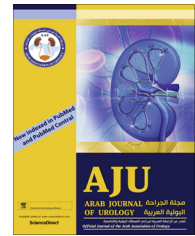




Arab Journal of Urology

(Official Journal of the Arab Association of Urology)

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ORIGINAL ARTICLE

Hyperprolactinaemia in male infertility: Clinical case scenarios

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Received 21 August 2017, Received in revised form 4 October 2017, Accepted 7 October 2017

KEYWORDS

Prolactin;
Male infertility;
Dopamine agonists;
Testosterone;
Pituitary adenoma

ABBREVIATIONS

DA, Dopamine;
HPG, Hypothalamic-Pituitary-Gonadal (axis);
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Abstract Objective: To explore the evaluation, treatment and impact of hyperprolactinaemia on male infertility and testicular function, as hyperprolactinaemia is commonly detected during the evaluation of infertile men.

Methods: A literature search was performed using MEDLINE/PubMed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify all studies exploring hyperprolactinaemia in male infertility.

Results: Elevated levels of serum prolactin have a detrimental effect on male reproduction through inhibition of the pulsatile release of gonadotrophins from the anterior pituitary gland, and a direct effect on spermatogenesis. Treatment of confirmed hyperprolactinaemia with dopamine agonists leads to significant improvements in both semen parameters and hormone levels.

Conclusion: Hyperprolactinaemia, both directly and indirectly, has a negative effect on sperm production, and its detection and management in men seeking fertility is mandatory.

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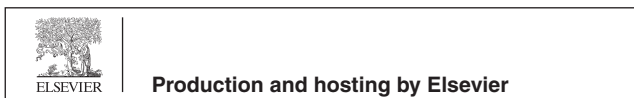
Introduction

Infertility is classically defined as the inability to conceive after at least 1 year of regular unprotected intercourse. It is a common medical condition affecting between 9% and 25% of couples worldwide [1,2]. A male factor contributes to roughly half the cases of infertility amongst couples [3]. Establishing a precise diagnosis via a thorough history, examination and

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Peer review under responsibility of Arab Association of Urology.



<https://doi.org/10.1016/j.aju.2017.10.002>

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Please cite this article in press as: Dabbous Z, Atkin SL. Hyperprolactinaemia in male infertility: Clinical case scenarios, *Arab J Urol* (2017), <https://doi.org/10.1016/j.aju.2017.10.002>

investigative protocol is essential for optimal male infertility management. During evaluation, the specialist investigates for the presence of endocrine dysfunction that may contribute to a patient's infertility. Current guidelines indicate hormone evaluation of infertile men in the presence of abnormal semen analysis, symptoms of hypogonadism, or other clinical findings suggestive of a specific endocrinopathy, such as gynaecomastia or testicular atrophy [4].

Hyperprolactinaemia is amongst the endocrine disorders known to influence male infertility. It is a common medical condition present in ~1% of the general population worldwide [5]. Hyperprolactinaemia in men is defined by the presence of a high serum prolactin level of > 15 µg/L. It can result from physiological or pathological conditions. Stress and exercise can cause small increases in prolactin levels and are important causes of physiological hyperprolactinaemia [6]. Medication-induced hyperprolactinaemia is usually associated with prolactin levels ranging from 25 to 100 µg/L, but metoclopramide, risperidone, and phenothiazines can lead to prolactin levels of > 200 µg/L [6].

Prolactinomas (lactotroph adenomas) are the most common pathological cause of hyperprolactinaemia and account for ~40% of pituitary adenomas [7]. The diagnosis is more commonly made in women than men due to the effect of hyperprolactinaemia on the female menstrual cycle giving an earlier indication of hormonal imbalance. Prolactinomas can be microadenomas (< 1 cm in diameter) or macroadenomas (> 1 cm in diameter), and the level of serum prolactin measured is directly proportional to the size of the adenoma [7].

Whilst hyperprolactinaemia is prevalent in up to 11% of infertile males [8], it is a diagnosis that is often missed because of its subtle clinical manifestations. In the present systematic review, we examine the available evidence for the effect of hyperprolactinaemia on male infertility, and highlight the approach for the evaluation and treatment of hyperprolactinaemia using clinical case-based scenarios.

Methods

Search strategy

This study was designed according to modified guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [9]. PubMed/MEDLINE databases were searched using the following search terms in titles and abstracts: 'hyperprolactinemia', 'male infertility', 'dopamine agonists', 'prolactin', 'medical treatment for male infertility', 'endocrine causes of male infertility'. The search was limited to studies performed on humans. The literature was searched from inception to 18 August 2017.

Study selection

The generated list of articles was screened by title and abstract by the authors (Z.D. and S.A.) and then relevant full papers were examined. Review articles were also explored to find additional appropriate papers. The exclusion criteria were based on gender (females), species (other animals), and study methods (retrospective, case report, editorial or commentary). Data were then extracted, cross-checked, and verified.

Data extraction

Eligible studies were reviewed and the following data were abstracted: (i) first author's name, (ii) year of publication, (iii) country where the study was performed, (iv) study design, (v) number of participants in the study and control groups, (vi) type of medication, (vii) duration of treatment, (viii) baseline and follow-up semen parameters/male fertility status.

Results

Overall, 39 articles were found following the multi-database search. After screening of titles and abstracts, 17 articles were assessed in full. Of these, nine articles were excluded because they did not meet the inclusion criteria. Therefore, eight articles were found to be eligible for inclusion in the systematic review (Fig. 1).

Study characteristics

The included studies were published between 1981 [10] and 2011 [11]. The range of treatment duration was from 2.25 [12] to 24 months [13]. Study designs of included trials were comparative studies [13–15] and prospective observational studies [10–12,16,17]. Selected studies enrolled patients with hyperprolactinaemia and oligospermia [12] or hyperprolactinaemia and infertility [17]. Medications assessed for the treatment of hyperprolactinaemia where bromocriptine [10,12,15,17],

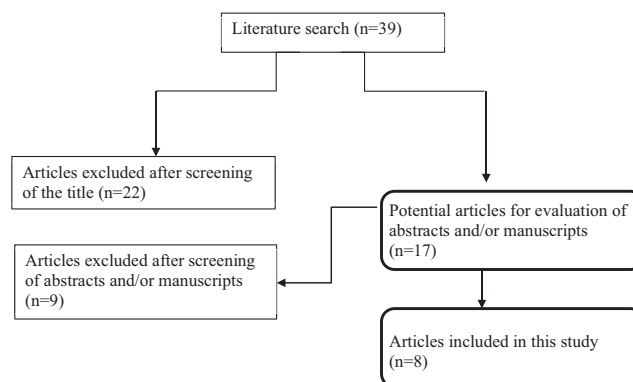


Fig. 1 PRISMA flowchart of literature search.

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