

### Introduction

The incidence of cancer is very high worldwide, and the primary mode of treatment is administration of chemotherapeutic agents. Fortunately, the National Cancer Institute has reported over 12 million cancer survivors in the US. Therefore, it is necessary to develop effective care plans to improve the quality of life of cancer survivors. Few reports exist regarding the influence of anti-cancer agents on voiding function. We reported previously that some anti-cancer agents caused endothelial dysfunction and erectile dysfunction in a study using an animal model.

In this study, we investigated the chronological change in voiding function after administration of the anti-cancer agent, oxaliplatin (L-OHP), using a rat model.

### Results

#### Cystometrography (CMG) analysis

![Graph showing Cystometrography analysis](image1)

Intercontraction intervals (ICI)

<table>
<thead>
<tr>
<th>Group</th>
<th>ICI (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cont</td>
<td></td>
</tr>
<tr>
<td>L-OHP</td>
<td></td>
</tr>
</tbody>
</table>

Maximum intravesical pressure (MIVP)

<table>
<thead>
<tr>
<th>Group</th>
<th>MIVP (cm H2O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cont</td>
<td></td>
</tr>
<tr>
<td>L-OHP</td>
<td></td>
</tr>
</tbody>
</table>

- The ICI in L-OHP group is shorter than that of Cont group.
- There are no change of MP between Cont and L-OHP groups.

#### Isometric tension study

![Graph showing Isometric tension study](image2)

- The contractile response for carbachol decreased in the L-OHP group compared to the Cont group.
- The contractile response for EFS in the L-OHP group is also lower than that of the Cont group.

#### real time PCR analysis

![Graph showing real time PCR analysis](image3)

- Muscarinic receptor (M2) mRNA expression was higher in the L-OHP group than in the Control group. However, M3 mRNA expression was lower in the L-OHP group than in the Cont group.
- Rho-associated protein kinase 1 (ROCK-1) mRNA was also lower in the L-OHP group than in the Cont group.

### Discussions

- L-OHP shortened the voiding interval in this study. L-OHP also up-regulated M2 mRNA expression, which could explain the shortened voiding interval.
- L-OHP weakened detrusor muscle contraction. L-OHP decreased not only M3 mRNA but also ROCK-1 mRNA expression. We think that the down-regulated M3 and ROCK-1 mRNA led to weakened detrusor muscle contraction.

Our findings indicate that anti-cancer agents can change voiding function and detrusor muscle contraction. If anti-cancer agents are repeatedly administered, they can result in an overactive bladder and eventually an underactive bladder. Therefore, follow-up care for cancer survivors should include some form of continence medication.

### Protocols

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1d 2d</td>
</tr>
<tr>
<td>L-OHP group</td>
<td>5d 4w</td>
</tr>
</tbody>
</table>

Cystometrography (CMG) Isometric tension study real time PCR analysis

Evaluation tests

*P < 0.05 **P < 0.01 Mean ± S.E. Student’s t-test (n = 4-6)

### Affiliations to disclose†:

- * Founding for speaker to attend:
  - Travel grant from The Nitto Foundation

---

**Anti-cancer agent, oxaliplatin, shortens voiding function and weakens detrusor muscle contraction in rats**

Tomoya Kataoka¹, Yuji Hotta², Yasuhiro Maeda³, Kazunori Kimura¹,²

¹) Department of Clinical Pharmaceutics, Graduate School of Medical Sciences, Nagoya City University, Japan
²) Department of Hospital Pharmacy, Graduate School of Pharmaceutical Sciences, Nagoya City University, Japan

---

**#158**

**Muscarinic receptors in smooth muscle**

M3

M2

ACh

Rho-A

PLC

AC

ROCK

IP3

cAMP

Contraction

Relaxation