

A One Health Issue: Hyperestrogenism and hyperandrogenism in dogs, cats and children due to secondary exposure

Ann Neubert

Introduction

Due to unintentional transmission of topically applied sex hormones, both, children and pets that have close physical contact with users of topical hormone replacement therapy can develop clinical symptoms of exogenous hyperestrogenism or hyperandrogenism [1,2,3]. These clinical signs can be serious. This risk for children is already addressed harmonized within the EU in the package leaflets of affected estradiol containing medicinal products [4]. Topical testosterone containing medicinal products authorized in Germany also contain respective warnings. Although androgen prescriptions have been increasing in Germany for years, the prescription volume of topical estrogen is four times higher than topical testosterone [5]. The objective of this research was to describe clinical signs in pets and children and compare case numbers in pharmacovigilance databases.

Material and methods

- Literature research
- Research in pharmacovigilance databases
- Descriptive statistical analysis

Results

Clinical signs of hyperestrogenism in:

Dogs	Cats	Children
<ul style="list-style-type: none"> • Premature puberty • Return to oestrus despite neutering • Ongoing oestrus signs like swollen vulva, vaginal discharge, behavioural changes • (Stump-)pyometra 	<ul style="list-style-type: none"> • Return to oestrus despite neutering • Ongoing oestrus signs like hyperactivity, vocalisation, inappropriate urination, anorexia, affectionate behaviour 	<ul style="list-style-type: none"> • Precocious puberty, premature and advanced thelarche • Vaginal discharge
<ul style="list-style-type: none"> • Feminisation in males (pendulous prepuce, reduced penis and testicle size, attractiveness for other males) • Linear preputial dermatosis 	<ul style="list-style-type: none"> • Reduced testicle size • Anxiety, increased sexual interest • Inappropriate urination 	<ul style="list-style-type: none"> • Male: female pseudo puberty
<ul style="list-style-type: none"> • Mammary hyperplasia, gynaecomastia 	<ul style="list-style-type: none"> • Mammary hyperplasia, gynaecomastia 	<ul style="list-style-type: none"> • Breast budding and breast masses in prepubertal females • Gynaecomastia and breast masses in prepubertal males
<ul style="list-style-type: none"> • Alopecia (bilateral symmetric, progressive, non- inflamed) • Hyperpigmentation 	<ul style="list-style-type: none"> • Stillbirth • Poor growth rate • Reduced general health • Euthanasia 	<ul style="list-style-type: none"> • Accelerated growth rate, advanced bone age, somatomegaly, gigantism • Cerebral seizures • Body odour

Clinical signs of hyperandrogenism in:

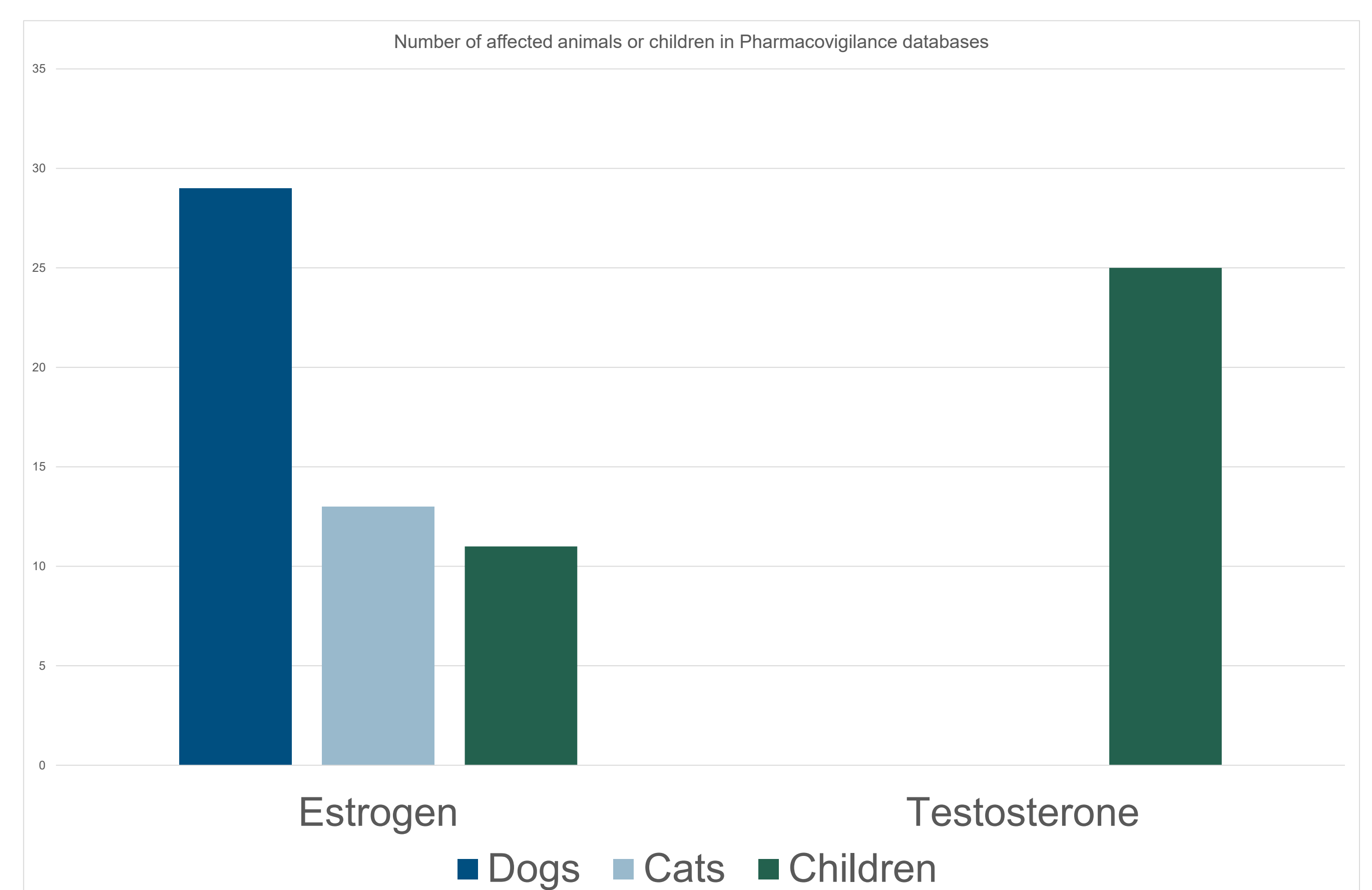
Dogs	Cats	Children
<ul style="list-style-type: none"> • Clitoromegaly 	<ul style="list-style-type: none"> • Clitoromegaly 	<ul style="list-style-type: none"> • Precocious puberty • Virilisation (clitoromegaly, hyperpigmentation of labia majora)
<ul style="list-style-type: none"> • Prostatic hypertrophy • Aggression, increased Libido • Seborrhoea • Liver dysfunction • Alopecia 	<ul style="list-style-type: none"> • Neutered male: visible testosterone-dependent penile spines • Prostatic hypertrophy • Aggression, increased Libido • Seborrhoea • Liver dysfunction • Inappropriate urination • Hyperactivity 	<ul style="list-style-type: none"> • Hypergonadism, penis enlargement/penile growth • Scrotal disorder • Accelerated growth rate, advanced bone age, advanced height • Premature development pubic hair • Acne, comedones, seborrhea • Aggression • Dysphonia



©Brett Wildermuth

©Brett Wildermuth

Fig. 1: Vulva swelling and progressive high grade alopecia in a female-neutered Toy Fox terrier due to secondary hyperestrogenism caused by owner's topical hormone replacement therapy.



©BVL

Fig. 2: Number of affected animals or children in pharmacovigilance databases (animals: cases from Europe, children: worldwide cases). As with any pharmacovigilance data a high rate of underreporting can be suspected.

Conclusion

- Hypothesis for further research: There might be an underdiagnosis of secondary hyperestrogenism in cats and children as well as hyperandrogenism in animals.
- A close dialogue between the medical and veterinary profession in the context of the One Health Concept is desirable to raise the awareness among both disciplines.

