ORIGINAL ARTICLE

Birth Control and Contraception: Has Profit Maximization Priority over Women's Safety?

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ABSTRACT

Background: On the background of severe adverse events caused by a contraceptive device – approved by the FDA in 2002 and removed from the market by the manufacturer in 2018 – the article aims at clarifying as to whether or not the health of women is unduly neglected in the pursuit of business interests by manufacturers. **Material and Methods:** The material encompasses pertinent publications on contraceptive methods emanating from the most influential institutions and from manufacturers. The method consists in an in-depth analysis of the most frequently consulted sources of information on contraceptive products provided by international market-leading manufacturers, by high-impact research publications, and by the most authoritative international health agencies. **Results:** An analysis of the most frequently accessed information on contraceptive products proves that women are not adequately informed by manufacturers about risks and potential complications capable of jeopardizing their health. In addition, counseling by physicians is not always sufficiently tailored to each patient's needs so that women are not enabled to make an intelligent choice – as required by the bioethical principle of "informed consent." As a solution for inadequate counseling, autodidactic strategies are recommended which should focus on publications in the area of pharmacovigilance and on ratings of contraceptive methods prioritizing the parameter safety. **Conclusions:** Profit maximization as the golden rule of free market economies constitutes a menace for the safety of women, as witnessed by repeated litigations and lawsuits brought against pharmaceutical companies. A new research discipline is needed -- most appropriately designated as pharmaceuticovigilance -- which complements pharmacovigilance by analysing and critically assessing documents which reveal manufacturers' authentic market strategies. Such an analysis can accomplish not only protection for the consumer from misleading information but also motivation for manufacturers to strive for highest ethical standards in their pursuit of capital gains.

Key words: Bioethics, consumer, contraception, FDA, pharmaceutical companies, physicians, sterilization

INTRODUCTION

Recently, the world press informed the reader about fatalities in conjunction with a device for contraception and a mortiferous *in vitro* fertilization as part of assisted reproductive technology. In the face of such menaces to the health of women it seems imperative to intensify efforts to advocate safety over business interests. The present paper aims at contributing to these efforts by illuminating the safety hazards associated with contraceptive products offered for sale in the world markets.

DISCUSSION

Millions of women worldwide are using contraceptive pills and devices, but not all of them are aware of the risks associated with the utilization of these products. The question of safety of contraceptive products has been smoldering latently since 1960 when the US Food and Drug Administration (FDA) approved the first pill "Enovid," which contained the progestogen norethynodrel and the estrogen mestranol. More recently, the adverse events and risks associated with contraceptive products have been brought to the forefront

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by a device for sterilization which caused severe harm to its users. During the year 2018, international media reported regularly about the harm experienced by women who had used this implant for permanent contraception, which had been approved as "safe" by the FDA as early as 2002.

The troubled history of a "safe" contraceptive device, and the harm experienced by its users

In 2018, one of the world's leading pharmaceutical companies had to withdraw its contraceptive device for permanent contraception – hailed as the first non-incisional option for sterilization – from the US market. The US press commented this withdrawal by highlighting the adverse events and the ensuing legal reverberations: "It has been the subject of an estimated 16,000 lawsuits or claims filed by women who reported severe injuries, including perforation of the uterus and the fallopian tubes. Several deaths, including of a few infants, have also been attributed to the device or to complications from it."[1] In Australia, the Therapeutic Goods Administration (TGA) had issued a hazard alert already earlier, which prompted the company to recall its product as early as 2017. According to Australian media, this alert was the consequence of reports about severe harm experienced by women: "'The reports have included changes in menstrual bleeding, unintended pregnancy, chronic pain, perforation, migration of the device, and allergy/hypersensitivity or immune-type reactions. Surgery, including hysterectomy, was required in some instances to remove the device,' the TGA said."[2]

In view of the numerous reports about harm caused by the implant, it came as a surprise to the consumers when the press reported also about the US FDA's persistent claims concerning the safety of the product: "Bayer announced that they will no longer sell or distribute Essure in the U.S. after December 31, 2018, for business reasons. This information does not change the FDA's understanding of the safety and effectiveness of the device…"[1] The company stands on firm ground, therefore, when it refers to the FDA to underscore the safety of its product: "The FDA has maintained for several years that the benefits of Essure outweigh its risks."[3]

According to the FDA, the stumbling block was not the device *per se* but lack of counseling about risks and potential complications. Apparently, physicians had failed to inform women adequately, although implantation of the device had been restricted to professionals who had signed a statement attesting appropriate counseling. "Despite previous efforts to alert women to the potential complications of Essure, we know that some patients still aren't receiving this important information," said FDA Commissioner Scott Gottlieb, in a statement. "That is simply unacceptable."[1]

Besides the lack of counseling criticized by the FDA, an additional problem area had been targeted by another influential agency, namely, the National Center for Health Research (NCHR). The president of this organization put the blame on the manufacturer for providing information that is inadequate: "How many people do you know who would carefully read a 22-page document before signing it?" said Diana Zuckerman, president of the NCHR, a consumer advocacy group. "In addition to being much too long and technical, the information provided will be confusing to many consumers."[1]

Are the manufacturer's "Instructions for Use" adequate?

Concerning the critique voiced by the NCHR, it should be noted that the "Instructions for Use" furnished by the manufacturer of the Essure implant as early as 2002 comprise 50 pages and contain not only a detailed product description but also extensive lists of warnings and precautions. Risks are classified into those that are associated with the insert placement procedure, with the Essure Insert Wearing, with follow-up procedures, and with future procedures. Among the risks associated with follow-up procedures – which include a modified hysterosalpingogram (HSG) – the death-bearing complications of anaphylaxis are clearly stated: "The use of contrast media, used to perform a modified HSG which may be required for the Essure Confirmation Test has been associated with allergic reaction in some patients. Allergic reaction can result in hives or difficulty breathing. In some individuals, an anaphylactic response may occur which may lead to death."[4] Concerning the essure confirmation test (a modified HSG), the consequences of exposure to X-rays are appropriately mentioned, but only in the News Release of 2018 and not in the Instructions for Use of 2002: "Some women may experience nausea and/or vomiting, dizziness and/or fainting, cramping, pain or discomfort. In rare instances, women may experience spotting and/or infection."[3] The News Release of 2018 draws attention also to the life-threatening complications of an ectopic pregnancy: "Ectopic pregnancies (pregnancy outside the uterus) may occur with Essure. This can be life threatening. If insert removal is indicated, surgery will be necessary."[3]

In light of the comprehensive "Instructions for Use" of 2002 and the "News Release" of 2018, it would be unethical to blame the manufacturer for not providing sufficient information. After all, the manufacturer admonishes women explicitly to read the patient information booklet, advises doctors to review the Patient-Doctor Discussion Checklist with the patient, and requests that "all of the patient's questions" be answered.[4] What gives rise to consumer dissatisfaction is not incompleteness or inaccuracy of information, including technical details and product description; rather, it is the ambiguity of the terminology utilized to describe the mechanism of action. Neither the lay person nor the experienced hysteroscopist are capable of understanding how the alleged in-growth of tissue due to polyethylene terephthalate (PET) fibers can occur as a spontaneous physiological and biochemical process. It

is not surprising therefore that some commentators speak unmistakably of an inflammation and an ensuing scar tissue: "The Essure implant consists of two small coils made of a nickel alloy and a polyester-like fiber. It is placed through the vagina into the fallopian tubes and is designed to create an inflammatory response that causes scar tissue to form, blocking the tubes."[5]

Obviously, an inflammation resulting in scar tissue is not the same as "benign tissue in-growth" due to PET fibers, as claimed by the company. Information deficit is conspicuous also in the table which provides data on pregnancy rates for birth control methods. As these data refer to typical use only and disregard perfect use, they do not stand up to the standards of statistical precision found in other publications, such as those by Contraceptive Technology[6] or by the World Health Organization (WHO).[7]

The shortcomings in the information material presented by the manufacturer for the user of the Essure implant are paradigmatic for other manufacturers worldwide. Quite a number of them fail to provide adequate instructions for use, as pointed out by the NCHR in its critique of the Essure implant. In addition, they fall short of enabling the consumer to make an "intelligent choice" – a requirement of the bioethical principle of "informed consent."[8] The consumer inquiring into the safety of products for contraception and birth control by means of information furnished by manufacturers notices that there are striking differences in the accuracy, comprehensibility, and comprehensiveness of these publications. The question arises, therefore, whether the lack of reliability is the consequence of business interests prioritizing profit maximization at the expense of considerations for users' safety.

Conflicting claims and the dilemma of lack of evidence

On the European market, a new contraceptive product – a copper-containing intrauterine device (IUD) made in Belgium – has been available for women since the end of the past century.[9] In contrast to the 50-page document offered by the manufacturer of Essure, the "Information for the User" provided by the Belgian company is limited to three pages. Despite its brevity, the document makes persuasive claims regarding the superiority of this product in comparison with "conventional" devices: "Conventional IUDs are less flexible and often too big, which will likely elicit uterine cramps and abnormal menstrual bleeding."[9]

In contrast to these deficits, the new device offers several advantages, such as small size, absence of a frame, and flexibility: "GyneFix differs from conventional IUDs by its very small size and because it has no frame which makes it completely flexible."[9] In addition to the optimal design, efficacy allegedly is superior to all other copper IUDs and even equals female sterilization: "GyneFix offers the same effectiveness as female sterilization."[9] Moreover, the device is "well tolerated," and – what seems almost inconceivable to the well-informed consumer – there are "almost no side effects."[9] Above all, the device does not cause an increase in menstrual blood loss, which – according to the manufacturer – is the primary reason for users to abandon a copper IUD: "Increased menstrual blood loss is the most common reason to stop using a copper IUD."[9] What further impresses but also surprises the consumer is the statement that "pregnancy and PID have been rarely observed."[9] Concerning these two complications it must be emphasized that ectopic pregnancy is generally considered a common problem with IUDs; and pelvic inflammatory disease has been recognized for a long time as the most serious drawback of IUDs. As early as 1995, the limitations of IUDs have been specified by scholarship in physiology: "Their usefulness is limited by their tendency to cause infections."[10] Along the same line, German authors underscored as early as 2000 ascending infection and spontaneous expulsion as "the most feared complications."[11]

Despite such potential complications, the virtues of the new device – underscored by the manufacturer in the "Information for the User" – are reiterated in scientific publications of 1999 and 2013.[12,13] In 1999, an International Study IUD Group on Intrauterine Drug Delivery at the University Hospital of Ghent claimed: "GyneFix has the lowest failure rate of all copper IUDs currently available"[12] – without, however, providing any pertinent data.

In 2013 several authors, including the inventor of GyneFix, not only hailed the new device but also highlighted convincingly the inadequacies of the conventional devices. On the basis of evidence-based research focusing on comparative measurements of the uterine cavity, shortcomings of these devices were specified as "increased expulsion rates, complaints of pain and erratic or increased menstrual bleeding, and subsequent high rates of discontinuation."[13] Regrettably, in their eulogy for the new device, the authors failed to mention a study by British authors published in 2003, which addresses specifically the problem of perforation with Gynefix and also draws attention to adhesions as a risk of copper-containing devices: "Copper IUDs such as the GyneFix are thought to predispose the patient to adhesions once inside the peritoneal cavity."[14] In addition to specifying risks, the British authors identified the device correctly as an "implant" and not as an "insert," as designated by the Belgian manufacturer. Regarding evidence for the advantages of GyneFix, the most comprehensive research has identified only continuing use advantages of GyneFix in an 8-year multicenter randomized comparative trial published in 2009: "The frameless IUD had more insertion failures, expulsions and pregnancies in the 1st year than TCu380A, but fewer pregnancies from the second through the 8th year, and by 8 years had fewer ectopic pregnancies and removals for pain."[15]

Besides these favorable findings by research, statements in the manufacturer's "Information for the User" deserve attention; above all the critique of the "conventional" devices, that is, ParaGard and Mirena, approved for and distributed on the US market. This critique seems convincing as it is the result of evidence-based research elucidating the inappropriate dimensions of the conventional devices. Interestingly enough, this critique has been ignored by the authors of one of the most pertinent publications on long-acting reversible contraception (LARC), which appeared in 2017 in one of the world's leading medical journals.[16]

These authors hail LARC justifiably as the most effective methods of contraception, but fail to take into account the critique of conventional devices voiced by Belgian authors. In sum, the US authors ignore the shortcomings found in conventional LARCs, GyneFix is not even mentioned as one of the devices belonging to LARC, and references regarding the publications on GyneFix are untraceable. Instead, the authors of the 2017 publication hail precisely those LARC devices that have been judged unsuitable in the publication of 2013. LARC methods are recommended by the US authors not only by virtue of their high effectiveness and safety but also owing to their noteworthy rate of continuation. Without paying heed to the deficits of "conventional" devices described by the Belgian authors, the US authors conclude: "All adolescents and adult women should be informed about the availability of LARC methods, given their extremely high effectiveness, safety, and high rate of continuation."[16]

The claim that LARC methods are extremely safe seems misleading in light of the findings published by the Belgian authors 3 years previously. Given such diametrically opposed assessments of LARC methods, the consumer has reason to seek clarification and finds an answer in the vexing problem of competing interests.[13,16] Indeed, scientific publications are increasingly adulterated by authors' interest in financial gains in the form of stipends, grants, and consulting remunerations. One avenue to circumvent these problems has been opened by pharmacovigilance, but it is not resolved whether the findings of this research are duly appreciated by pharmaceutical companies, by research institutes, or by health agencies.

Are warnings by pharmacovigilance sufficiently acknowledged?

Recent findings in oncology about leukemia in children of mothers taking hormonal contraceptives remain almost unmentioned by manufacturers, although the authors of a scientific publication of 2018 speak unequivocally of the "… biological plausibility, on the basis of evidence that hormonal exposure in utero causes cancer in children."[17]

In the same year, the risk of depression and suicidal action owing to hormonal contraception has been emphasized by the European Medicines Agency: "Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use…Depression can be serious and is a well-known risk factor for suicidal behavior and suicide."[18] One year previously, in 2017, an investigation on the association of hormonal contraception with suicide among Danish women had been published in a US journal of psychiatry.[19] It is true, of course, that most "Instructions for Use" provided by manufacturers of contraceptive pills mention the risk of depression. Suicidal action, on the other hand, has never been addressed so far to this author's knowledge.

Oral hormonal contraceptives have been identified also as causally related to increased intraocular pressure and the associated risk of blindness: "The association between female sex hormones and intraocular pressure (IOP) changes has long been known… However, reports on the increased risk of an open-angle glaucoma in females taking oral contraceptive pills for 3 years or more are a recent finding, which requires further studies to probe the causal association between estrogen, progesterone, and rise in IOP."[20] These warnings about the risk of open-angle glaucoma are patently absent in most product descriptions, where alerts pertaining to ophthalmologic adverse events are limited to brief comments on possible complications due to contact lenses.

Studies on the impact of hormonal contraceptives on the quality of life receive only marginal attention.[21] At times, print media are instrumental in disseminating new findings, such as the risk of breast cancer highlighted by the US press[22] on the basis of a publication by Danish authors of 2017.[23]

In view of the above discussed problems of inadequate information for the consumer furnished by manufacturers and of conflicting statements in research publications, women are well-advised to turn to products whose safety is established by reliable research. In fact, women implementing autodidactic strategies are nowadays in a position to identify the personally most suitable method of contraception by consulting trustworthy ratings and rankings prioritizing safety, such as the "Synoptic Overview of Contraceptive Methods" of 2019.[24] By consulting publications in pharmacovigilance and using social media, women can remedy the lack of counseling which is likely to be perpetuated as long as doctors have to abide not only by bioethical principles but also by maxims of a free market economy.[25]

SUMMARY AND IMPLICATIONS

Information on contraceptive products emanates not only from manufacturers but also from national and international health agencies as well as from researchers. This information is not always reliable as it contains inaccuracies, errors, and misleading claims. Women and their physicians are advised to seek information on contraceptive products in

publications of pharmacovigilance and in trustworthy ratings of contraceptive methods.

The free market economy would be unthinkable without the unwritten law of profit maximization. For the market of contraceptive products, this law must be limited by two factors, namely, the bioethical principle of nil nocere (no harm) and the constitutional right to bodily integrity. Manufacturers are faced with the challenge of achieving maximum of profit without violating ethical principles and constitutional rights. Companies subscribing to principles of business ethics should refrain from using a confusing or misleading terminology for the description of their products, including adverse events and potential risks. For each product, the consumer should be provided with complete and comprehensible information which enable her to make an intelligent choice. Failure to do so might result not only in severe hurt to users but also in equally damaging economic consequences for the manufacturer.

CONCLUSIONS

Profit maximization will remain an inextinguishable guiding doctrine in free market economies. Manufacturers of contraceptive products will strive with the same rigor as car producers at achieving their economic goals. Along the same line, doctors will be tempted to fall prey to the financial gains in the form of stipends and grants offered by companies in return for supporting their marketing strategies in scientific publications. Women and consumers in general should be informed about these economic priorities and the ensuing health hazards by their health professionals, by public media, and by government agencies. The safety of women must remain the highest good not only in bioethical deliberations but also on economic markets worldwide.

REFERENCES

1. Available from: https://www.washingtonpost.com/…/2018/...sales-of-essure-birth....html. [Last accesed on 2018 Apr 11].
2. The Guardian. Available from: https://www.upi.com/…/2018/…/13/Bayer.../5611534172665. [Last accessed on 2018 Aug 13].
3. Bayer Pharmaceutics Company. Bayer to Voluntarily Discontinue U.S. Sales of Essure at End of 2018 for Business Reasons. Whippany, NJ: Bayer Pharmaceutics Company; 2018.
4. Bayer Pharmaceutics Company. Essure Permanent Birth Control. United States: Bayer Pharmaceutics Company; 2002.
5. New York Times. Available from: https://www.nytimes.com/2018/07/20/health/bayer-essure-birth-control.html. [Last accessed on 2018 Jul 20].
6. Trussell J. Contraceptive efficacy. In: Hatcher RA, Trussell J, Nelson AL, Cates W, Kowal D, Policar M, editors. Contraceptive Technology. 20th ed. New York: Ardent Media Limited; 2011.
7. World Health Organization. Effectiveness to Prevent Pregnancy. Geneva: World Health Organization; 2017. Available from: https://www.who.int/news-room/fact-sheets/detail/family-planning-contraception. [Last accessed on 2019 Nov 20].
8. American Medical Association. Code of Medical Ethics: Current Opinions. Chicago, Illinois: American Medical Association; 1992.
9. GyneFix. Information for the User, CONTREL Manufacturer. CONTREL EUROPE NV, Incubatie-en Innovatiecentrum, Technologiepark 3 B1 (Universiteit Gent), HYPERLINK; 2014. http://www.b-medical.eu/media/uploads/en/products/upload/2.pdf; https://www.soyin.be/gynefix/how-safe-is-gynefix. [Last accessed on 2020 Oct 31].
10. Ganong WF. Review of Medical Physiology. 17th ed. Norwalk, CT: Prentice Hall International, Appleton and Lange; 1995.
11. Gröger S, Grüne B. Kontrazeption. In: Diedrich K, editor. Gynäkologie und Geburtshilfe. Berlin: Springer; 2000. p. 60-87.
12. Wildemeersch D, Batár I, Webb A, Gbolade BA, Delbarge W, Temmerman M, *et al*. GyneFIX. The frameless intrauterine contraceptive implant--an update for interval, emergency and postabortal contraception. Br J Fam Plann 1999;24:149-59.
13. Wildemeersch D, Pett A, Jandi S, Hasskamp T, Rowe P, Vrijens M. Precision intrauterine contraception may significantly increase continuation of use: A review of long-term clinical experience with frameless copper-releasing intrauterine contraception devices. Int J Womens Health 2013;5:215-25.
14. Aust TR, Kirwan JN, Herod JO, McVicker JT. Perforation with the GyneFix intrauterine implant: Is there a common factor? J Fam Plann Reprod Health Care 2003;29:155-6.
15. Meirik O, Rowe PJ, Peregoudov A, Piaggio G, Petzold M. The frameless copper IUD (GyneFix) and the TCu380A IUD: Results of an 8-year multicenter randomized comparative trial. Contraception 2009;80:133-41.
16. Curtis KM, Peipert JF. Long-acting reversible contraception. N Engl J Med 2017;376:461-8.
17. Hargreave M, Mørch LS, Andersen KK, Winther JF, Schmiegelow K, Kjaer SK. Maternal use of hormonal contraception and risk of childhood leukaemia-authors' reply. Lancet Oncol 2018;19:e659.
18. European Medicines Agency. PRAC Recommendations on Signals. London: European Medicines Agency, Pharmacovigilance Risk Assessment Committee; 2018.
19. Skovlund CW, Mørch LS, Kessing LV, Lange T, Lidegaard O. Association of hormonal contraception with suicide attempts and suicides. Am J Psychiatry 2018;175:336-42.
20. Bhanwra S, Ahluwalia K. The association of oral contraceptive pills with increase in intraocular pressure: Time for pharmacovigilance to step in. J Pharmacol Pharmacother 2015;6:51-2.
21. Zethraeus N, Dreber A, Ranehill E, Blomberg L, Labrie F, Von Schoultz B, *et al.* A first-choice combined oral contraceptive influences general well-being in healthy women: A double-blind, randomized, placebo-controlled trial. Fertil Steril 2017;105:1238-45.
22. Rabin R. New York Times. Available from: https://www.nytimes.com/2017/12/06/health/birth-control-breast-cancer-hormones.html. [Last accessed on 2017 Jun 12].
23. Mørch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard O. Contemporary hormonal contraception and the risk of breast cancer. N Engl J Med 2017;377:2223-39.
24. Kraetschmer K. How women in search of suitable contraceptive

methods can remedy the lack of counseling and circumvent untrustworthy information disseminated by various media. ARC J Gynecol Obstetr 2019;4:1-7.
25. Kraetschmer K. Is the "lege artis" principle obsolete? J Forensic Res 2013;4:3.

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