inaccurate aldosterone to catecholamines ratios.

Other alternatives to dexamethasone premedication were the use of GBCM or CO2 during AVS, as described in 4 case reports [10-13]. Allergic reactions to GBCM occurred in 0.04% to 0.17% of patients [23, 26, 48], less common than ICM allergy. Only 0.024% of patients had a reaction to both ICM and GBCM [48]. Yet, both techniques are not without toxicities and technical difficulties [15-17, 49]. Finally, sensitivity of adrenal scintigraphy to identify lateralized PA is highly variable, and with less accuracy for small adrenal lesions [14, 18, 50-54]. Because dexamethasone is often given 2 to 7 days before injection of radiotracer and continued during imaging acquisitions in adrenal scintigraphy to reduce uptake by zona fasciculate and reticulate, aldosterone may be suppressed for a longer period of time, explaining the lower sensitivity of adrenal scintigraphy under dexamethasone [53]. This was not an issue in this study as dexamethasone was administered only a few hours before AVS.

The main limitation of this report is that only 7 patients with ICM allergy were included in our analysis. Additionally, most of our patients had history of only mild to moderate allergic reactions to ICM. While severe reactions are rarely described, we could not study safety and reliability of AVS under dexamethasone in such patients.

Conclusion

This study provides the largest number of patients with PA and ICM allergy who underwent successful AVS with dexamethasone premedication. Dexamethasone did not affect AVS interpretation, neither for the SI nor for the LR (basal and post-ACTH). Correct lateralization with subsequent unilateral adrenalectomy was achieved, with documented cure of PA on postoperative follow-up. Although no adverse reaction was reported in our patients despite known allergy to ICM, dexamethasone premedication should be reserved to patients with PA presenting with severe clinical features such as hypokalemia, multidrug resistant hypertension, and cardiovascular comorbidities, who would mostly benefit from surgery and require documentation of lateralized disease. Prospective multicenter collaborative studies with a larger number of patients would be useful to confirm the usefulness of premedication with dexamethasone to perform AVS in patients with ICM allergy.

Author Contributions

A.L. conceived the objectives and plan of this report, N.Y. performed the data analysis and wrote the first draft of the manuscript. E.T., I.B., and A.L. critically revised the article. All authors approved the final manuscript.

Disclosure Summary

The authors have nothing to disclose.

Data Availability

Some or all datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

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