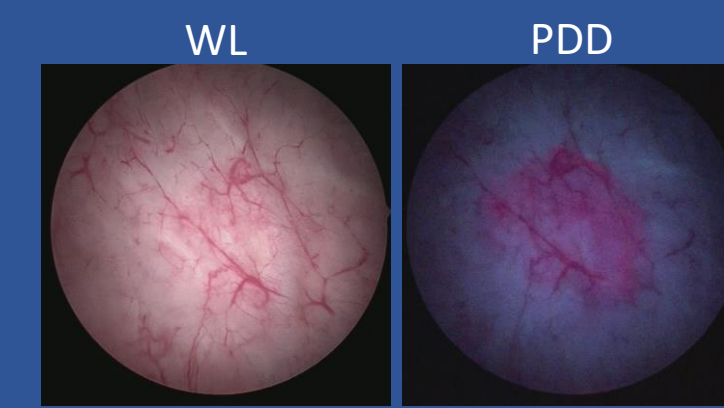


MP72-09: Intraoperative Hypotension due to the Oral Administration of 5-Aminolevulinic Acid for Photodynamic Diagnosis in Patients with Bladder Cancer

Takahiro Nohara, Hiroshi Kano, Takafumi Shimada, Yuki Kato, Taito Nakano, Tomomi Nakagawa, Hiroaki Iwamoto, Hiroshi Yaegashi, Masashi Iijima, Shohei Kawaguchi, Kazuyoshi Shigehara, Kouji Izumi, Yoshifumi Kadono, Atsushi Mizokami

Department of Urology, Kanazawa University Hospital



ABSTRACT

INTRODUCTION AND OBJECTIVE:

The patients in some instances experienced hypotension after the oral administration of 5-ALA. In this study, we analyzed the pre- and intraoperative SBP to safely perform a TURBT with PDD.

METHODS:

The participants included 109 consecutive patients who underwent PDD-TURBT in our institution and were categorized as the PDD group. The clinical data were collected, and the perioperative SBP and vasopressor usage were analyzed. On the other hand, the consecutive patients who previously underwent conventional TURBT (without the use of oral 5-ALA) were included and categorized as the control group.

RESULTS:

The SBP before anesthesia, lowest SBP from the anesthesia induction to the start of operation, and lowest SBP during operation were significantly lower in the PDD group than those in the control group. The rate of vasopressor use was significantly higher in the PDD group. Furthermore, using the multivariate analysis, we found that the general anesthesia and regular use of RAS inhibitor pose a hypotension risk (lowest SBP from the anesthesia induction to the start of operation <80 mmHg).

CONCLUSIONS:

The oral intake of 5-ALA obviously cause a drop in the intraoperative SBP. Therefore, urologists and anesthesiologists should consider withdrawal of RAS inhibitors and monitor the SBP carefully during PDD-TURBT.

Introduction

- Several randomized control trials and meta-analyses showed the efficacy of PDD in reducing tumor recurrence rates after TURBT in patients with superficial bladder cancer.
- In Japan, oral 5-ALA was approved as an insurance adaptation in December 2017.
- At our institution, oral 5-ALA (ALAGLIO®; SBI Pharmaceuticals Co. Ltd., Tokyo, Japan) has been used in >100 NMIBC patients who underwent PDD-TURBT since the insurance approval.
- However, we experienced some cases who suffered pre- and intraoperative hypotension after oral 5-ALA intake (e.g. a case shown on the right side).
- In the present study, we aimed to prove that hypotension occurs because of the oral intake of 5-ALA in patients with NMIBC and show the characteristics of patients at risk of hypotension under oral administration of 5-ALA.

Case (80 y.o. male)
The patients does not have any comorbidities except for mild diabetes.
On the day of PDD-TURBT, he was orally administered 5-ALA (20 mg/kg) at 6:00 AM.
At the entrance of the operating room (8:30 AM), his SBP was below 80 mmHg.
It took 60 minutes of rapid infusion until SBP increased to 90 mmHg. Then, spinal anesthesia was started at 9:30 AM.

Patients & methods

Figure 1. Study design

The retrospective study was performed as follows.

PDD group: Patients underwent PDD-TURBT with oral 5-ALA (20 mg/kg) given 3 h before surgery)

Control group: Patients underwent conventional TURBT (without PDD)

The clinical data (perioperative SBP, vasopressor usage, anesthesia type, etc.) were analyzed.

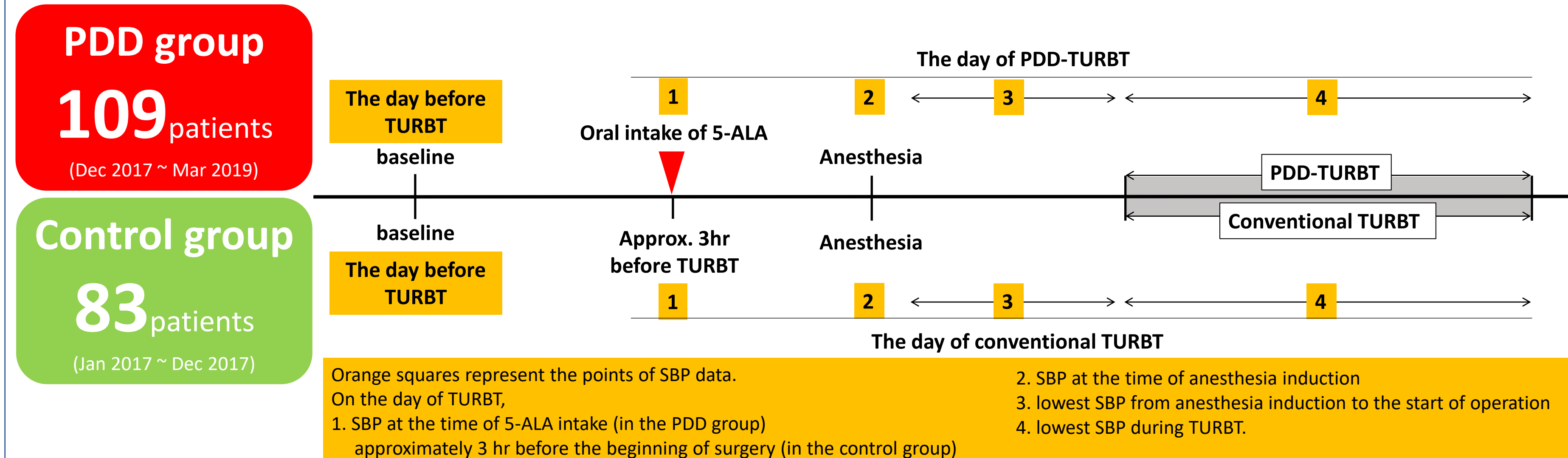


Table 1: The comparison of the patient characteristics and perioperative data.

	PDD group	Control group	P
Age (y.o.)	74.3 ± 8.3	73.1 ± 9.1	0.407
Gender			
Male	89 (82%)	65 (78%)	0.588
Female	20 (18%)	18 (22%)	
Body mass index (kg/m ²)	23.4 ± 3.2	23.3 ± 3.3	0.742
Coexistence of hypertension	56 (53%)	45 (54%)	0.771
Administration of antihypertensive medicines on the day of TURBT	38 (35%)	30 (36%)	0.880
Anesthesia	General 48 (44%) spinal 61 (56%)	General 29 (35%) spinal 54 (65%)	0.235
Operation time (min)	59 ± 31	54 ± 36	0.083
Intraoperative infusion volume (ml)	887 ± 335	731 ± 268	<0.001
Cases using vasopressor during anesthesia and surgery	50 (46%)	18 (21%)	<0.001

Abbreviations

PDD: Photodynamic diagnosis
TURBT: Transurethral resection of bladder tumor
5-ALA: 5-aminolevulinic acid
NMIBC: Non-muscle invasive bladder cancer
SBP: Systolic blood pressure
RAS: Renin-angiotensin system
ASA-PS: American Society of Anesthesiologists physical status classification

References

- Bondad J, et al. Photodiagn. Photodyn. Ther. 2013; 10: 39–41.
- Chung IW, et al. Photodiagn. Photodyn. Ther. 2013; 10: 362–7.
- Eichhorn V, et al. World J. Urol. 2013; 31: 371–6.
- Mingone CJ, et al. Am J Physiol Lung Cell Mol Physiol. 2006; 291: 33–44

Results

- The patient characteristics and perioperative data were not significantly different between both groups, except for Intraoperative infusion volume and rate of vasopressor use during anesthesia and operation (table.1).
- The SBP before anesthesia, and lowest SBP from the anesthesia induction to the start of operation and during operation were significantly lower in the PDD group (figure 2).
- Age, regular RAS inhibitor usage and general anesthesia were the risk factors for hypotension on univariate analysis. Multivariate analysis showed that general anesthesia and regular RAS inhibitor use presented a hypotension risk (table 2).

Discussion and Conclusion

- This is the first report about hypotension due to orally administered 5-ALA in patients with NMIBC (Hypotension by orally 5-ALA is reported in only few studies¹⁻³).
- The mechanism of hypotension due to the oral intake 5-ALA remains unclear⁴.
- We showed that the oral administration of 5-ALA in PDD-TURBT was more likely to cause hypotension in patients with NMIBC. Regular RAS inhibitor use and general anesthesia might pose a hypotension risk.**
- Limitations: small sample size, retrospective analysis, time bias, difference of anesthesiologists.

Table 2: Logistic regression analysis in the PDD group to show the risk factors for the SBP <80 mmHg from anesthesia induction to the operation.

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Age (y.o.)	1.062 (1.011-1.116)	0.016	1.053 (0.989-1.121)	0.106
Gender (Ref. female)	1.067 (0.397-2.869)	0.897		
Body mass index (kg/m ²)	1.060 (0.938-1.197)	0.351		
Coexistence of diabetes (Ref. (-))	1.447 (0.578-3.620)	0.430		
Coexistence of hypertension (Ref. (-))	1.607 (0.746-3.464)	0.226		
Regular use of calcium blocker (Ref. (-))	0.703 (0.461-2.161)	0.168		
Regular use of RAS inhibitor (Ref. (-))	3.378 (1.155-9.880)	0.026	4.964 (1.409-17.490)	0.013
Past history of heart disease (Ref. (-))	1.657 (0.751-3.657)	0.211		
Preoperative Hemoglobin (g/dl)	0.831 (0.656-1.052)	0.124	0.915 (0.667-1.254)	0.580
Preoperative Albumin (g/dl)	0.423 (0.145-1.235)	0.116	2.093 (0.465-9.422)	0.336
Charlson Comorbidity Index	1.323 (0.953-1.838)	0.095	1.354 (0.872-2.103)	0.177
ASA-PS ≥3 (Ref. score 1 or 2)	1.064 (0.350-3.232)	0.913		
Administration of antihypertensive medicines on the day of TURBT (Ref. (-))	1.329 (0.592-2.983)	0.491		
General anesthesia (Ref. spinal anesthesia)	6.240 (2.572-15.141)	<0.001	8.782 (3.154-24.451)	<0.001
SBP on the day before TURBT (mmHg)	0.982 (0.960-1.005)	0.133		
SBP at 3 hours before TURBT (mmHg)	0.996 (0.973-1.020)	0.744		
SBP at the time of starting anesthesia (mmHg)	0.983 (0.964-1.002)	0.079	0.979 (0.955-1.003)	0.080
Manifestation of nausea (Ref. (-))	1.447 (0.578-3.620)	0.430		

Figure 2. The chronological SBP change in both groups.

