

USE OF GnRH AGONISTS PRIOR TO AN ENDOMETRIOSIS DIAGNOSIS

In today's age of rapid-paced medicine, the premise of "faster, better, more" pervades the healthcare industry. To be certain, a multitude of positive developments has been made in the realms of disease research and treatment. For every ailment, there is a readily available solution in our doctors' offices. In the interest of "faster, better, more," however, is the single most important piece of the healthcare puzzle - the patient - being trodden on? Have some industry players begun overstepping their bounds?

An example of such conduct is the ideology of a number of practitioners and pharmaceutical corporations that GnRH agonists can - and should - be used to diagnose Endometriosis. This practice is inherently flawed at best; of questionable ethics at worst.

A case in point is the recent "Consensus Statement Regarding the Management of Chronic Pelvic Pain and Endometriosis."¹ The statement, issued on behalf of a self-appointed "expert panel" comprised of 52 gynecologists and experts in consensus guideline development, concluded that "for women in whom Endometriosis is the suspected cause of pain, laparoscopic confirmation of the diagnosis is unnecessary." The authors instead recommend a course of medical therapy, including Danazol, GnRH agonists and progestins to potentially diagnose and treat the symptoms. For the purposes of this document, we will be limiting our statements to the use of GnRH agonists in such a manner; specifically, the most commonly prescribed agonist in the United States, Leuprolide acetate (Lupron®).

Presumably, an "expert" is one who has dedicated the majority of his or her practice to the study, care and treatment of Endometriosis. Said expert would most undoubtedly be well researched on Endometriosis and highly trained in thorough surgical eradication of the disease, utilizing medical therapy only when specifically relevant to the patient's unique situation. Unfortunately, such Endometriosis experts are in the minority; there are but a few of these true authorities practicing within the United States. Interestingly enough, the participation of such experts was conspicuously absent from this consensus panel. David Redwine, MD, of the St. Charles Endometriosis Treatment Center in Bend, OR is one such pioneer. Dr. Redwine has advanced not only the understanding of the disease, but has pioneered the most effective treatment approaches as well.

Unfortunately, Dr. Redwine's successes were minimized in the consensus paper, his studies called "inconsistent."² Other highly regarded experts in Endometriosis are markedly missing from the Panel as well, including those from The Center for Endometriosis Care in GA; The Center for Advanced Laparoscopic Surgery in NY; The Athena Institute of Health in CA; The C. Paul Perry Chronic Pelvic Pain Clinic in AL; Georgia Reproductive Associates in GA; and Helena Women's Health in CA, just to name a few.

There are, however, several "Advisors" to Takeda Abbott Pharmaceuticals, the manufacturers of Lupron®, present on the panel.³ Inevitably, their presence naturally leads to speculation as to the validity of their conclusions and raises the question of bias.

Having noted the lack of many recognized experts from the panel, we believe it is unjust to arrive at a conclusion advocating the use of pre-surgical GnRH therapy (i.e., Lupron®) in Endometriosis patients, without considering the contributions of those experts who effectively treat the disease without GnRH intervention everyday. We further recommend that far more research be performed on the long-term effects of GnRH therapies such as Lupron® before advocating their

usage in a manner which may ultimately prove more harmful than helpful.

Research data is replete with confirmation of the fact that Endometriosis, while suspected, cannot be firmly diagnosed without biopsy. GnRH therapy has a place in Endometriosis treatment; however, it lacks good judgment on the part of the physician to put his or her undiagnosed patient on such a powerful medication without a confirmed diagnosis via laparoscopy or where appropriate, laparotomy. To do so thereby causes further delay in offering a true diagnosis; delays surgical removal of the Endometriotic implants; exposes her to potentially negative and lasting side effects as a result of GnRH usage; and in many cases, fails to resolve her pain, thereby extending the length of time she continues to suffer. Lupron®, for example, is known far and wide throughout the Endometriosis patient community for significantly negative and long-lasting side effects, yet the many complaints of those patients suffering from such effects are largely ignored and invalidated by the medical community. This situation is difficult enough for those who know the cause of their pain; are we to now expect undiagnosed patients to undergo the same maltreatment?

In their Newsletter, Endometriosis experts at the Center for Endometriosis Care wrote, "Lupron doesn't get rid of Endometriosis. It is expensive and has significant and sometimes permanent side-effects. That's a lot of items in the "no" column."⁴ This is not an appropriate or acceptable standard of care for Endometriosis patients.

Rather than promoting "quick fix" injections which enable practitioners to spend less time studying expert surgical techniques and thereby reducing their hours in the operating room, but allows them to spend many billable hours in the office setting, we should instead be focusing on the best way to serve Endometriosis patients: rapid diagnosis and thorough disease removal - both of which can be accomplished via the laparoscopic excision procedure pioneered by Redwine et. al.

To be certain, a decrease of pain during Lupron® therapy does not prove that the patient has Endometriosis,⁵ and proven Endometriosis experts have shown time and again that medications are only short term relievers for Endometriosis in many cases. Timely and efficient diagnosis accompanied by careful and thorough removal of the disease offers far better results - without exposing the patient to harmful and potentially long-term side effects.

There are a number of discussions attempting to rationalize the use of pre-diagnostic GnRH therapy as a cost-effective treatment approach. What about the cost to the patient's well being? Again, the significantly negative effects of GnRH therapies like Lupron® are not adequately addressed; rather, the side effects are referred to repeatedly in the literature as "temporary and related to hypoestrogenism, including vasomotor flushes, headache, and vaginal dryness." Also of note is the "reversible" vertebral bone density loss. There are hundreds, if not thousands, of women in the Endometriosis community who suffer far worse effects, and have been for upwards of 5 years since their last injection. The ERC hears from many such women, who convey to us that the effects they suffer from GnRH therapy "are worse than their Endometriosis pain ever was." One must ask, why are the concerns of these women not being addressed?

In two data collection studies performed by the Endometriosis Research Center, women were asked to share feedback about their experience with Lupron®. The results (both data collections were limited to Lupron® users only):

27.71% found Lupron® to be tolerable and helpful at symptom relief;
7.23% found Lupron® to be tolerable, but not helpful at symptom relief;
16.87% found Lupron® to be intolerable, but nonetheless helpful at symptom relief;
48.19%, almost half of the participants, indicated that Lupron® WAS INTOLERABLE AND NOT HELPFUL AT SYMPTOM RELIEF.

These impartial and unbiased results are strikingly different from the experiences propagated throughout the medical community and TAP's various websites.

For example, one woman, "Lisa," tells her positive Lupron® experience on TAP's corporate site at <http://www.tap.com/patients/endometriosis>:

"I felt awesome after I started the treatment," Lisa said. "I know that endometriosis is not a 'curable' condition. But I'm glad I took this treatment [sic]." "Lisa's" story becomes questionable when we read further down the page, where it is revealed that she is an "employee of TAP."

In a second study, patients were asked for feedback regarding their POST-Lupron® experience. The results were even more startling:

21.67% did not suffer any lasting effects from Lupron®;
26.67% suffered lasting effects for up to 6 mos. after Lupron®;
10.00% suffered lasting effects for up to 1 year after Lupron®;
5.00% I suffered lasting effects for up to 2 years after Lupron therapy®;
6.67% suffered lasting effects for up to 3 years after Lupron therapy®;
6.67% suffered lasting effects for up to 4 years after Lupron therapy®;
23.33%, a staggering amount of participants, suffered lasting effects for UP TO 5 OR MORE YEARS after Lupron®.

"Effects" included but were not limited to seizures, cardiac problems, and fibromyalgia. Yet, these effects are largely unrecognized in the medical literature. Again, such effects continue to be ignored and invalidated by healthcare providers at large.

Our results strongly contradict Takeda Abbott's own statements, which claim that Lupron® is "well tolerated." TAP's literature also acknowledges only those side effects "related to hypoestrogenism, including vasomotor flushes, headaches, vaginal dryness and an average of 3.2% reversible bone loss;" and states that "side effects will also disappear as your estrogen levels gradually return to normal once you have finished your course of treatment with Lupron Depot®" [see www.endofacts.com/expect/after.htm]. According to TAP, no patient should suffer any effects beyond approximately 3-6 months after terminating Lupron® therapy. On the contrary, as reflected in the ERC's second data collection study, this is simply not the case for many who have undergone treatment with Lupron®.

We also know that young women treated with GnRH agonists for Endometriosis may never achieve peak bone mass density, increasing their risk for osteoporosis later in life.⁶ Endometriosis is found during laparoscopy in 35%-70% of adolescents (including ages 12-17) presenting with chronic pelvic pain.⁷ Lupron® has only been approved for treatment in those women ages 18 and above. How then does the consensus panel address the patients' age as well as the bone mass density concern? Should these young patients presenting with possible Endometriosis be forced to wait until their late teens or early twenties - or even beyond - to have their pain adequately diagnosed and treated?

One need only open a newspaper to note that Takeda Abbott Pharmaceuticals has been the subject of ongoing investigations and was in fact fined \$875 million for illegal promotion of their drug, Lupron®. Yet, they continue to spend thousands of dollars marketing the drug direct to patients via no less than four patient oriented websites⁸ and through the financial support of various

physicians and organizations within the Endometriosis community. Again, the question of bias comes to the forefront of the issue. Are their efforts paying off? Drug company ties sometimes "influence and/or distort study results," according to Yale University researchers, who noted "strong and consistent evidence [exists] that industry-sponsored research tends to draw pro-industry conclusions."⁹

Beginning in 1938, DES (Diethylstilbestrol) was prescribed to an estimated 4.8 million pregnant women in the U.S.,¹⁰ touted as the recommended prophylaxis "in ALL pregnancies." Advertisements for the drug at the time boasted "96% live delivery with desPLEX in one series of 1200 patients - bigger and stronger babies, too. No gastric or other side effects with desPLEX - in either high or low dosage."¹¹ It was not until over 30 years later in 1971 that researchers began realizing the extremely dangerous effects DES held for the woman, her children and possibly her grandchildren. We are still researching the extensive and injurious effects of DES today. Lupron has only been used in Endometriosis treatment since the early 1990s. Must we wait 20 more years to discover that Lupron®, like DES, has far-reaching consequences? Are we creating another generation of women who have been harmed by overzealous utilization of a so-called "miracle drug?"

The Endometriosis Research Center strongly maintains: the long-term effects of Lupron® (and GnRH medications in general) is not known. The application of GnRH therapy to those women who have not been surgically diagnosed must stop. More research must be given to the long-term effects of GnRH therapy on a woman - and possibly her offspring. Indeed, GnRH medications have a place in Endometriosis treatment; however, caution must be exercised to avoid the cookie-cutter approach to therapy. What works for one patient will not work for another. Subjecting patients to potential negative effects that outweigh the benefits of treatment is unethical. Patient needs and the uniqueness of each case must be thoroughly considered before any therapies are offered.

References:

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HOW DO I RECEIVE ADDITIONAL INFORMATION? Where can I get further materials, resources and support?

ERC Support & Contact Network - The ERC hosts over 50 active, in-person support groups throughout the US, Canada and Caribbean. To find a group near you, call us at 800/239-7280 or visit <http://www.endocenter.org/supportgroups.html> for more information. The ERC is also proud to host the Internet's largest electronic support group for Endometriosis, the ERC EndoAngel™ Listserv. The Listserv will allow you the opportunity to exchange ideas, experiences, information and support with others who are dealing with similar issues related to the disease. For more information, please join the ERC EndoAngel™ Listserv (for free, of course) by visiting the following URL: <http://groups.yahoo.com/group/erc>

Additionally, the ERC also offers a moderated discussion group specifically designed for the unique perspective and Endometriosis needs of Military dependents and personnel, located online at: <http://groups.msn.com/EndometriosisandtheMilitary>

Not online? No problem! If you would like to take part in the ERC contact network, but do not have Internet access or would prefer to speak with someone in an offline setting, please contact us with your full name, phone number and Endometriosis topic. We will put you in touch with one of our contact network volunteers, who have offered to speak with others on the subject.

Contact Us - Please do not hesitate to contact our offices. The ERC is an established 501(c)3 Tax Exempt-Tax Deductible Organization which was founded to address the International need for Endometriosis education, research and support. We are dedicated to finding a cure for this disease; providing support and helping to improve the quality of life for all those affected by Endometriosis; raising public awareness about the disease; educating healthcare providers, patients, policymakers and the public; providing an international network in which women can exchange information and ideas; and facilitating research on all aspects of the disease.

We are a resource center for education and support. Each individual who contacts the ERC will receive an initial Contact & Information Packet. The ERC offers educational literature on Endometriosis, accurate fact sheets on many topics pertaining to the disease, a monthly Newsletter, and much more. Please visit us on the web at www.endocenter.org or call our offices toll free at 800/239-7280 to obtain the ERC's Material Request Form, which contains an updated list of all our educational materials. Being added to the ERC's mailing list will enable you to be kept informed of the latest research and developments surrounding the disease. If you would like to receive a sample copy of our Newsletter, we will be happy to provide you with an edition. Simply send your request to us along with a self-addressed, stamped, #10 envelope (the SASE helps cover our postage costs). The ERC has maintained a strict privacy policy since we were founded; any personally identifiable information collected by the ERC is used solely for the purposes of sending materials. Your information is never shared outside headquarters for any reason, at any time.

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