

Human urethral reconstruction: is there a perfect animal model?

Olsen Ekerhult T¹, Ortac M², De Kort L.M.O.³, De Graaf P³

1. Sahlgrenska Academy, Institute of Clinical Sciences, Dept. of Urology, Gothenburg, Sweden, 2. Istanbul Faculty of Medicine, Department of Urology, Istanbul, Turkey, 3. UMCU, Department of Urology, Utrecht, The Netherlands

Introduction

Urethral disease in males is common and reconstruction surgery depends on availability of graft material. If there is not enough (local) tissue, tissue engineering may be a solution. To extrapolate data from the bench to the clinic, animal models are needed. However, it is necessary to understand the real power and limitations of these animal models.

Purpose:

We tried to compile the existing literature on mouse, rat, rabbit, dog, pig and primate penile anatomy and urethral development, as well as disease models of hypospadias and urethral stricture, to compare them with the human penis, both sick and healthy.

Methods

A literature search was performed using PubMed over the last 3 decades. The search keywords used were “urethra” “animal model,” “urethral disease,” and “preclinical studies”. We only included English original manuscripts, no reviews, editorials or congress abstracts.

Discussion

The human penis is an organ with a unique anatomy that does not have a perfect homologous in the animal kingdom, much less among the animals commonly used to model disease. The lack of good representative animal models is one of the main causes why advances in preclinical studies are not being translated to standard healthcare¹.

While rodents are far out the most used animal model, they are not the first choice for urethral reconstruction due to size and the presence of cartilage and bone structures in the penis. While pigs have been claimed to share main urethral characteristics with human, their penises do not. Ruminants lack the corpus spongiosum, an dogs have an os penis. Lastly, primate penises have more similarities with human than any other, even if they are not as identical as commonly believed.

Considering all this, we suggest rabbit as the model of choice. It has big similarities with human and it does not contain an os penis, most important, it is big enough to surgically work with.

Results: Overview of different animal models for urethral reconstruction in literature

	size	os penis	ethical concerns	costs	Used in literature
Mouse	--	yes	low	low	No
Rat	-	yes	low	low	Yes
Rabbit	+	no	low	intermediate	Yes, most
Pig	+	no	low	high	yes
Dog	+	yes	high	high	Yes, often female
Ruminant	+	no	low	high	no
Primate	+	some	highest	highest	no

Conclusion:

Overall, there is not a perfect animal model that can give urethral tissue engineering new approaches a boost to the clinic, since human penis has a unique anatomy with no accurate homologous in nature. Nevertheless, among the available animal models, we propose the use of rabbits. Balance between responsible animal experimentation and reasonably good translation to clinic is found in rabbit penis and urethra.

Reference: ¹Versteegden, L. R. M., et al (2017). Eur Urol, 72(4), 594-606. doi:10.1016/j.eururo.2017.03.026