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# Exploring alternative treatment options for a patient with heavy menstrual bleeding and mistrust of the healthcare system

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## Erratum

This clinical decision report was originally published under the wrong title ("Exploring alternative treatment options for heavy menstrual bleeding for a patient with mistrust of the healthcare system"). The title has been corrected. (2022.12.08, The Editors).

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# Exploring alternative treatment options for a patient with heavy menstrual bleeding and mistrust of the healthcare system

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**ABSTRACT** A clinical decision report using:

Tinelli A, Gustapane S, D'Oria O, Licchelli M, Panese G. Nutraceuticals in fibroid management after ulipristal acetate administration: An observational study on patients' compliance. *International Journal of Gynecology and Obstetrics*; 2022;156(1):133-138. https://doi.org/10.1002/ijgo.13692

for a patient with chronic, symptomatic anemia with menorrhagia and uterine fibroid.

***Keywords***: *uterine fibromas, heavy menstrual bleeding, menorrhagia, anemia, natural, nutraceuticals, alternative medicine*

## Clinical-Social Context

Lilianna Borgias (a pseudonym) is a 44-year-old African American woman who presented to the emergency department for increasing dizziness and shortness of breath. She had a past history of chronic microcytic anemia, asthma, and urticaria associated with blood transfusions. At the ED, it was found that she had a hemoglobin of 6.7g/dL but she refused blood transfusions because she previously experienced urticaria that developed within one week of blood transfusions which lasted for months. Blood transfusion would be a last resort.

Ms. Borgias had a pronounced history of menorrhagia since she was a young adolescent and had been on oral iron supplementation since that time. She stopped the oral iron supplementation because the gastrointestinal side effects became intolerable. Despite oral iron supplementation, she still required multiple blood transfusions; however, when she began to receive intravenous iron infusions, she ceased the need for blood transfusions for several years prior to her current hospitalization. While in the hospital, we discovered she had uterine fibroids which may have contributed to her menorrhagia and anemia. However, when possible oral medical options were discussed, Ms. Borgias made it clear that she was not comfortable with the idea of medications or surgical interventions, expressing instead an interest in natural alternatives. She held a strong belief in controlling her health through diet and supplementation and felt a strong distrust in any use of standard medical treatment. Her distrust seemed to be rooted in decades of feeling ignored by the medical professionals and her perceived lack of answers by them for her heavy bleeding and lack of improvement with medical treatment during this time. The patient's sex and ethnicity may have contributed to previous practitioners' dismissal of her opinion, leading to her seeking alternative medical treatments. Understanding the patient's past experiences and wishing to respect her preferences led us to a clinical question not previously explored.

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## Clinical Question

Are there safe and effective alternative treatments for uterine fibroids that can improve the patient's quality of life?

## Research Article

Tinelli A, Gustapane S, D'Oria O, Licchelli M, Panese G. Nutraceuticals in fibroid management after ulipristal acetate administration: An observational study on patients' compliance. *International Journal of Gynecology and Obstetrics*; 2022;156(1):133-138. https://doi.org/10.1002/ijgo.13692 [1]

## Description of Related Literature

A review of the literature was begun by searching the terms "natural" and "uterine fibroid" using a summon search of the databanks owned by the Wayne State University Library and sorted by newest articles first. The search yielded 6,294 journal articles and 257 reports. The search was then narrowed by limiting the results to the last five years and selecting only journal articles leaving 1,981 articles to review. The field was further narrowed by replacing the search term "natural" for the term "nutraceuticals" following the review of several articles and their terminology. This search narrowed the results to 245 Journal articles. Only articles from journals that were unlikely to have a contributing bias were considered including the International *Journal of Molecular Biology*. Journals such as *Nutrients* were ruled out for this paper, as were papers that covered other gynecological issues such as endometriosis or uterine cancer.

The search was then supplemented to compare the use of traditional medical approach in the treatment of uterine fibroids. This was first begun by referring to UpToDate for the current classifications of, and methods of treatment for, uterine fibroids. The search term was "uterine fibroids treatment" and the top article was "Uterine fibroids (leiomyomas): Treatment overview".[2] This article supplied the context for further research using the summon feature with the terms "uterine myoma", "heavy menstrual bleeding", and "treatment" resulting in 343 Journal articles. The MeSH terms were found to be "dietary supplement" and "leiomyoma".

Biro R et al.[3] was a 6-month trial of the chemical epigallocatechin gallate (EGCG) in 25 women with asymptomatic or oligo-symptomatic uterine fibroids that measured quality of life using SF-12 questionnaire and a custom myoma related questionnaire as well as objective measurements of fibroid size. The study found that quality of life improved via the SF-12 questionnaire, but there was no objective improvement or subjective improvement as measured by their custom questionnaire. This study was not chosen because its population did not represent that of Ms. Borgias because the patients were asymptomatic, and the custom symptomology test may have been a confounding variable. Ciebiera M et al.[4] was an excellent review article that summarized the current medications and alternative therapies being explored for uterine fibroids, but it was not chosen because it was not the most current research (published in 2017) and because it did not offer specific treatment regimens unlike the chosen article by Tinelli A et al.[1]

Included in the articles concerning traditional Western medicine was the 12-month trial by Neri M et al.[5] that examined the use of ulipristal acetate (UPA) in women with heavy menstrual bleeding. The benefits of the article were both the population and its length. Its results were however limited by its small sample size of 19. The review article by Donnez J.[6] excellently summarized the current advantages of UPA as both a presurgical treatment and a possible alternative to surgery entirely as well as the risks and benefits to administering the drug. Both were not chosen as the focus of this review because of Ms. Borgias' personal wishes to avoid medication and were included as supplementary information should the patient wish to discuss what the possible risk and benefits for each medical approach were.

The article chosen for discussion was the 3-month trial of EGCG and vitamin D3 by Tinelli A et al. The trial was begun after the Italian government banned the use of UPA due to its potentially hepatotoxicity and followed 30 women for 3 months after they were switched to EGCG and vitamin D3. The trial measured quality of life via the Uterine Fibroid symptoms and Quality of Life (UFS-QOL) questionnaire and split the analysis into symptoms severity (SS) and health-related quality of life (HRQL). This article was chosen because the patient population best matched that of Ms. Borgias since all the patients were symptomatic enough to require UPA treatment and because it focused on quality-of-life improvement, the question most relevant to Ms. Borgias situation. It was also chosen because it investigated a combination of two of the most promising nutraceuticals under investigation right now.

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According to the SORT criteria the literature concerning the treatment of uterine fibroids with nutraceuticals was Strength of Recommendation B, based on the limited, medium quality clinical trials.[7]

## Critical Appraisal

The impetus for the initiation of nutraceuticals was the government's sudden ban of UPA and the need to find a way to sustain patients reliant on UPA. The studies unique strength and downfall is that it was begun during the COVID-19 pandemic. The status of the global pandemic drove the consideration of treatments that were not only proven safe but had limited side effects because they could not be managed in an office. Limitations included the limited sample size and length of the study due to a lack of access to in-person physicals and meetings. The circumstances contributed to the choice of study type as an open-label trial since it was conducted as a stop gap for patients reliant on UPA. This prevented randomization and blinding on both sides of the study allowing for the placebo effect to be a confounding variable. A variable that may have compounded by the recruitment technique requiring women to agree to a "natural" alternative possibly introducing a selection bias to participants interested in natural alternatives. Although it must be remembered that this was studied in women who were well acquainted with a prior traditional medical management of their condition. An additional weakness of the study is that it began therapy immediately following the cessation of UPA. Meaning it is possible that the women continued to feel residual effects of the UPA and contributed it to the new regimen.

The setting also limited the study to more subjective form of measurements such as the UFS-QOL as opposed to previous studies that focused on objective measurements such as the reduction of fibroma size. The information was collected by asking patients to anonymously fill out the UFS-QOL at the time they stopped taking UPA (T0) and at the end of 3 months of natural therapy (T1). The UFS-QOL was comprised of 37 questions using a scale of 1-5. 8 of the questions concerned symptom severity (SS), in which a higher score corresponded to worse symptom severity and the rest were comprised of the Health-Related Quality of Life (HRQL) question in which a higher score was associated with an improved state of living. The subsection of the HRQL included: Concern, Activities, Energy and Mood, Control, Self-consciousness, and Sexual Function. The reliance on a such a subjective form of measurement alone limits the study, but it also places the emphasis of importance on the experience of those suffering from the condition. It also recognizes that fibroid size does not always correspond with quality of life.

The study found that there was a significant improvement in all the life-related parameters analyzed with the "control" subgroup increasing the most by 16.76% on average. The other subgroups increased by the following: "concern" rose by 10.16%, "activity" increased by 11.5%, "energy and mood" rose by 9.4%, "self-consciousness" increased by 12.5%, and "sexual function" increased by 12.5%. Overall, the SS category decreased by 10.28% and the HQRL increased by 10.6%. These results demonstrate that EGCG and vitamin D could represent an improvement in quality of life as well as medication compliance. The results were complete and documented several subcategories of quality-of-life while continuing to measure significant improvement as analyzed by the student t-test with a p value of $< 0.05$.

The treatment method of EGCG 150 mg plus vitamin D3 25 µg plus vitamin B6 5 mg is a feasible therapeutic plan and option for women who are fearful of new medications and have had prior negative experiences with the medical field before. The ease of compliance with this therapy is demonstrated by the ability of the women to participate in the study without attrition. Although it is possible that the study selected for patients that were already motivated to taking daily medication. The small size of the trial, qualitative measurements, and short-term follow up place the individual quality of the study as a Level of Evidence 2 using the SORT criteria.[7] However this study is an important first step in the implementation of larger blinded trials as in-person monitoring can now be implemented and provides enough preliminary evidence of feasibility, low side-effect profile, and subjective improvement to offer it as possible treatment in those fearful of traditional medicine.

## Clinical Application

The therapy offered by Tinelli A et al. trial is an excellent alternative to beginning discussions with a nervous or wary patient like Ms. Borgias. Ms. Borgias had previously faced decades of menorrhagia and symptomatic, uncontrolled anemia that had dictated her life. She was willing to discuss treatment that could be helpful, but it was clear that knowledge of natural alternatives was important for her to be able to consider and would help her maintain her autonomy. These compounds have several trial demonstrating significant improvement in quality of life and the compounds have been shown to decrease fibroma size in animal studies. It is also beneficial in terms of

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cost and reduced need for close follow up care given the lack of side effects, especially when compared to the risk of hepatotoxicity seen with treatments like UPA. In the case of Ms. Borgias, this would be both freeing and enabling since she has had had multiple hospital stays a year for low hemoglobin requiring iron transfusions and she has been lost to follow up in the past. The supplements present the opportunity to build trust and return autonomy to a patient who had long been ignored or patronized. This research article presented a promising alternative for patients in many walks of life in terms of feasibility, compliance, and cost. However, communicating with the patient about the potential for escalation of care should the treatment fail to show improvement in their case must be discussed.

## New Knowledge Related to Clinical Decision Science

Part of the duties of a physician is the ability to interpret our patients' requests. In this case, when Ms. Borgias asked for a "natural" treatment, it was important to learn that the academic discourse used the term "nutraceuticals" to refer to naturally derived supplements for a proper review of the literature. Similarly, referring to reference texts such as UpToDate can provide additional terminology that can both broaden your search by incorporating specific language in the current academic discussion.

Considering the use of nutraceuticals when possible is important as a physician especially in the context of critically underserved populations. Often these populations have faced mistreatment or have been ignored by medical practitioners and rightfully have a distrust of medications. This distrust is only emphasized by using powerful medications with potentially harmful side effects that require the expense of the medication and rigorous follow up. Working with patients to find a solution with products that they are more comfortable with and are more affordable builds trust and helps them find a treatment plan that can work for them. In the case of uterine fibroids, they are rarely life threatening, even if they have a tremendous impact on quality of life. However, the key to helping populations like Ms. Borgias with large blood loss is to build trust and emphasize when it is vital to return to the hospital in cases with heavy bleeding such as if the patient begins to demonstrate symptoms of extreme fatigue, light-headedness, and dizziness. It also important to state that escalation of treatment to traditional Western medications and surgery may still be necessary if their quality of life has not been achieved on supplementation alone.

While providing nutraceuticals as a traditional physician may be uncomfortable or unfamiliar, as physicians we have the education to help meet and guide our patient's treatment goals by providing timely advice and expertise to their questions. Restoring trust was an important part of this clinical decision.

## Conflict Of Interest Statement

The author declares no conflicts of interest.

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