



# Is Fever a Marker of Infection or Side Effect of Misoprostol?

Amber Edinoff, University of Arizona College of Medicine, Phoenix

Dean Coonrod, MD, MPH, Maureen Sutton, MPH, CCRP, Bikash Bhattarai, PhD. Maricopa Integrated Medical System



## Abstract

Endometritis complicates 6-27% of cesarean deliveries. Our study will look at the rates of endometritis from three time periods – prior to and after the implementation of vaginal cleansing at time of cesarean delivery as well as an interim group. A retrospective chart review was performed on women undergoing cesarean delivery prior to and after the policy change. Misoprostol administration was also recorded since there is a routine use of 400µg of buccal misoprostol policy implemented at the midpoint of the interim group. The frequency of fever was 4.5% in the pre-policy group compared with 22.2% in the post-policy group which was hypothesized to be due to misoprostol use. The rate of endometritis without removing patients receiving misoprostol was 3.8% in the pre-policy period and 15.2% in the post-policy period. The rates of endometritis with the excluding those receiving misoprostol were 3.8% in the pre-policy period and 6.7% in the post policy period, however, the difference was not significant. The rates of endometritis were higher in the post policy group. It was found that if a patient received Misoprostol, then they were 3 times more likely to be diagnosed with endometritis

## Introduction

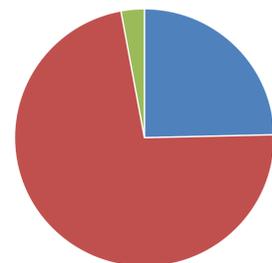
Cesarean delivery is one of the most common surgical procedures that is performed in the United States. One cause of infection after a cesarean delivery is endometritis. This is defined as an infection of the decidua and is a common cause of postpartum febrile morbidity leading to prevention intervention. For example, a decrease in endometritis was > 60% in both elective and non-elective groups with the use of prophylactic antibiotics. A Cochrane review evaluated four trials regarding preoperational vaginal cleansing. This review found that with immediate preoperational vaginal preparation there was a significant reduction in endometritis.

Misoprostol is a uterotonic used to reduce postpartum hemorrhage. Current randomized control trials have shown an increase in both pyrexia and shivering in the group receiving misoprostol. In April 2016, a policy instituting routine use of 400 µg of misoprostol after cesarean delivery at MIHS. The original study was a retrospective chart review looking at the use of vaginal cleansing in reducing the rates of endometritis and found a paradoxical increase. This lead to the current study to examine if the routine use of misoprostol at MIHS was a potential cofounder.

## Materials and Methods

Retrospective chart review of charts from July 2015- November 2015, February 2016-June 2016 and February 2017- June 2017 which comprises the pre, interim and post policy periods. The inclusion criteria included all women undergoing non-emergent cesarean delivery (Category II-IV) and had postpartum visit. The exclusion criteria includes allergy to iodine containing solutions and planned cesarean hysterectomy. Definition of the outcome measure was endometritis which was defined as postoperative fever  $\geq 38^{\circ}\text{C}$  plus fundal tenderness, in the absence of clinical or laboratory evidence of alternative source of infection, and wound infection. Endometritis was defined in this study as having 2 or more symptoms and/or having a diagnosis code of Endometritis. These symptoms are defined as fever, tachycardia, and/or fundal tenderness

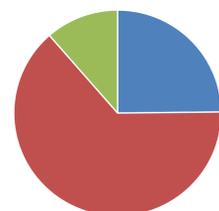
Endometritis in the Pre-Policy Period



■ Without Endometritis (DX or 2 SX)  
■ Endometritis with 1 sx  
■ Endometritis With dx code or 2+ SX

Rates of Endometritis in the Pre-Policy Period including patients who received Misoprostol

Endometritis in the Post-Policy Period



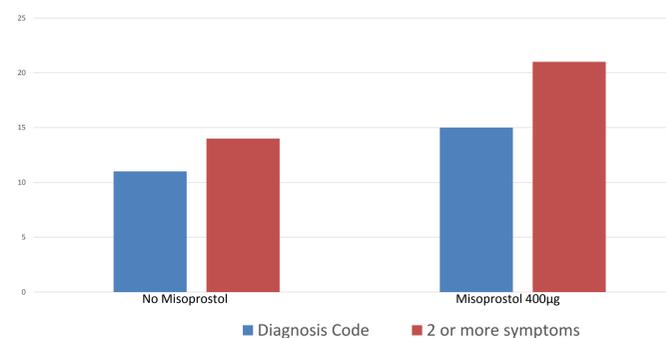
■ Without Endometritis (DX or 2 SX)  
■ Endometritis with 1 sx  
■ Endometritis With dx code or 2+ SX

Rates of Endometritis in the Post-Policy Period including patients who received Misoprostol

## Results

There was an increase in the incidence of fever between the pre and post policy groups (4.5% vs 22.2%). In the pre-policy group, 1.5% of patients had endometritis defined as a diagnosis code or 2+ symptoms while 6.5% of patients in the post policy group had the same ( $P>0.016$ ). Breaking down the diagnosis and symptoms groups, 1.5% had an endometritis diagnosis code and 1.5% had 2 or more symptoms in the pre-policy group while 6.0% had an endometritis diagnosis code and 7.0% had 2 or more symptoms in the post-policy group. We broke up the interim group into pre-implementation of misoprostol policy which we call interim 1 and post implementation of the misoprostol policy called interim 2. In the Interim 1 group, 3.0% of patients had an endometritis diagnosis code while 8.9% had two or more symptoms. In the Interim 2 group, 7.6% of patients had a diagnosis code of endometritis and the same percentage had two or more symptoms. The odds ratios regarding endometritis between the pre policy and the interim 1 groups is 2.2 ( $p=0.381$ ) and between interim 2 and the post policy group is 1.3 ( $P= 0.642$ ). When we looked at patients who received misoprostol across the policy periods, we found that 47.7% of patients in the study had a diagnosis code of endometritis and 60.0% of patients had two or more symptoms of endometritis. Overall, we found that patients were three times more likely to be diagnosed with endometritis if they received misoprostol (OR 3.2,  $P=0.004$ ).

Rates of Endometritis



Rates of Endometritis in patients who did and in those who did not receive misoprostol 400 µg ( $P> 0.004$ )

## Discussion and Conclusions

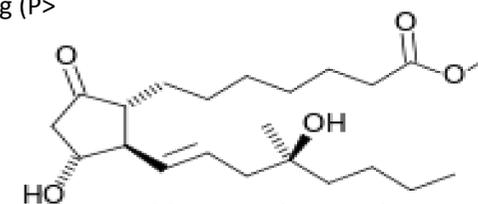
The original study had surprising results. It found that there was a higher incidence of endometritis in the post policy period. This is both counter intuitive and not what has been found in other recent studies regarding preoperational vaginal cleansing. The higher frequency of fever could have lead to an increase in patient evaluation by providers which could have lead to an increased in the diagnosis of endometritis. This was thought that perhaps be due to the fact that misoprostol was being routinely used during the post policy period as adjunct therapy for postpartum hemorrhage prophylaxis. Our data did show that there was a 3 times greater likelihood to be diagnosed with endometritis if the patient was given misoprostol which lends support to our idea that misoprostol was a cofounder in the original study. The next step with the current data is to do a stratified analysis to control for misoprostol use to further test this conclusion. Our study points to the importance of evaluating for misoprostol use when considering a potential diagnosis of endometritis in the clinical setting

## Acknowledgements

I would like to thank Dr. Coonrod and Maureen Sutton for their support and guidance on this project. I would also like to thank Bikash Bhattarai, PhD for help with statistical analysis. I also want to thank Chelsea Drake, MD and Rachel Pile for their work on the initial project.



Misoprostol 200µg Tablets



Molecular formula for misoprostol



Preoperational Vaginal Cleansing Solution