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Original article

Risk of hormonotherapy in transgender people: Literature review and data from the French Database of Pharmacovigilance

Risque de l'hormonothérapie chez les transsexuels : état des lieux de la littérature et données de la Base française de pharmacovigilance

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Abstract

Objective. – After the diagnosis of transsexualism, hormone therapy is an established stage of gender identity disorder treatment for inducing secondary sex characteristic development of the target gender while reducing that of the birth sex. The aim of this study was to review existing data about the risk of hormone therapy in transsexual people. *Methods.* – A PubMed search was done to identify relevant data about adverse drug reactions (ADRs) and mortality associated to hormones exposure. Furthermore, case reports of hormonal therapy-induced ADRs were identified in the French Pharmacovigilance DataBase (FPDB). *Results.* – Review of currently available data showed an increase of thromboembolic effects and hyperprolactinemia with oestrogens. Both oestrogens and testosterone derivatives could induce hepatic effects. Currently, there is no significant association between hormone exposure and cancer or mortality in transsexual people. Five ADRs were found in FPDB, and two of them were related to misuse (voluntary overdose and prescription error). *Conclusion.* – Potential for under-reporting and under-identification in the FPDB of hormonal therapy-induced ADRs in transsexual people should be underlined. Technical improvement of the FPDB could facilitate further identification of reports concerning the risk associated with hormonal therapy in transsexual subjects.

Keywords: Transsexual; Hormone therapy; Adverse drug reactions

Résumé

Objectif. – Après le diagnostic du transsexualisme, le processus de transformation débute par une expérience en vie réelle suivie par l'hormonosubstitution, réversible puis irréversible. L'objectif étant de bloquer les hormones stéroïdes du sexe génotypique et d'acquérir les caractères sexuels secondaires du sexe désiré. L'objectif de ce travail est une revue des données sur le risque de l'hormonothérapie chez les transsexuels. *Matériel et méthodes.* – Nous avons réalisé une recherche Pubmed sur les effets indésirables des hormones ainsi que les données disponibles sur la mortalité. Par ailleurs, nous avons interrogé la Base nationale de pharmacovigilance française (BNPV) pour identifier les effets indésirables induits par les hormones chez les transsexuels. *Résultats.* – La revue des données montre essentiellement une augmentation du risque thromboembolique et une hyperprolactinémie avec les estrogènes. Des effets hépatiques peuvent être survenus aussi bien avec les estrogènes que la testostérone. Il ne semble pas exister un effet significatif sur la densité osseuse. De même, l'augmentation du risque de cancer ou de mortalité n'est pas à ce jour établie. Nous avons par ailleurs identifié 5 cas d'effets indésirables dont 2 liés à un mésusage (surdosage volontaire et erreur de prescription).

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Conclusion. – Il existe clairement une sous-notification des EI survenant chez les transsexuels sous hormonothérapie, liée aussi à la difficulté de leur codage dans la BNPV. Une optimisation de la BNPV s'avère nécessaire afin de pouvoir identifier de façon optimale les déclarations sous hormonothérapie chez les transsexuels pour améliorer l'accessibilité aux données sur le risque médicamenteux chez cette population.

Mots clés : Transsexuel ; Hormonothérapie ; Risque médicamenteux

1. Introduction

According to the tenth edition of the international classification of diseases, transsexualism is defined as "the desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatment" [1]. Two additional definitions have also been noted: the definition of the Council of Europe [2], which defined transsexualism as "a syndrome characterised by a dual personality, one physical, the other psychological, together with such a profound conviction of belonging to the other sex that the transsexual person is prompted to ask for the corresponding bodily 'correction' to be made". Finally, the European Court of Human Rights defined the term "transsexual" as "those who, whilst belonging physically to one sex, feel convinced that they belong to the other; they often seek to achieve a more integrated, unambiguous identity by undergoing medical treatment and surgical operations to adapt their physical characteristics to their psychological nature. Transsexuals who have been operated upon thus form a fairly well-defined and identifiable group" [2]. The aim of this study was to review existing data about the risk of hormone therapy in transsexual people by the literature review and extraction of data of the French pharmacovigilance database.

2. Epidemiology

Data on prevalence of transsexualism during childhood are limited. In adults, data are also scarce, and limited to subjects requesting sex reassignment surgery [2,3]. A literature review has compared data from 1960–1970 to those collected in 1990. This study suggested an increase in the prevalence of transsexualism, which could be partly accounted by the improvement in patients' access to information (Internet, media, etc.). According to these data, incidence of transsexualism remains constant. Estimated sex ratio is 3/1, namely 3 men wanting to become women for one woman wishing to became a man [4]. In Europe, the prevalence is estimated between 1/10,000 and 1/45,000 for male to female transsexuals (MtoF), and from 1/30,000 to 1/200,000 in female to male transsexuals (FtoM). In France, apart from statistics from the National Health Insurance Scheme [2] on sex reassignment surgery claims, no exhaustive record is available. Thus, at the time of the study, it is not possible to get reliable estimates of the prevalence and incidence of transsexualism in France [2,3,5].

3. Healthcare pathway

In 2009, French National Authority for Health (*Haute Autorité de santé*, HAS) has published a report to precise the steps and modalities of care pathway in transgender people. According to current recommendations, the treatment pathway begins with a diagnosis phase, followed by a test in real life, accompanied by psychological support, cross-gender hormonal replacement therapy (HRT) and finally by sex reassignment surgery [2–6].

3.1. Diagnosis

In current recommendations, which were based on the experience of medical teams involved in the management of transsexualism, psychiatrists play a central role. They must confirm the diagnosis of gender identity disorder and exclude differential psychiatric disorders, like schizophrenia with delusions of sex change and body dysmorphic disorder or transvestic fetishism (consisting in cross-dressing behaviour to induce sexual excitement, without change of the birth sex). Several consults are recommended (2 to 10), during a period lasting from 6 to 9 months according to clinical situations, in order to establish a diagnosis of gender identity disorder (Fig. 1). A confirmatory diagnosis is required to ensure the motivation of the patients in following the rest of the program and to limit the risks of regrets and negative consequences for the patient [2–6]. A study realized on the future of transgender people has shown that 1 to 8% of them express transitory beliefs of regrets and 1 to 2% definitive regrets concerning their sexual transformation [7].

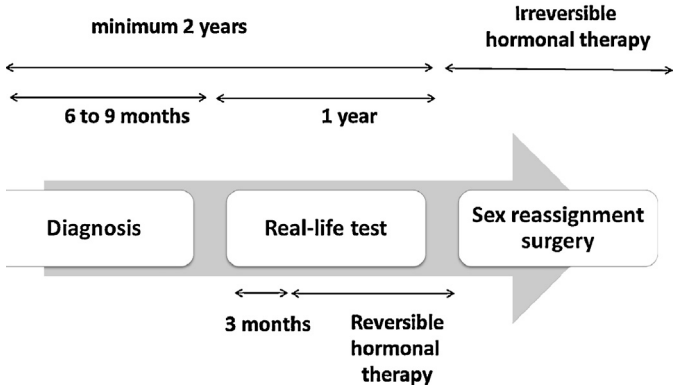

Fig. 1. Stages of treatment in the transsexual population.