Antibiotic therapy for active Crohn’s disease

1. **The patient:**
   39 year old man known to have Crohn’s disease presents to the Emergency Treatment Center complaining of crampy abdominal pain and worsening watery diarrhea. He is afebrile and abdominal exam is benign. He has mild leukocytosis without a left shift. As per patient, his presenting symptoms correspond to his usual “Crohn’s flare-ups”. In addition to a course of oral steroids, does he need to be started on antibiotics?

2. **Searching for evidence:**
   PubMed search was done using “Crohn’s” and “antibiotics” as key words with the following limits: Humans, Randomized Controlled Trial, and English.

3. **Description of the study:**
   This was a double blind, multicenter, randomized controlled trial conducted in Canada. The objective was to assess if adding antibiotics (Metronidazole and Ciprofloxacin) to oral steroids would improve the remission rate in patients with active Crohn’s disease.

4. **The research question:**
   Population: patients with active Crohn’s disease of the ileum, right colon, or both.
   Intervention: adding antibiotics to oral steroids.
   Control: using only oral steroids.
   Outcome: remission rate after 8 weeks of therapy.

5. **Importance of the study:**
   Antibiotics are often given to patients with active Crohn’s disease treated with steroids with the assumption that broad-spectrum antibiotics might enhance the efficacy of the anti-inflammatory drugs. This is based on evidence from animal models showing that the enteric bacterial flora may be contributing to the chronic pathologic inflammatory responses.

6. **Detailed description of the study:**
   Population: 134 patients from 14 university medical centers and 2 community-based gastroenterology practices were recruited to participate in this study. They all had active Crohn’s disease involving the ileum, proximal colon or both. Disease location was determined by either colonoscopy or air-contrast barium enema performed within 2 years. Disease activity was defined using the Crohn’s Disease Activity Index (CDAI)
   Intervention: adding oral ciprofloxacin and metronidazole both 500 mg twice daily to oral budesonide 9 mg once daily for a total of 8 weeks.
   Control: using only oral budesonide 9 mg once daily for 8 weeks.
   Outcome: there was no difference was noted between the treatment groups in the rate of remission at any time during the 8 week follow-up period. However there was a non-significant tendency towards improved outcome with adding antibiotics when there is involvement of the colon. Patients treated with antibiotics were significantly more likely to experience diarrhea.

7. **Validity of the study:**
Baseline characteristics of both treatment groups were similar
The patients were randomized
It was a double blind study
Analysis was done based on “intention to treat” but 2 in each treatment group, took at least 1 dose of the study medication but failed to provide efficacy data and were excluded from analysis.

8. **Summary of primary results:**
   After 8 weeks of treatment, 33% (21%-44%) of the patients treated with antibiotics were in remission versus 38% (26%-50%) in the placebo group (p=0.55). However, in patients with disease of the ileum and colon, 53% of the patients receiving antibiotics were remission compared to 25% of those receiving placebo (p=0.10). Conversely, patients with disease of the ileum only, 26% of the patients receiving antibiotics therapy were in remission compared to 42% of those receiving placebo (p=0.09). However, significantly more patients in the antibiotics group had diarrhea at the end of the 8 weeks (20% vs. 6%, p<0.05)

9. **Applying the results of the study:**
The patient had previously evidence of colonic inflammation on previous colonoscopy. The study showed that there was no benefit from using antibiotics in active Crohn’s. In the sub-group analysis there was a tendency toward higher remission rates with antibiotics in patients with colonic involvement but this study failed to show statistical significance. This might be secondary to the small sample size and to the fact that the latter conclusion came from subgroup analysis.

10. **Decision:**
The patient reported that he has been successfully treated using only oral steroids. Therefore, the decision was not to add oral antibiotics.

11. **Conclusion:**
The addition of antibiotics to oral steroids has not been proven to be beneficial for the treatment of patients with active Crohn’s disease. In patients with evidence of colonic involvement, it may improve outcome. However, it may cause more diarrhea.