The effects of PDE-5 and DPP-4 inhibitors on testicular morphology in a porcine model for heart failure

Background
Heart failure affects many Americans, and there have been numerous attempts by researchers and clinicians to find better ways to treat this disease syndrome.

Studies aimed at evaluating the effects of novel heart medications, including PDE-5 and DPP-4 inhibitors, are currently under way.

PDE-5 breaks down cGMP, which promotes relaxation of cardiac muscle, along with modulating testosterone production in the testes.

DPP-4 breaks down incretins, like GLP, and some studies have shown DPP inhibitors to be cardioprotective. These have unknown effects on the testes.

One of these classes of drugs is used in the treatment of erectile dysfunction (PDE-5 inhibitor), and the other is used in the treatment and control of diabetes (DPP-4 inhibitor).

Both classes of drugs are thought to have potential as medications for the treatment and control of heart failure.

However, there is little known about the effects of long-term use of these drugs on spermatogenesis.

Histopathologic evaluation of the testes and staging of the seminiferous tubules are considered the gold standards for evaluating spermatogenesis, especially when semen is not being collected.

Experimental Hypothesis
Six months of aortic band-induced heart failure, plus or minus oral administration of a PDE-5 or DPP-4 inhibitor, will adversely affect porcine spermatogenesis.

Method for Staging Seminiferous Tubules

<table>
<thead>
<tr>
<th>Stage</th>
<th>Stages of the Seminiferous Tubules</th>
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<tr>
<td>I</td>
<td>Stage I, Stage II, Stage III</td>
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<tr>
<td>II</td>
<td>Stage IV, Stage V, Stage VI</td>
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<tr>
<td>III</td>
<td>Stage VII, Stage VIII, Seminiferous tubule degeneration</td>
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Other Observed Histological Changes
From left: Giant cell (arrowhead), normal Leydig (interstitial) cells, hyperplastic Leydig cells

Conclusions
Chronic oral administration of a high dosage of the PDE-5 inhibitor, tadalafil, appeared to cause an increased incidence of degeneration of seminiferous tubules and a decreased frequency of spermiogenesis in a porcine model for heart failure.

Results

Gross Measurements
There were no statistically significant differences among the means of the lengths (p=0.54), heights (p=0.73), or widths (p=0.90) of any of the groups tested.

Histological Examination
- The tadalafil group differed significantly from the mean of the Control group in both stage VIII (P=0.042, Figure 1) and in degenerated seminiferous tubule frequencies (P=0.005, Figure 2).
- The other groups displayed no significant differences from the Control group mean (Figures 1 and 2 below).
- Furthermore, other abnormalities were much more apparent in the tadalafil group. Common abnormalities observed included giant cells, vacuolization, hyperplastic Leydig cells, and the absence of spermatocytes in the cauda of the epididymides.
- In the control group (n=6), one specimen showed slight hyperplasia of the Leydig cells, with limited giant cells and vacuolization.
- In the control with heart failure group, most of the testes displayed vacuolization with two slides showing giant cells.
- The tadalafil group (n=8) showed mostly hyperplastic Leydig cells (six), with low sperm numbers in the epididymis, vacuolization, and giant cells throughout.

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References

的带领研究

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研究目标

研究两种新型心力衰竭药物对睾丸形态的影响。