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Finasteride, the Controversial Drug that Medical Authorities Continue to Defend

There are now serious doubts about finasteride's safety. This case spotlights the failings of drug-monitoring systems.

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Can we trust drug-monitoring agencies? The Mediator and Dépakine scandals have certainly made us wonder. The same goes for another case, one perhaps less known in the media, that of finasteride, also known as Propecia. The suffering of thousands of men exposed to this substance is worth exploring. They hoped, with the help of this little pill, to slow their hair loss. What happened instead? Depression, suicidal ideation, severe insomnia, serious sexual dysfunction, and an inability to work. Romain Mathieu, whose story we have told along with other victims' stories, took his life in June of 2016 to escape the pain he attributed to Propecia, the commercial name for finasteride.

30,000 men in France – and millions around the world – take the drug every day, with statistically insignificant benefits. Patients may experience 10% hair growth, and only on the top of their heads, not, for example, on the temples. In several countries, including France, hundreds of people are considering legal action against the extremely powerful laboratory Merck & Co (MSD), whose commercialization of Propecia since 1997 has earned them billions of dollars.

Today, health authorities are only formally linking finasteride to issues of a sexual nature (loss of libido, erectile dysfunction). What about the range of psychiatric, cognitive and physical side effects that victims call "post-finasteride syndrome"? Science seems incapable of choosing a side in this debate.

Prof. François Desgrandchamps, head of urology at the St. Louis Hospital, says:

"We don't know the exact impact of finasteride on our patients, but we also can't discount their stories. They aren't complaining randomly or for pleasure."

In spite of this medical mystery, the Agencies for French Drug Safety (ANSM) and the European Medicines Agency (EMA), as well as certain doctors, are not convinced that finasteride is the cause.

They don't know if there is a link between these troubles and the drug, but they appear to think that such a link does not exist. The finasteride case does, however, imply that there are flaws and failings in the drug-security systems – and for the moment the benefit of the doubt is going to the labs, not the patients.

The Inertia of the EMA

To better understand this, let us examine the source of the health agencies' data, the "pharmacovigilance" centers, which document reports of adverse drug reactions reported by patients and/or their physicians. These reports only represent a small portion of reality – perhaps 5% at most – of adverse side effects. However, it was based on this data that the EMA created a Pharmacovigilance Risk Assessment Committee (PRAC) to evaluate the benefit/risk of the involved medications. Although the EMA declined our request for an interview, the agency did make available to us a detailed, 160-page report, summarizing the PRAC's meetings about finasteride over the past two years. [1, 2]

In theory, it is supposed to be the drug companies themselves that give health authorities the data that may include reports of harm to those taking their products. And it was [Merck's] MSD Laboratory, which held the original patent on finasteride, that sent the EMA committee information about cases of adverse reactions reported by its patients. It was also MSD that analyzed this information. And after receiving it, the PRAC merely wrote a comment on its report. The drug company may also provide health agencies with scientific studies.

Did this procedure, somewhat surprising but nonetheless legal, influence the EMA's decisions? There's no way to know for sure. The agency only says that "a mechanism for financial sanctions is provided for in case of violation or breach." We must also note that the time the EMA takes to examine such case(s) may extend over a period of years. In 2007, Sweden asked MSD about a possible link between finasteride and depression. [3] But it took until June 2017 for the accumulation of adverse drug reaction (ADR) reports, between 2014 and 2016, to push the PRAC to add "depression" and "suicidal ideation" to the warnings on the product insert.

In April 2018, the PRAC decided to add the risk of anxiety to the insert [4]. In 2013, however, the director of AFSSAPS (ANSM's predecessor) claimed that these side effects were "well known," citing only passing sexual difficulties or issues.

The failings of 'pharmacovigilance'

Why did these contradictions, and the belated label changes, happen? It has to do with how these pharmacovigilance committees function, since it is their job to examine ADRs. The experts ask, Is a specific disorder caused by taking a drug? It is often impossible to answer this with the minimal data provided by the drug company.

According to epidemiologist Catherine Hill: "Examining [ADR] cases and eliminating them one by one because certain information is missing, or because they don't see why there is a link, is a fundamental error."

Another example is the representation of psychiatric problems. In 2016, 124 cases were reported in Europe. Nineteen people were considered to be in a "grave" state, but the information in their case files does not provide "enough information to establish a causal relationship."

Additionally, five men committed suicide. The PRAC chose to ignore two of these cases, stating that there was "not enough medical information" available. For the other three cases, involving men ages 24 to 49 years old, the drug company was skeptical of the possibility of linking their action to its product. MSD focused on the psychiatric history of one of the men, and says that for the two others, the suicide happened several months or years after they had stopped treatment.

The report concludes: “The cases reported during this interval do not indicate a need for regulatory action.” In short, the committee dismissed all the security alerts and did not delve further to remove any doubt.

Says Catherine Hill: “This method prevents any discoveries of new problems. This is how, among others, the valvulopathies attributable to Mediator were dismissed. And who could have imagined that one of the side effects of the PandemrLx vaccine (which combats the H1N1 flu) would be narcolepsy?”

In conclusion, the authorities stated that the risk/benefit quota of finasteride 1mg would remain “unchanged,” but they did order the product insert to be modified. Will this change be effective? It is doubtful.

In 2017, ANSM did not communicate this information to health professionals, only to academic associations and groups – and waited five months to communicate it to the press. Sylviane Mathieu, president of the French [Finasteride] Victims’ Association, cites a recent case of a dermatologist who discovered the change in the product insert too late – under pressure from the parents of one of her patients to whom she had prescribed finasteride. Their son had fallen into a severe depression.

Note that this is not the first time that information did not circulate in a timely fashion between the watchdog agencies and physicians. This was also a thorny point in the Levothyrox affair. There again, doctors were not sufficiently informed of the arrival of a new formula in local pharmacies.

Clinical trials riddled with uncertainty

What can be done to dispel doubts regarding the causality linking finasteride and what they call post-finasteride syndrome?

Says Catherine Hill: “We need to do comparative studies: do finasteride users have more psychiatric problems than those who do not take the drug?”

This method is currently used by pharmaceutical companies when they do clinical trials, to evaluate the effectiveness and innocuity of a new drug before it is goes to market.

“No signs of depression or suicide were detected over a series of trials,” says Dr. [Pascal] Reygagne, a dermatologist at the Sabouraud Center, specializing in hair [loss]. He was the physician mandated by MSD to participate in their clinical trials in 1997, and he was a zealous prescriber of finasteride.

In a document dated February 2017 [(5)], Sweden says the same thing, including for the trials of finasteride 5mg, the same drug used at a higher dose to treat enlarged prostate.

But does the fact that they did not detect these problems during their clinical trials authorize physicians and the health authorities to conclude that finasteride does not cause them to occur?

“In general, in organized studies, certain adverse, serious effects are very rarely detected,” objects Dr. Lotfi Benslama, a maxillofacial surgeon, who was mandated several times to evaluate the effectiveness of reimbursed drugs [by French Social Security].

Why does this happen? In the case of finasteride 5mg, Sweden based its comments on a study that lasted seven years [6] and did not incorporate the presence of adverse effects. Rather, it focused on the action of the drug on prostate cancer. It is therefore possible that suspicious or questionable cases were not noticed.

In the case of finasteride 1mg, it has been impossible to obtain from the ANSM any documentation from clinical trials, despite asking them over a six-month period. In the end it was on the website of the FDA, the American regulatory agency, that we found them, riddled with ambiguities and uncertainty.

First, the sample sizes were too small to pick up on rare effects: only 1,781 patients received finasteride 1mg in the studies with a control group.

Catherine Hill confirms: “If for example 1% of the population of this age had psychiatric problems and if the drug raised the risk to 1.1% of that population, we would not be able to detect it with a trial involving only 2000 patients.”

Is this risk, even such a small one, really negligible? “The clinical analysis of adverse events occurring with a small number of patients during these trials does make us think that their number may become problematic when scaling to the general population,” estimates Dr. Benslama. This is what happened with Acomplia, an anti-obesity drug that came on the French market in 2007, and which was pulled a year later, having caused 250 cases of serious psychiatric problems as well as four suicides. Clinical trials run by Sanofi had noted these adverse effects, but clearly also underestimated them.

There is also the fact that finasteride trials using a control group were at first limited to a duration of one year, which was then extended for another year – but only for certain patients: those who were healthy. So these trials, like so many others studying other medications, all had one failing: they included people in good health and avoided the inclusion of other categories of patients. For example, many pregnant women taking Dépakine, which is a teratogenic [capable of interfering with the development of a fetus] anti-epileptic drug, suffered from this trial bias. The clinical trials were not able to demonstrate the risk of fetus malformation and development since they did not include this kind of [pregnant] patient.

Finally, the trials missed the adverse effects experienced or appearing one or two years after starting treatment. Many victims suffering from this post-finasteride syndrome experienced significant problems after several years.

Finasteride: a medical mystery

Without certainty from the pharmacovigilant watchdog agencies and the initial clinical trials, what can medicine tell us about this famous post-finasteride syndrome? We have not found a lot of reliable data. In the reports issued by the PRAC, the scientific studies that were factored in do not show any element that would allow us to definitely settle the risk issue.

“Available information about toxicity released by clinical trials of finasteride on men suffering from androgenic alopecia is very limited, of poor quality and seems systematically biased,” says Dr. [Steven] Belknap, a dermatological researcher at Northwestern University in Chicago, who with his colleagues performed a meta-analysis of 34 clinical trials. In addition, wide-ranging studies of finasteride were all performed on individuals 55 years or older who were taking a 5mg

dose for their prostate, and therefore excluding younger men and the biological specificities inherent to their age.

Prof. [Roberto] Melcangi, from the University of Milano, directed a study in which 16 patients claiming to suffer from post-finasteride syndrome were given a battery of neurological tests. The result: the study leaned toward a hypothesis of neurotoxicity. Reminder: finasteride blocks the action of an enzyme that transforms testosterone into a different hormone, DHT (dihydrotestosterone), which causes the acceleration of hair loss in men who are genetically predisposed to hair loss. However, “when you stop treatment, the enzyme should in theory function as it did before, which is absolutely not the case. Finasteride seems to activate mechanisms which we do not comprehend. It’s incredible!” exclaims Prof. Melcangi.

Another study, financed by the Post-Finasteride Syndrome Foundation, published in 2015 and led by researcher [Shalender Bhasin], expands this hypothesis of neurological problems. The researchers used functional MRI examinations, measuring activity in the brain when it was in action. They showed a series of erotic images to patients and were surprised to see that the zones that lit up in their brains were not those which habitually link to physical desire, but instead to those linked to depression. In this rather disturbing context, certain health professionals are currently warning their patients repeatedly before prescribing finasteride.

Others, such as Dr. Benslama, are now bluntly recommending that the drug be pulled from the market.

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