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Intradialytic Hypotension during Dialysis for Acute Kidney Injury in Congolese Patients: Prevalence, Risk factors and Outcome

Hypotension intra dialytique en cas d'agression rénale aigüe chez les patients Congolais : fréquence, déterminants et issue

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Résumé

Contexte et objectif. En dépit des progrès faits dans l'hémodialyse (HD), l'hypotension intradialytique (hID) reste courante. Les objectifs de la présente étude étaient de déterminer l'ampleur et l'issue de l'hID lors des séances d'hémodialyse pour agression rénale aigüe (ARA). *Méthodes*. Etude documentaire des patients souffrant d'ARA requerant des séances d'HD réalisées dans 2 centres HD de Kinshasa entre 2008 et 2018. L'hID était définie par la pression systolique sanguine (PAS) < 90 mmHg ou une baisse d'au moins 40 mmHg durant la séance d'HD. Les déterminants de l'hID ont été recherchés par l'analyse de régression logistique multivariée. *Résultats*. Soixante-trois patients (41,0 ± 15,7 ans, 65% d'hommes) ont été inclus. Ils ont réalisé 219 séances. La fréquence de l'hID était de 8,7%. Elle était associée à un volume d'ultrafiltration horaire > 750 ml [p = 0,017; OR a 1,97 (1,12-4,21)], une anurie [p = 0,021; ORa 2,72 (1,33-6,19)], une session de plus de 3 heures [p = 0,025; ORa 2,78 (1,48-6,05)], un sepsis [p = 0,020; ORa 3,89 (1,24-12,18)], une PAS initiale plus basse [p <0,001; ORa 0,97 (0,96-0,98)] et une déshydratation [p = 0,032; ORa 5,57 (1,16-26,64)]. Aucun décès n'a été signalé. *Conclusion*. En cas de dialyse aiguë, environ 1 séance sur 12 se complique d'hiD liés au patient et à l'HD elle-même. Une prise en charge anticipative est à encourager pour assurer une meilleure sécurité des patients.

Mots-clés: hypotension intra dialytique, Kinshasa, agression rénale aiguë
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Summary

Context and objective. Despite progress in hemodialysis (HD), intradialytic hypotension (IDH) remains common. This study aimed to determine the frequency, risk factors and outcome of IDH during acute hemodialysis. *Methods*. We compiled the records of acute HD sessions in 2 HD centers of Kinshasa between 2008 and 2018. IDH was defined by blood systolic pressure <90 mmHg or a drop of ≥ 40 mmHg during HD session. The risk factors for IDH were defined by logistic regression. *Results*. 63 patients (41.0 ± 15.7 years, 65 % man) were included. They performed 219 sessions including 169 conventional HD and 50 hemodiafiltrations (HDF). The prevalence of IDH was 8.7%. It was associated with an hourly ultrafiltration volume> 750 ml [p=0.017; aOR 1.97 (1.12-4.21)], anuria [p=0.021; aOR 2.72 (1.33-6.19)], a session of more than 3 hours [p=0.025; aOR 2.78 (1.48-6.05)], sepsis [p=0.020; aOR 3.89 (1.24-12.18)], lower initial systolic blood pressure [p<0.001; aOR 0.97 (0.96-0.98)] and hydration status [p=0.032; aOR 5.57 (1.16-26.64)]. No deaths have been reported, but we had 3 ICU admissions. *Conclusion*. In the event of acute dialysis, approximately 1 session in 12 is complicated by IDH with a good prognosis. This depends on factors related to the patient and to the dialysis method itself.

Key-words: Intradialytic hypotension, Kinshasa, acute kidney injury

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Introduction

Intradialytic hypotension (IDH) is one of the most frequent complications in conventional hemodialysis (HD) for acute kidney injury (AKI), and relates to 5-20% of HD sessions, depending of the definition used (1-3). It occurs once the intravascular volume reaches the threshold of 50 mL/kg of body weight (4). Before that happens, the body uses other mechanisms to keep mean arterial pressure (MAP) stable despite the decrease in pulse pressure (PP): a sympathetic stimulation results in peripheral vasoconstriction and tachycardia, a stimulation of the renin angiotensin aldosterone system (4). IDH is a worrying problem because of its association with an increased incidence of cardiovascular events (arrhythmia, myocardial ischemia, thrombosis, etc), loss of residual urine volume, vascular access failure and mortality (4-5).

Pathophysiologies of IDH and methods to prevent this complication have been extensively investigated (4). Over the years, HD techniques have improved, and there is more attention for the prevention of HD hypotension, for example, by lowering the dialysate temperature and monitoring of relative blood volume changes (4, 6-7). At the same time, the average age of dialysis patients as well as the proportion of patients with significant comorbidities such as diabetes mellitus and heart failure has increased worldwide (8).

In a multicenter prospective cohort study from Kinshasa hospitals, Masewu *et al* observed that AKI is a prevalent problem in intensive care unit (ICU) and it affects short-term survival of critically ill patients, multiplying by six the risk of dying versus patients without AKI, especially during the first 3 days of hospitalization (9). The development of HD centers in Kinshasa, and gradually in other towns of DR Congo, has saved lives of many patients suffering from severe AKI. In order to assess the tolerance of the HD technique in patients with severe AKI, the objectives of this study were to determine the frequency and risk factors of IDH, to describe the treatment administered to patients with IDH, and specify their outcome.

Methods

The study was conducted in dialysis centers of Kinshasa University Hospital (KUH) and Ngaliema Medical Center (NMC) by collecting data from January 2008 to December 2018. We have included all patients with AKI in whom HD was performed. Our sampling was exhaustive given the limited number of cases. Each HD session constituted a statistical unit. Patients with confirmed or suspected chronic kidney disease (CKD) were excluded from the study.

Collected data

The following data was collected in the present study:

- Sociodemographic data: age, sex;
- Clinical data: weight at the start and at the end of each HD session, heart rate (HR) and Glascow Coma Scale (GCS) before, during and at the end of the HD session, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), pulse pressure (PP) before, during and at the end of the HD session.

Blood pressure (BP) was measured in the sitting position immediately prior to the start of the dialysis treatment using integrated automatic oscillometric devices. During the procedures, BP monitoring was performed every 30 min.

- Treatment that patients received and comorbidities;
- Biological data: urea, creatinine and potassium levels in the blood before the HD session;
- Etiologies of AKI: pre-renal, renal or post-renal;
- Indications for dialysis: acute pulmonary edema (APE), threatening hyperkalemia, uremic coma, anuria, severe acidosis, other indications;
- Data related to the HD session: technique used (conventional HD or hémodiafiltration=HDF), blood flow rate (BFR), duration of HD session, ultrafiltration rate (UFR), ultrafiltration profile (standard or sloping), value of the sodium conductivity, temperature of the dialyzate, type of buffer (acetate or bicarbonate), total dose of

anticoagulant, dialysis range (first session, second session, third, ...);
- During the session, the management/treatment received in the event of IDH: Trendelenburg position, reduction of the BFR, reduction of the UFR, increase in sodium conductivity, infusion of solutes during the session (crystalloids, macromolecules, hypertonic glucose), recourse to vasoactive amines, recourse to anti-arrhythmics, oxygen supply, mechanical ventilation, cardiac massage, the presence of the doctor (nephrologist), the presence of the resuscitator;
- Outcome of unstable patients: stopping or continuing the dialysis session, transfer to the intensive care unit (ICU), death or survival.

Operational definitions

The main variables of the present study are defined as follows:
- IDH: was defined as systolic blood pressure at nadir less than 90 mmHg or a decrease of at least 40 mmHg in hypertensive patients (10);
- Intradialytic tachycardia: increase in heart rate of more than 20 bpm during the HD session or at the end of the HD session (10);
- Intradialytic bradycardia: when the heart rate drops below 55 bpm during the HD session or at the end of the HD session (10);
- Intradialytic arrhythmia/cardiac arrest: appearance of the complication during or at the end of the HD session (10);
- Hemodynamic parameters during HD session: average of all the parameters taken during the HD session (parameters at the start and at the end of the session being excluded);
- Uremic coma: was defined as coma in setting of patient with AKI AKIN stage 3;
- Severe acidosis: was defined in the setting of patient with alkaline reserve less than 12;
- Anuria was defined as passage of less than 100 milliliters of urine in day.

Statistical analysis

Statistical analyzes were performed using SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Each HD session was considered to be a statistical unit. Comparisons between groups were performed using Student's t test, Fisher's exact test, Mann-Whitney test and Pearson Chi square test, as appropriate. Logistic regression analysis was used to identify risk factors of IDH. Association measures were calculated with 95% confidence intervals. $P< 0.05$ defined the level of statistical significance.

Ethical considerations

The data was collected anonymously and confidentially. The privacy and personalities of patients have been preserved according to the Helsinki Declaration.

Results

General characteristics and particularities of dialysis sessions

63 patients (41 men [65%] and 22 women [35%]) were included in the study. Their average age was 41.0 ± 15.7 years. Men were older than women (43.9 ± 15.9 years vs 35.6 ± 14.2 years; p=0.035). The reported comorbidities were arterial hypertension (5 cases), diabetes (2 cases), heart disease (2 cases), HIV infection (1 case) and viral hepatitis C (1 case). The causes of AKI in the present study encompasses sepsis (n=25), malaria (n=23), Non-steroidal anti-inflammatory drug (n=5), Obstructive uropathy (n=4), Shock (n=4), Severe dehydration (n=3), nephrotoxic plants (n=2) and Ovarien hyperstimulation syndrome (n=2).

During the study, 219 dialysis sessions were evaluated (63 first sessions and 156 later sessions), i.e. an average of 3.5 ± 1.4 sessions per patient, with the extremes of 1 and 16 sessions. Conventional HD represented 77% of sessions vs 23% for HDF. We noted that prolonged anuria, hyperkaliemia, uremic coma and acute pulmonary edema were the main indications for both conventional HD and HDF. Severe acidosis was more common when HDF was indicated (Table 1).

Table 1. Indications of HD sessions in the study population

Indications	All sessions, n=219	HD, n=169	HDF, n=50	p value
Hyperkalaemia > 6.5 mmol/l	40 (18.3)	34 (20.1)	6 (12.0)	0.192
Acute pulmonary edema	52 (23.7)	40 (23.7)	12 (24.0)	0.961
Severe acidosis	10 (4.6)	4 (2.4)	6 (12.0)	0.011
Uremic coma	37 (16.9)	31 (18.3)	6 (12.6)	0.752
Anuria > 12 hours	61 (27.9)	50 (29.6)	11 (22.0)	0.293
Anuria > 6 hours	80 (36.5)	59 (34.9)	21 (42.0)	0.360

Results are presented as absolute frequency (%)

The dialysis parameters were identical regardless of the technique used (HD or HDF). However, in HDF sessions, sloping ultrafiltration was used more frequently and several sessions were performed without resorting to anticoagulants. The majority of sessions lasted at least 3 hours. Only bicarbonate was used as a buffer for dialysis. The mean sodium conductivity was 138.2±1.2 µs/cm, and the mean dialyzate temperature was 36.9 ± 0.2 °C (Table 2).

Table 2. Dialysis parameters in the study population

	All sessions, n=219	HD, n=169	HDF, n=50	P value
Duration of treatment, hours	3.5 ± 0.8	3.5 ± 0.8	3.3 ± 0.9	0.189
2 < hours	47 (21.5)	33 (19.5)	14 (28.0)	0.368
2 - 3 hours	19 (8.7)	14 (8.3)	5 (10.0)	
≥ 3 hours	153 (69.9)	122 (72.2)	31 (62.0)	
Bicarbonate	219 (100.0)	169 (100.0)	50 (100.0)	-
Initial ultrafiltration modality				
Sloping mode	22 (10.0)	0	22 (44.0)	< 0.001
Standard mode	197 (90.0)	169 (100.0)	28 (56.0)	
UFR/session, Ml	1873 ± 874	1852 ± 891	1948 ± 816	0.503
Na conductivity, µs/cm	138.2 ± 1.2	138.2 ± 1.1	138.3 ± 1.6	0.882
Dialysate temperature, °C	36.9 ± 0.2	36.9 ± 0.2	36.7 ± 0.3	< 0.001
Dose of anticoagulant, UI	4108 ± 1440	4147 ± 1509	3935 ± 1071	0.439
Sessions without anticoagulant	32 (14.6)	16 (9.5)	16 (32.0)	< 0.001

Results are presented as absolute frequency (%) or as mean ±standard deviation

The comparison of the hemodynamic parameters between the two techniques did not show any statistically significant difference before, during and at the end of the treatment sessions (table 3).

Table 3. Hemodynamic parameters in the study population

Variables	All sessions, n=219	HD, n=169	HDF, n=50	p value
At the start of dialysis				
SBP, mmHg	138.3 ± 19.8	138.7±19.5	137.0±20.9	0.596
DBP, mmHg	78.1 ± 14.3	78.2 ± 14.4	77.6 ± 14.1	0.782
MAP, mmHg	98.2 ± 14.2	98.4 ± 14.2	97.4 ± 14.5	0.666
PP, mmHg	60.3 ± 17.2	60.5 ± 17.1	59.4 ± 17.6	0.703
HR, bpm	88.7 ± 22.1	88.2 ± 21.8	90.3 ± 23.3	0.546
During of dialysis				
SBP, mmHg	143.2 ± 26.8	142.8±26.8	144.6±26.9	0.680
DBP, mmHg	78.9 ± 17.9	78.9 ± 17.9	79.0 ± 18.3	0.986
MAP, mmHg	150.6 ± 29.0	150.4 ±28.9	151.3±29.7	0.841
PP, mmHg	64.2 ± 18.9	63.8 ± 19.2	65.5 ± 18.2	0.570
HR, bpm	90.6 ± 24.8	90.7 ± 23.1	90.4 ± 30.1	0.950
At the end of dialysis				
SBP, mmHg	142.7 ± 20.7	141.9±20.5	145.3±21.3	0.309
DBP, mmHg	79.4 ± 16.8	79.2 ± 16.7	80.2 ± 17.2	0.690
MAP, mmHg	100.8 ± 15.6	100.4±15.4	101.9 ±16.4	0.542
PP, mmHg	62.9 ± 17.6	62.3 ± 17.1	65.1 ± 19.1	0.327
HR, bpm	89.4 ± 25.8	90.0 ± 25.5	87.3 ± 27.2	0.511

Results are presented as means ± standard deviation. Abbreviations: DBP= diastolic blood pressure, SBP=systolic blood pressure, MAP=mean arterial pressure, PP=pulse pressure, HR=heart rate, bpm=beats per minute.

Prevalence of intradialytic hypotension

Depending on the technique used, 8 to 10 percent of dialysis sessions were complicated by IDH. The other complications observed were tachycardia and bradycardia. Arrhythmia and cardiac arrest were rarely reported (table 4).

Table 4. Complications during HD sessions

Complications	All sessions, n=219	HD, n=169	HDF, n=50	p value
IDH	19 (8.7)	14 (8.3)	5 (10.0)	0.446
Arrhythmia	2 (0.9)	2 (1.2)	0	0.595
Cardiac arrest	2 (0.9)	0	2 (4.0)	0.051
Tachycardia	21 (9.6)	14 (8.3)	7 (14.0)	0.228
Bradycardia	15 (6.8)	10 (5.9)	5 (10.0)	0.238

Results are presented as absolute frequency (%).

Factors associated with intradialytic hypotension

Given the limited number of dialysis sessions (only 219), two logistic regression models were tested. In a first logistic regression model, the volume of ultrafiltration > 750 ml/hour [OR: 1.97 (95% IC: 1.12-4.21); p=0.017], anuria < 100 ml [2.72 (1.33-6.19); p=0.021] and the duration of the HD session ≥ 3 hours [2.78 (1.48-6.05); p=0.025] were the independent factors associated with IDH (table 5).

Table 5. Factors associated with intradialytic hypotension in AKI patients (first logistic regression model)

	Univariate analysis		Multivariate analysis	
Variables	p value	OR (CI 95%)	p value	aOR (CI 95%)
Sex				
Men		1		1
Women	0.031	1.84 (1.01-3.47)	0.831	1.18 (0.26-2.25)
Severe acidosis				
No		1		1
Yes	0.031	1.91 (1.31-3.43)	0.659	1.52 (0.29-3.38)
UF > 750 ml/hour	0.001	1.68 (1.02-3.61)	0.017	1.97 (1.12-4.21)
Diuresis (ml)				
>500		1		1
100-500	0.998	1.00 (0,40-2,48)	0.905	1.06 (0,41-2,75)
<100	0.031	3.96 (1,51-8,45)	0.021	2.72 (1,33-6,19)
Duration of the dialysis session				
< 2 hours		1		1
2-3 hours	0.398	1.21 (0.81-4.01)	0.283	1.19 (0.90-3.01)
≥ 3 hours	0.029	2.98 (1.21-4.59)	0.025	2.78 (1.48-6.05)
Malaria				
Yes		1		1
No	0.042	1.96 (1.02-3.58)	0.996	1.13 (0.28-3.67)

Abbreviations: UF = ultrafiltration

In a second model, factors independently associated with IDH were sepsis [3.89 (1.24-12.18); p=0.020], dehydration [5.57 (1.16-26.64); p=0.032], and pre-dialytic SBP [0.97 (0.96-0.98); p<0.001] (table 6). The factors not retained in the first model were: age, sex, severe acidosis, heart failure, obstructive uropathy and malaria. In the second model, the conductivity, temperature of the dialyzate, diabetic status, the electrolyte disturbances in pre-dialysis and first session vs later were not retained.

Table 6. Risk factors of intra-dialytic hypotension in AKI patients (second logistic regression model)

	Univariate analysis		Multivariate analysis	
Sepsis	P value	OR (CI 95 %)	P value	aOR (CI 95 %)
No		1		1
Yes	0.043	2.65 (1.00-7.25)	0.020	3.89 (1.24-12.18)
SBP1 mmHg	<0.001	0.98 (0.97-0.99)	<0.001	0.97 (0.96-0.98)
Dehydration				
Yes		1		1
No	0.033	6.06 (1.39-26.54)	0.032	5.57 (1.16-26.64)

Abbreviations: SBP1 = systolic blood pressure before dialysis session

Therapeutic attitudes and outcome

The Trendelenburg position was systematic in the event of IDH (figure 1). The use of physiological saline (78.9%), the decrease in ultrafiltration (63.2%) and the reduction of the blood pump (43.2%) were also very common.

No case of cardiac arrest was reported. However, dialysis was stopped in 26.3 % of cases; 2 patients (10.5%) received oxygen and one patient was intubated and put on mechanical ventilation. Three intensive care admissions were reported for better surveillance, but there were no deaths. The use of vasoactive amines and macromolecules was less common.

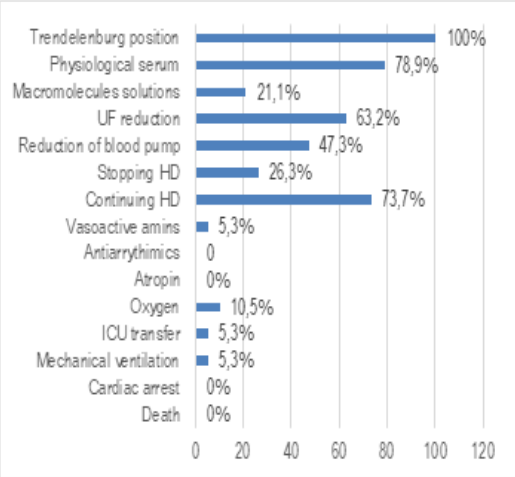

Figure 1. Therapeutic attention and frequency of complications in case of intradialytic hypotension

Discussion

This study has shown that IDH is common during dialysis sessions indicated for AKI, but with a good prognosis. The risk factors found are those generally described in the literature. The technique used (HD or HDF) did not influence the risk of the occurrence of IDH.

The prevalence of IDH of 8.7% is of concern. However, it is lower than recent data in the literature. Indeed a recent meta-analysis estimated the prevalence of HD sessions complicate by IDH to be 11.6% when the nadir <90 mmHg definition was used; and 10.1% when IDH was defined as a > 20 mm Hg decrease in SBP in combination with clinical events and interventions (11). The small sampling and the retrospective nature of our study can influence our results. On the other hand, the relatively young age of patients is an advantage as they had less comorbidity. Reduced tolerance to fluid removal may occur more often in patients with multiple comorbidities (12). In Chronic kidney disease (CKD), it is known that patients with regular HD who experience moderate or severe IDH have significantly higher prevalence of myocardial ischemia and stress induced myocardial dysfunction, than those who experience no or mild IDH (13).

To date there is no objective assessment tool to determine the needed UFR during each HD session. Higher volume overload or higher UFR is associated with poor outcomes including worse mortality and unfavorable clinical outcomes. Unlike the protocol followed in Kinshasa HD centers, which limit the hourly UFR to 1 liter, the present study reports a risk of IDH as soon as 750 mL/h is exceeded. Without data of the body weight of patients, it is difficult to conclude definitively, because a good evaluation had to take into account the weight and/or the size of the patients. More recently in a HD cohort, Flythe *et al*. found that UFR of >13 mL/Kg/h increased all-cause mortality (14).

Anuria is not cited as a risk factor for IDH. In patients with severe AKI, anuria is more likely to lead to hypervolemia or even hypertension. It is known that in the context of chronic HD, anuria impairs both the removal of fluids and the clearance of solutes, resulting in increasing morbity and morality (15). The fact that in a second logistic regression model, dehydration was retained as risk factor of IDH, raises questions about the evaluation of blood volume in patients. It is not formally excluded that some patients with anuria were hypovolaemic; this could therefore explain their risk of IDH. The risk associated with sepsis, can be explained by an increase in body temperature, and dilation of the cutaneous vascular system which counteracts the vascular response to hypovolaemia and contributes to IDH (16). This appears to be at least partly mediated through nitric oxide (17).

In chronic HD, Stidley *et al*. demonstrated that in the first 2 years after initiation of HD, predialysis SBP less than 120 mmHg is associated with a twofold to threefold higher risk of mortality compared with predialysis SBP of 140 to 149

mmHg (18). Observational studies in patients on HD have consistently shown a strong association between lower SBP and higher risk of mortality. In patients suffering from AKI, the drop in SBP is a situation often indicating a pre-shock, which can quickly evolve into shock; this fits well with the operational definition of IDH (19).

The use of HD represents a mainstay of supportive care of patients with AKI. However, a number of fundamental questions regarding its optimal management remain unanswered. There is no consensus on the ideal duration of an acute HD session. In the case of conventional HD or HDF, the first session is generally short (2 hours) in order to prevent an osmotic imbalance linked to a significant elimination of urea. The other sessions last about 4 hours. Our study has shown that the risk of IDH increases beyond 3 hours. On the other hand, we did not find any advantage of HDF over conventional HD. No renal replacement therapy mode is ideal for all patients with AKI as they all have advantages and disadvantages. Systematic reviews and meta-analyzes concluded that there is no evidence that any single modality is associated with improved outcomes of patients with AKI (20-21). The experience of the practitioners plays an important role in the evolution of the patients, whatever the technique used. Hemodynamic instability and IDH may be decreased by using variable dialyzate sodium profiles (≥ 140 meq/L), variable ultrafiltration rates and setting dialyzate temperature to below 37°C (7, 15-16,22).

The outcome of the patients was favorable in all cases. Respect for treatment protocols in accordance with international standards, and very probably the presence of nephrologists or resuscitators during sessions are an asset. The number of sessions stopped sufficiently shows that priority is given to the stability and comfort of the patient.

The small sample size is a limitation for the present study. This is also the case for the nature of the study which was retrospective and limited to two centers. Some parameters of interest such as the KT/V and the BVM modulus were not evaluated. No patient in the study benefited from hemofiltration, which is commonly used in the West in the management of cases of AKI.

However, we can retain that in the event of acute dialysis, approximately 1 session in 12 is complicated by IDH with a good prognosis. This depends on factors related to the patient and to the dialysis method itself. Anticipatory management should be promoted to ensure better patient safety.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be considered as a potential conflict of interest.

Author's contribution

JRRM and SMM conceived the idea, designed and supervised the study, had full access to all data and took responsibility for the integrity of the data. JRRM and YMN wrote the first version of the article. All coauthors reviewed and approved the final version.

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