



Optimal Ureteric Jet Visualization at the Time of Pelvic Reconstructive Surgery: A Double-Blinded, Randomized Controlled Trial Comparing Vitamin B2 to 5% Dextrose in Water

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Disclosures – C.D. McDermott



MEDICAL ADVISOR FOR SZIO INC.



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The Need for Cystoscopy

- Rate of ureteric injury 3 – 5.1% after pelvic reconstructive surgeries
- Recommended by American College of Obstetricians and Gynecologists (ACOG) and American Urogynecologic Society (AUGS)

- With Thanks
- Conclusions
- Limitations
- Results
- Methods
- Objectives

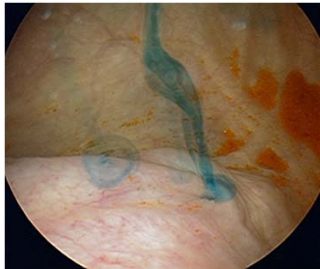
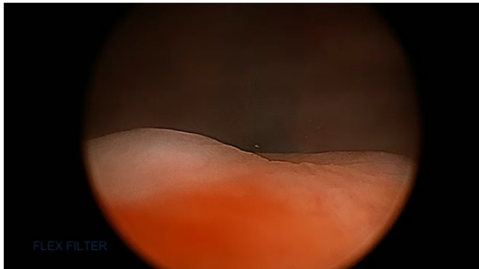
Cystoscopy increases the detection rate of ureteric injuries from 18% to 95%

- Background
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The Need for a New Agent

- Indigo carmine was previously the most commonly used agent
- Given intra-operatively and colours the urine blue
- A world-wide shortage of the active ingredient has prompted the need to search for alternatives

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Vitamin B2 (Riboflavin)

- Given pre-operatively
- Colours the urine bright yellow
- Lack of adverse side effects
- Inexpensive - \$0.11 USD (\$0.14 CAD) per 100mg dose (current market price)

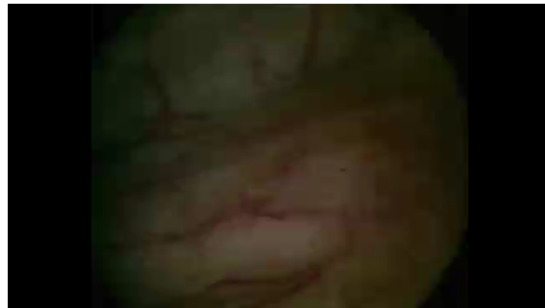


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5% Dextrose in Water (D5W)

- Given intra-operatively
- Relies on the difference in viscosity between D5W and urine
- No previous studies on adverse effects
 - Evidence showing 50% and 10% dextrose in water to increase the risk of post-operative UTIs
- Inexpensive - \$1.16 USD (\$1.48 CAD) per 1000mL bag (current market price)



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Objectives

To compare two highly available and inexpensive agents as ureteric jet visualization methods: pre-operatively vitamin B2 versus intra-operative cystoscopy distension using D5W

- 1 **Primary outcome:**
 - Rate of accurate detection of both ureteric jets
- 2 **Secondary outcomes:**
 - Time from start of cystoscopy to visualizing both ureteric jets
 - Use of IV furosemide to aid visualization
 - Use of IV fluorescein as a rescue agent for visualization
 - Surgeon satisfaction
 - UTI rates at one week after surgery



Study Design

- Double-blinded, Health Canada authorized randomized controlled trial
- Performed at 3 tertiary hospitals between Aug 2018 – June 2021
 - Mount Sinai Hospital
 - Sunnybrook Health Sciences Centre
 - Women’s College Hospital

Inclusion Criteria
Age of 18
Undergoing female pelvic reconstructive surgery where intra-operative cystoscopy was necessary
Exclusion Criteria
Renal Disease
Ureteric disease
Previous ureteric compromise
Hypersensitivity to cyanocobalamin or cobalt
Malabsorption disorder
Allergy to fluorescein dye
Unable to present for one week post-operative assessment due to geographic or transportation issues
Unable to provide written consent



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Study Design

n=238

Vit B2/Normal Saline

D5W/Placebo

Post-op Day 3-10

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- Simple randomization scheme in a 1:1 ratio
- Allocation concealed from those involved in recruitment
- Sample size
 - 15% difference in detection rate chosen by consensus as significant
 - Given previous detection rate of vitamin B2 as 72% \Rightarrow 1226 patients required (238 patients if estimating 5% drop-out rate)
- Intent-to-treat analysis was used

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Results: CONSORT Flow of Study

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238 out of 513 patients agreed to participate (the most common reason of exclusion was inability to attend one-week follow-up)

2 out of 238 patients were unable to complete surgical intervention

Follow-up data was available for all 236 patients

Results: Baseline Characteristics

	Vitamin B2 (n=117)	D5W (n=119)
Age (years)	65 (53-71)	63 (53-70)
BMI (kg/m ²)	26.0 (23.5-30.0)	27.3 (24.3-30.7)
Gravidity	2 (2-3)	3 (2-3)
Parity	2 (2-3)	2 (2-3)
Vaginal delivery	2 (2-3)	2 (2-3)
Cesarean delivery	0 (0-0)	0 (0-0)
Post-menopausal	90 (76.9)	91 (76.5)
Smoker	6 (5.1)	11 (9.2)
Diabetic	19 (16.2)	9 (7.6)
Immunocompromised	1 (0.9)	1 (0.8)
History of recurrent UTI	7 (6.0)	9 (7.6)
Pre-operative vaginal estrogen use	62 (53.0)	67 (56.3)
ICS stage of pelvic organ prolapse		
Stage 1	17 (14.5)	20 (16.8)
Stage 2	38 (32.5)	37 (31.1)
Stage 3	50 (42.7)	49 (41.2)
Stage 4	12 (10.3)	13 (10.9)

Groups were similar for all variables with no significant difference

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Results: Intra-Operative Outcomes

	Vitamin B2 (n=117)	D5W (n=119)	P
Types of surgical procedure			
Prolapse surgery only	65 (55.6)	58 (48.7)	0.359
Incontinence surgery only	11 (9.4)	12 (10.1)	1.000
Other surgery only	2 (1.7)	7 (5.9)	0.171
Prolapse and incontinence surgery	38 (32.5)	42 (35.3)	0.749
Prolapse and other surgery	1 (0.9)	0 (0)	0.496
Study medication intake time			1.000
Before 12PM	95 (81.2)	97 (81.5)	
After 12PM	22 (18.8)	22 (18.5)	
Time from taking study medication to looking for ureters (minutes)	140.4 (100.0-167.0)	127.6 (98.4-162.1)	0.209

Groups were similar for types of surgical procedure, medication intake time, and time from study medication to looking for ureters

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Results: Intra-Operative Outcomes

	Vitamin B2 (n=117)	D5W (n=119)	P
Primary outcome			
Detection of both ureteric jets	112 (97.3)	108 (90.8)	0.062
Detection of one ureteric jet	4 (3.4)	5 (4.2)	0.181
Detection of no ureteric jet	1 (0.9)	6 (5.0)	
Secondary outcomes			
Time looking for ureter 1 (seconds)	32.0 (12.3-93.0)	29.0 (15.0-115.0)	0.325
Time looking for ureter 2 (seconds)	81.5 (35.8-178.5)	83.0 (43.5-201.0)	0.456
Furosemide use	4 (3.4)	7 (5.9)	0.539
Fluorescein rescue	4 (3.4)	14 (11.8)	0.025**
Surgeon satisfaction \geq "satisfied" (4/5 on a Likert scale)	95 (81.2)	63 (52.9)	<0.001**

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Both vitamin B2 and D5W showed high rates of ureteric jet detection with no significant difference between groups

Results: Intra-Operative Outcomes

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There was no significant difference in the time to visualization of both ureters

Results: Intra-Operative Outcomes

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There was no difference in the use of IV furosemide to aid visualization

Results: Intra-Operative Outcomes

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Vitamin B2 group had significantly lower use of IV fluorescein as a rescue for visualization

Results: Intra-Operative Outcomes

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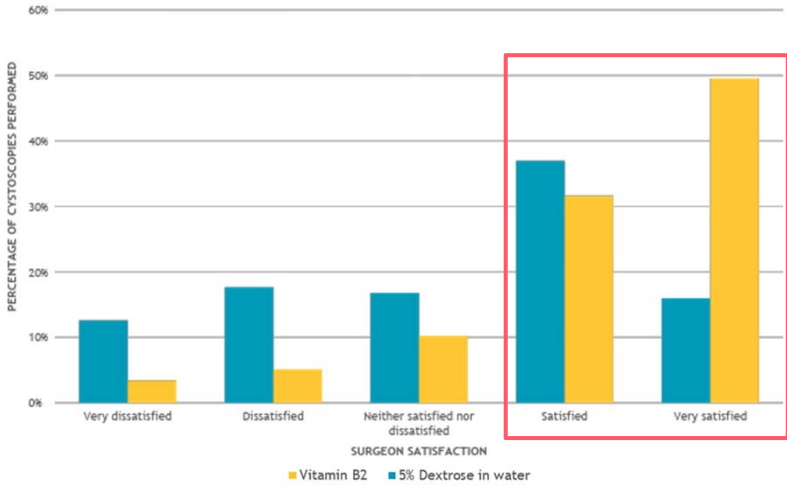
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Surgeon satisfaction ≥ "satisfied" (4/5 on a Likert scale)	95 (81.2)	63 (52.9)	<0.001**

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Vitamin B2 group was shown to have significantly higher surgeon satisfaction rates

Results: Surgeon Satisfaction

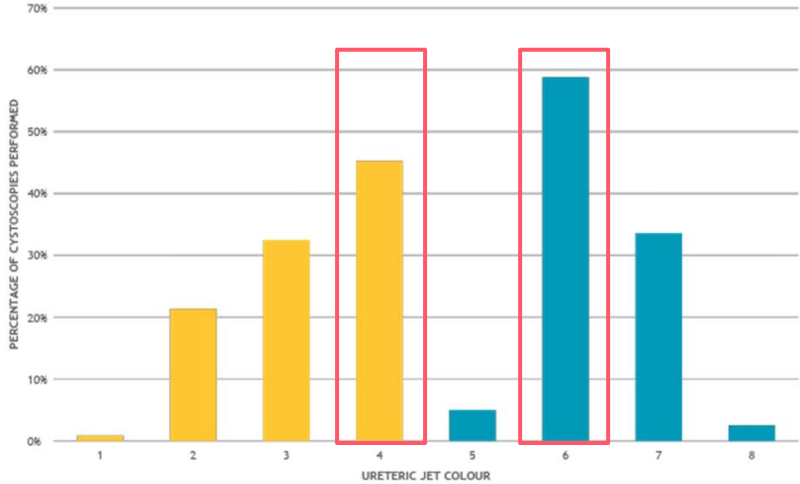
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Results: Ureter Jet Colours



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Results: Post-Operative Outcomes

	Vitamin B2 (n=117)	D5W (n=119)	P
Discharged home with catheter	85 (72.6)	71 (59.7)	0.099
Foley catheter	19 (16.2)	18 (15.1)	
Suprapubic tube	66 (56.4)	53 (44.5)	
Post-operative follow-up day	6 (5-7)	6 (5-7)	0.855
Using catheter at follow-up visit	84 (71.8)	66 (55.5)	0.013**
Currently on antibiotics	84 (71.8)	66 (55.5)	0.013**
Length of catheterization (days)	5 (1-7)	3 (1-6)	0.014**
Positive urine culture	21 (17.9)	19 (16.1)	0.839

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There was no significant difference in the rate of positive urine cultures at one-week after surgery

Limitations

- Tertiary centre setting – many patients who were screened for recruitment could not be enrolled due to inability to present for a one-week post-operative assessment
- Routine urine culture at 1 week post-operative visit – may not be as generalizable to other centres that diagnose/treat UTIs based on symptoms alone +/- urinalysis and culture results
- Higher than expected detection rate for both agents – limited our power and possibly ability to detect a difference

	Vitamin B2 (n=117)	D5W (n=119)	P
Primary outcome†			
Detection of both ureteric jets	112 (97.3)	108 (90.8)	0.062
Detection of one ureteric jet	4 (3.4)	5 (4.2)	0.181
Detection of no ureteric jet	1 (0.9)	6 (5.0)	

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Conclusions

- Both pre-operative vitamin B2 and intra-operative cystoscopy with D5W showed high rates of ureteric jet detection
- Vitamin B2 was shown to have
 - Significantly higher surgeon satisfaction rates
 - Significantly lower rate of IV fluorescein use
- There was no significant difference in the time to visualization of both ureters or the use of IV furosemide
- There was no significant difference in the rate of positive urine cultures at one week after surgery

With Thanks

Both are effective, inexpensive, and widely available agents for ureteric jet visualization at the time of pelvic reconstructive surgery

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