NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*
- Email correspondence between the editorial office and the authors*

*The corresponding author has opted to make this information publicly available.

Personal or nonessential information may be redacted at the editor’s discretion.

Questions about these materials may be directed to the Obstetrics & Gynecology editorial office: obgyn@greenjournal.org.
Date: Nov 30, 2018
To: "Allison Marie Wyman" em@greenjournal.org
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2015

RE: Manuscript Number ONG-18-2015

Title: THE EFFECT OF FUROSEMIDE ON TIME TO CONFIRMATION OF URETERAL PATENCY DURING INTRAOPERATIVE CYSTOSCOPY: A RANDOMIZED CONTROL TRIAL

Dear Dr. Wyman:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 21, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is an interesting study looking at the effect of furosemide on the time to confirmation of ureteral patency. I think this is an interesting question which could be very clinically relevant. Although as you mention, the clinical relevance in saving 79 seconds may not be important, it is still a possible option for clinical use. The use of a randomized controlled trial is very helpful and I appreciate the work that goes into setting this up.

Comments/suggestions:

1) Women were excluded if they had abnormal renal function - how did you define this (previous diagnosis, elevated creatinine, etc)?

2) Were there any concerns regarding hypotension during the study - either after giving the furosemide or as a concern prior to the study drug being given?

3) In table 1 it is clear that the results given are a median, I recommend adding that to the text as well (lines 218 and 221)

4) I know the study was not powered to look at adverse reactions, any further concerns about using chart review to determine whether there were adverse events or delayed diagnosis?

Reviewer #2:

This is a double blinded RCT looking at the use of furosemide at the time of routine cystoscopy after gynecologic surgery to assess the time it takes to identify bilateral ureteral patency vs. placebo.

Overall this was a well designed and executed trial. The authors and participants ought to be credited with a very clean trial with well defined primary and secondary outcomes.

Abstract:

Line 55 Explain the 2nd outcome of delayed ureteric injury. According to the introduction if patency is not seen within 30
Further assessment is recommended. Was this the protocol in this study? If so a more relevant 2nd outcome may be the 30 min further assessment which would include stent placement or removal of obstructive stitches.

Line 64-65 It is unclear what is meant by ureteral patency being greater at any given time period. How is this different from the primary outcome?

Line 69-70 As written the conclusion supports a statistically significant shorter time until identification of ureteral patency. Although the time may not be clinically significant it is not directly supported within the abstract. This is explained in detail in the discussion section.

Introduction:
This is a good overview of the incidence and complications of lower urinary tract injury during gynecologic surgery. The position of the AAGL and AUGS in regards to the use of routine vs. indicated cystoscopy is a very helpful perspective putting the objective of this study in proper context.


Line 138 Discuss what further evaluation is done after 30 min.? Did this include either stitch removal or stent placement? These may be more clinically relevant 2nd outcomes if available.

Line 144-147 This is a concise description and rationale for the objectives of this study.

Materials and methods:
Line 164 Why were patients excluded if it took > 30 min to identify ureteral patency? This is a clinically relevant endpoint. What etiology was found in these patients?

Line 169 Explain why patients were stratified by age 65?

Line 187 Was there standardization of the amount of distention fluid used for cystoscopy and or recorded? This may impact the ease of identifying the ureteral orifice and jets.

Line 194 What available literature was used to justify the power analysis and assumption of 3 min. reference?

Results:
Table 1.
Are there demographics available for hypertension, diuretic use, ERAS protocol and urine output? These could confound the results and should be listed if available.

Table 2.
There was a significant number of patients missing data on urine output. Was the urine output for the entire case or just during cystoscopy? This is a limitation if it is for the entire case since it is an indirect measure of GFR in conjunction with IFV.

Discussion:
Overall this is a good review of the literature and alternatives to indigo carmine for ureteral patency. The limitations of the study are acknowledged.

Line 233-243 Although the study did not show the predefined difference of 3 min., there is a good argument for clinical and cost effectiveness based upon the OR cost per min as stated.

Line 265 What is the clearance and half life of furosemide? Is it less than 30 min as listed in the protocol? This could impact the primary outcome of intention to treat.

Line 269 There should be a more detailed description of the type of surgeries listed in table 1. This could potentially impact risks of kinking and ureteral jet identification.

Reviewer #3: This is a concise, well-written, easy-to-read paper. Despite the lack of significance, this paper adds to the body of knowledge about a drug that we use commonly in clinical practice without much prospective comparison to placebo.
I am glad that the authors make a distinction between statistical and clinical significance: although their results reach statistical significance, they admit that clinical significance is limited.

The abstract is precise and clear.

The introduction frames the question adequately.

In the methods, I would have liked to see a brief discussion of the inclusion and exclusion criteria (if any) relative to renal function. Were there any patients whose renal function or lasix dependence was thought to be a relative contraindication to furosemide use? Alternatively, if there were no such contraindications, perhaps include a paragraph in your discussion about the appropriateness of lasix use in populations with renal disease or insufficiency.

The results are clearly presented.

The discussion well-written and does a nice job of not over-inferring the clinical significance of the statistical differences in time to ureteral jets.

Reviewer #4:

This is a double-blind randomized controlled trial to investigate the effect of furosemide on the time to confirmation for ureteral patency during intraoperative cystoscopy. Other outcomes included adverse reaction to study medication and delayed diagnosis of ureteric injury. The authors conclude that patients that received furosemide were 2.3 times more likely to have ureteral patency confirmed compared to placebo. Of note, no adverse events were noted and there were no delayed diagnoses of ureteric injury. This is a well planned and executed study. The authors should consider adding to the discussion that indigo carmine is once more available. The weaknesses of this study are addressed by the authors - mainly not following kidney function or other markers to assess the safety of furosemide. Although limited to urogynecologic procedures this is still applicable to all hysterectomies.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 240-243: This is relevant only if the OR times were different for the two cohorts. If these comments are included, then should provide in Tables a comparison of OR times for the two cohorts.

Table 1: Since this was a RCT, the p-values should be omitted. There is no need to statistically compare the baseline differences. The estimated blood loss and IV fluids should be cited as post-op surgical comparisons.

Tables 2, 3: Need to separate and clearly identify the primary (T₂ - T₀ time in seconds) outcome from the secondary outcomes. Drug time, time to 1st ureteral jet, urinary output, and hazards ratios of time to T₂, drug time and time to 1st ureteral jet are all secondary outcomes, ie, not powered in the methods section. Similarly, the Discussion section should clearly delineate the primary outcome from all secondary ones.

Fig 1: Need to include, along the x-axis, the number of patients remaining in each cohort. Since the Q3 times for the cohorts were 137 and 280 seconds, should include time increments at 100 second intervals, not 200 seconds.

EDITOR COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
   1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
   2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.
2. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. This statement must appear at the end of your Materials and Methods section. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Examples of statements can be found online at http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf.

3. Author Agreement Forms: Please note the following issues with your forms. Updated or corrected forms should be submitted with the revision.

Isabel Prieto, MD - Did not agree to be accountable for the work.

Elisha Jackson, MD - Did not indicate a conflict of interest disclosure. Did not draft the work or give final approval of the version to be potentially published.

Please note:

a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.

b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org):

* Substantial contributions to the conception or design of the work;
OR
the acquisition, analysis, or interpretation of data for the work;
AND
* Drafting the work or revising it critically for important intellectual content;
AND
* Final approval of the version to be published;
AND
* Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The author agreement form is available online at http://edmgr.ovid.com/ong/accounts/agreementform.pdf. Signed forms should be scanned and uploaded into Editorial Manager with your other manuscript files. Any forms collected after your revision is submitted may be e-mailed to obgyn@greenjournal.org.

4. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained."

*The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women’s Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.
7. Title: Please delete, "The Effect of," from the title.

8. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

9. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

10. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows:
Original Research articles, 300 words. Please provide a word count.

11. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf. Please edit your abstract as needed.

12. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

13. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

14. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

15. The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly. If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at http://www.acog.org/Resources-And-Publications.

16. Figures

Figure 1 (CONSORT): Please update or clarify n values (216-65 does not equal 150).

Figure 2 (Kaplan-Meier): Please provide a higher resolution version of this figure. Note that this manuscript has 2 Figure 1s. Please cite both in the body of the manuscript and update the figure numbers based on the order they appear.

17. If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.
Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 21, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

In compliance with data protection regulations, please contact the publication office if you would like to have your personal information removed from the database.
16 December 2018

Dear Editors of Obstetrics and Gynecology,

The coauthors and I would like to thank you for the opportunity to have our research published in Obstetrics and Gynecology. We appreciate the effort that was put forth in reviewing and commenting on this paper. Please find our responses to your questions and comments in the following pages.

I, Allison Wyman affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Once again, thank you for the opportunity to work together in publishing our research.

Sincerely,

Allison Wyman
Reviewer #1:

Comments/suggestions:

1) Women were excluded if they had abnormal renal function - how did you define this (previous diagnosis, elevated creatinine, etc)?

Response
Thank you for this point of clarification. Abnormal renal function was defined as any diagnosis of chronic kidney disease or an abnormal creatinine which was >1.1mg/dL in our laboratory. The manuscript has been changed to make this more clear.

2) Were there any concerns regarding hypotension during the study - either after giving the furosemide or as a concern prior to the study drug being given?

Response
This is also an important point as furosemide, especially if given rapidly, can cause hypotension. In discussing with the pharmacists and anesthesiologists at our institution during protocol development the thought was that the relatively small dose given in a controlled manner made concern for hypotension very low. The anesthesia team did, however, have the ultimate decision about whether or not to administer the study drug (the “drug not given for any reason” in exclusion criteria). In this study there were no patients in whom the anesthesia provider did not feel comfortable administering furosemide (the one who was not given the drug was due to oversight on the anesthesia team).

3) In table 1 it is clear that the results given are a median, I recommend adding that to the text as well (lines 218 and 221)

Response
Thank you, this has been changed in the manuscript, though due to editing the lines have changed now to 195/197.

4) I know the study was not powered to look at adverse reactions, any further concerns about using chart review to determine whether there were adverse events or delayed diagnosis?

Response
Thank you, this is an important point as ureteric injury and subsequent kidney damage could be diagnosed more remotely than 6 weeks. Additionally patients could have presented to other institutions. These considerations are added to the manuscript.
Reviewer #2:

Abstract:

Line 55  Explain the 2nd outcome of delayed ureteric injury. According to the introduction if patency is not seen within 30 min further assessment is recommended. Was this the protocol in this study? If so a more relevant 2nd outcome may be the 30 min further assessment which would include stent placement or removal of obstructive stitches.

Response
Thank you for this comment. The secondary endpoint of delayed ureteric injury came from our review of the literature review which found a case report where ureteric injury was missed, with the hypothesis being that furosemide had somehow masked the injury. In our study, if there was no jet seen after 30 minutes then the appropriate work up was carried out. There was one such patient and removing the kinking stitches resolved the lack of patency.

Line 64-65  It is unclear what is meant by ureteral patency being greater at any given time period. How is this different from the primary outcome?

Response
Thank you for this point of clarification. The primary endpoint was the time to ureteral patency. When looking at the data in aggregate, the Kaplan Meier curve showed that at any given time, patients in the group receiving furosemide were 2.8 times more likely to have had bilateral patency confirmed than patients in the placebo group.

Line 69-70  As written the conclusion supports a statistically significant shorter time until identification of ureteral patency. Although the time may not be clinically significant it is not directly supported within the abstract. This is explained in detail in the discussion section.

Response
Thank you for this comment. The conclusion section of the abstract has been amended to not that the findings are statistically significant as well as a line regarding the small clinical significance.

Introduction:

This is a good overview of the incidence and complications of lower urinary tract injury during gynecologic surgery. The position of the AAGL and AUGS in regards to the use of routine vs. indicated cystoscopy is a very helpful perspective putting the objective of this study in proper context.
Thank you.
There should be further discussion of undiagnosed urinary tract injury. Although bladder injury is greater overall ureter injury is more likely to go undiagnosed. J Minim Invasive Gynecol, 2012. 19(4): p. 407-11

Response
Thank you, this is an important point however we had difficulty including it given space restraints in the introduction.

Discuss what further evaluation is done after 30 min.? Did this include either stitch removal or stent placement? These may be more clinically relevant 2nd outcomes if available.

Response
After 30 minutes then either stent placement or stitch removal would be reasonable and these have been added to our manuscript. Given the primary endpoint of time to confirmation of ureteral patency it was our opinion that any case where a lower urinary tract injury was sustained would have to be excluded from the analysis as it would skew the results.

This is a concise description and rationale for the objectives of this study.

Response
Thank you.

Materials and methods:

Why were patients excluded if it took > 30 min to identify ureteral patency? This is a clinically relevant end point. What etiology was found in these patients?

Response
Thank you. This point was explained better in our protocol and it should be clarified in the manuscript. The >30min is from drug administration to cystoscopy-not that it took >30 min to identify the patency. Due to the pharmacokinetic properties of furosemide, after 30 minutes the effect would be minimal. Clinically, this happened in patients receiving a robotic sacrocolpopexy in whom the surgeon asked for the study drug to be given anticipating performing cystoscopy soon, but due to unanticipated delays in the case found that the time the cystoscopy was performed was >30min after the drug was given. This happened in two patients.

Explain why patients were stratified by age 65?

Response
The thought was that due to the natural decline in renal function with age it would be appropriate to account for this by stratifying by age.

Line 187 Was there standardization of the amount of distention fluid used for cystoscopy and or recorded? This may impact the ease of identifying the ureteral orifice and jets.

Response
Thank you, this is a good point. Distention was performed until the ureteral orifices were adequately visualized (this has been added to the manuscript). By only having FPMRS fellows or attendings perform this part of the cystoscopy we believed that over distention that would possibly influence results would be minimized.

Line 194 What available literature was used to justify the power analysis and assumption of 3 min. reference?

Response
We found no literature directly relating to the time to confirmation of time to ureteral patency, but did find a reference in the Female Pelvic Medicine and Reconstructive Surgery textbook discussing typical cystoscopy time of 5-8 minutes. This reference has been added to this line (it is used elsewhere as well).

Results:

Table 1.
Are there demographics available for hypertension, diuretic use, ERAS protocol and urine output? These could confound the results and should be listed if available.

Response
Unfortunately these data were not collected, and we would agree that these could be confounders. At our institution during study period the ERAS protocol was not in place.

Table 2.
There was a significant number of patients missing data on urine output. Was the urine output for the entire case or just during cystoscopy? This is a limitation if it is for the entire case since it is an indirect measure of GFR in conjunction with IFV.

Response
The urine output was for the entire case and was not always available from the record. Additionally, the urine output (when recorded) was recorded by the anesthesia team which was unblinded.
Discussion:
Line 233-243  Although the study did not show the predefined difference of 3 min., there is a good argument for clinical and cost effectiveness based upon the OR cost per min as stated.

Response
Thank you, we felt it best to not belabor this point as this study was not designed to evaluate cost effectiveness.

Line 265 What is the clearance and half life of furosemide? Is it less than 30 min as listed in the protocol? This could impact the primary outcome of intention to treat.

Response
Furosemide is principally cleared renally and the half life is 0.5-1 hour. It is possible patients may have still had effect after 30 minutes and exclusion was not appropriate, but as noted before this happened to two patients in the study.

Line 269 There should be a more detailed description of the type of surgeries listed in table 1. This could potentially impact risks of kinking and ureteral jet identification.

Response
This is a valid point, though unfortunately we do not have the specific data available as to which procedure was performed. The exclusion of any patients with lower urinary tract injury will hopefully decrease the chance of surgical procedure being a confounder.

Reviewer #3:
This is a concise, well-written, easy-to-read paper. Despite the lack of significance, this paper adds to the body of knowledge about a drug that we use commonly in clinical practice without much prospective comparison to placebo.

I am glad that the authors make a distinction between statistical and clinical significance: although their results reach statistical significance, they admit that clinical significance is limited.

The abstract is precise and clear.

The introduction frames the question adequately.

In the methods, I would have liked to see a brief discussion of the inclusion and exclusion criteria (if any) relative to renal function. Were there any patients whose renal function or lasix dependence was thought to be a relative contraindication to furosemide use? Alternatively, if there were no such
contraindications, perhaps include a paragraph in your discussion about the appropriateness of lasix use in populations with renal disease or insufficiency.

Response
Thank you for these comments. The exclusion criteria have been clarified, as patients with renal disease were indeed excluded.

The results are clearly presented.

The discussion well-written and does a nice job of not over-inferring the clinical significance of the statistical differences in time to ureteral jets.

Response
Thank you for your comments

Reviewer #4:

This is a double-blind randomized controlled trial to investigate the effect of furosemide on the time to confirmation for ureteral patency during intraoperative cystoscopy. Other outcomes included adverse reaction to study medication and delayed diagnosis of ureteric injury. The authors conclude that patients that received furosemide were 2.3 times more likely to have ureteral patency confirmed compared to placebo. Of note, no adverse events were noted and there were no delayed diagnoses of ureteric injury. This is a well planned and executed study. The authors should consider adding to the discussion that indigo carmine is once more available. The weaknesses of this study are addressed by the authors - mainly not following kidney function or other markers to assess the safety of furosemide. Although limited to urogynecologic procedures this is still applicable to all hysterectomies.

Response
Thank you for these comments and the suggestion regarding indigo carmine, which is important in any discussion of cystoscopy.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

lines 240-243: This is relevant only if the OR times were different for the two cohorts. If these comments are included, then should provide in Tables a comparison of OR times for the two cohorts.
Response
Thank you for this comment. Unfortunately the data for overall OR time was not available so will not include these comments.

Table 1: Since this was a RCT, the p-values should be omitted. There is no need to statistically compare the baseline differences. The estimated blood loss and IV fluids should be cited as post-op surgical comparisons.

Response
Thank you, these changes have been made to Table 1.

Tables 2, 3: Need to separate and clearly identify the primary (T₂ - T₀ time in seconds) outcome from the secondary outcomes. Drug time, time to 1st ureteral jet, urinary output, and hazards ratios of time to T₂, drug time and time to 1st ureteral jet are all secondary outcomes, ie, not powered in the methods section. Similarly, the Discussion section should clearly delineate the primary outcome from all secondary ones.

Response
Thank you for this comment, these points of clarification have been made in the table and manuscript as requested.

Fig 1: Need to include, along the x-axis, the number of patients remaining in each cohort. Since the Q3 times for the cohorts were 137 and 280 seconds, should include time increments at 100 second intervals, not 200 seconds.

Response
This figure has been updated to reflect these suggestions, which do help present the data more clearly, thank you.

EDITOR COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

  1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.

Response
Thank you for your work to increase transparency, we gladly opt-in.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. This statement must appear at the end of your Materials and Methods section. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (e.g., study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Examples of statements can be found online at http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf.

Response
This statement has been included, thank you.

3. Author Agreement Forms: Please note the following issues with your forms. Updated or corrected forms should be submitted with the revision.

Response
These forms will be included.

Isabel Prieto, MD - Did not agree to be accountable for the work.

Elisha Jackson, MD - Did not indicate a conflict of interest disclosure. Did not draft the work or give final approval of the version to be potentially published.

Please note:

a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.

b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org):

* Substantial contributions to the conception or design of the work;
OR
the acquisition, analysis, or interpretation of data for the work;
AND
* Drafting the work or revising it critically for important intellectual content;
AND
* Final approval of the version to be published;
AND
* Agreement to be accountable for all aspects of the work in ensuring that
questions related to the accuracy or integrity of any part of the work are
appropriately investigated and resolved.

The author agreement form is available online
be scanned and uploaded into Editorial Manager with your other manuscript files.
Any forms collected after your revision is submitted may be e-mailed
to obgyn@greenjournal.org.

Response
Thank you, these requirements have been reviewed.

4. Our journal requires that all evidence-based research submissions be
accompanied by a transparency declaration statement from the manuscript's lead
author. The statement is as follows: "The lead author* affirms that this manuscript
is an honest, accurate, and transparent account of the study being reported; that
no important aspects of the study have been omitted; and that any discrepancies
from the study as planned (and, if relevant, registered) have been explained."

*The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the
lead author is a different person, please ask him/her to submit the signed
transparency declaration to you. This document may be uploaded with your
submission in Editorial Manager.

Response
This statement is included on the opening to this cover letter, thank you.

5. Standard obstetric and gynecology data definitions have been developed
through the reVITALize initiative, which was convened by the American College
of Obstetricians and Gynecologists and the members of the Women’s Health
Registry Alliance. Obstetrics & Gynecology will be transitioning as much as
possible to use of the reVITALize definitions, and we encourage authors to
familiarize themselves with them. The obstetric data definitions are available
at [http://links.lww.com/AOG/A515](http://links.lww.com/AOG/A515), and the gynecology data definitions are
available at [http://links.lww.com/AOG/A935](http://links.lww.com/AOG/A935).

Response
Thank you, the data definitions were reviewed and the manuscript reviewed for any discrepancies.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

Response
Thank you, the discussion is 606 words and the Introduction has been modified to now be 245 words

7. Title: Please delete, "The Effect of," from the title.

Response
This change has been made, with the title now reading:
FUROSEMIDE USE AND TIME TO CONFIRMATION OF URETERAL PATENCY DURING INTRAOPERATIVE CYSTOSCOPY: A RANDOMIZED CONTROL TRIAL

8. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

Response
Thank you, these have been reviewed.
9. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

**Response**
*Furosemide and cystoscopy*

10. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

**Response**
*Thank you, the abstract has been reviewed and changes made per reviewer comments and to maintain consistency with manuscript. The word count is 252 words*

11. Abstracts for all randomized, controlled trials should be structured according to the journal's standard format. The Methods section should include the primary outcome and sample size justification. The Results section should begin with the dates of enrollment to the study, a description of demographics, and the primary outcome analysis. Please review the sample abstract that is located online here: [http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf](http://edmgr.ovid.com/ong/accounts/sampleabstract_RCT.pdf). Please edit your abstract as needed.

**Response**
*Thank you, the manuscript was structured according to these standards.*

12. Only standard abbreviations and acronyms are allowed. A selected list is available online at [http://edmgr.ovid.com/ong/accounts/abbreviations.pdf](http://edmgr.ovid.com/ong/accounts/abbreviations.pdf). Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

**Response**
*The manuscript was reviewed for standard abbreviations and acronyms ensuring that these expectations are met.*

13. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data
or a measurement.

Response
These changes have been made where appropriate.

14. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

Response
The checklists have been reviewed and appropriate changes made.

15. The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly. If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at http://www.acog.org/Resources-And-Publications.

Response
Thank you for pointing this out. The redacted Practice Bulletin has been removed as a reference, thank you.

16. Figures

Figure 1 (CONSORT): Please update or clarify n values (216-65 does not equal 150).

Response
Thank you, this has been fixed to reflect the actual numbers (215-65).

Figure 2 (Kaplan-Meier): Please provide a higher resolution version of this figure. Note that this manuscript has 2 Figure 1s. Please cite both in the body of the manuscript and update the figure numbers based on the order they appear.

Response
A figure with higher resolution is included and the figure titles updated and cited appropriately.
17. If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Dec 21, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief
Dear Randi,

Thank you very much for the emails and clarifications. I am attaching a revised manuscript with changes tracked and replies to comments.

I am unable to log into the system to change my Precis, but I am now giving written authority for you or the editors to change it appropriately to reflect the requested changes. I did add intravenous administration to the abstract and the body text.

Please let me know if I missed anything or need any further changes prior to the final review.

Thank you very much for your time and help

Sincerely,
Allison Wyman, MD

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The Editors have two additional requests:

1. Please edit your Precis to say: “Compared with placebo, intravenous administration of 10mg furosemide... confirmation of ureteral patency.”
2. Please make it clear in the Abstract and body text that it is “intravenous administration” of the furosemide.

Thank you,
Randi
Your revised manuscript is being reviewed by the Editors. Before a final decision can be made, we need you to address the following queries. Please make the requested changes to the latest version of your manuscript that is attached to this email. **Please track your changes and leave the ones made by the Editorial Office.** Please also note your responses to the author queries in your email message back to me.

1. General: The Editor has made edits to the manuscript using track changes. Please review them to make sure they are correct.

2. Line 137-140: Order reassigned for clarity. Please review to make sure this is correct.

3. Line 192-193: For articles submitted to O&G after July 1, 2018, we require a data sharing statement indicating what we’ve listed here. Your answers (in italics) may be different from what I’ve listed here. If so, please edit the responses accordingly.

4. Line 202: Where is the in-text citation for table 2? Tables should be cited in order at first mention. Please add the in-text citation and reorder your tables if needed.

To facilitate the review process, we would appreciate receiving a response by December 28.

Best,
Randi Zung

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Randi Zung (Ms.)
Editorial Administrator | Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
409 12th Street, SW
Washington, DC 20024-2188
http://www.greenjournal.org
Dear Stephanie

Thank you for the email and the updated figures. They look great to me! As far as your query, I would like to keep it saying "intervention" instead of the lasix administration. Unless the editors desire it to be changed, then of course I am amendable.

Thank you again,
please let me know if you need any thing else or have any further questions

sincerely
Allison

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Wednesday, December 19, 2018 11:52:25 AM
To: Wyman, Allison
Subject: O&G Figure Revision: 18-2015

Hello again Dr. Wyman,

Your figures and legend have been edited, and PDFs of the figures and legend are attached for your review. Please review the figures CAREFULLY for any mistakes. In addition, please see our query below.

AQ1: In Figure 1, would you like to specify the intervention rather than say “allocated to intervention?”

PLEASE NOTE: Any changes to the figures must be made now. Changes at later stages are expensive and time-consuming and may result in the delay of your article’s publication.

To avoid a delay, I would be grateful to receive a reply no later than Friday, 12/21. Thank you for your help.

Best wishes,

Stephanie Casway, MA
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