Experimental evidence that a combination of sGC stimulator BAY 60-4552 and PDE5 inhibitor vardenafil might salvage patients with insufficient response to PDE5 inhibitors after cavernous nerve injury

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OBJECTIVES

- Promoting cGMP accumulation via PDE5 inhibitors constitutes currently the first-line therapy and the gold standard treatment of erectile dysfunction (ED).
- In several pathological conditions, including post-radical prostatectomy (RP)-associated ED, the NO release is impaired. It results in insufficient response to PDE5 inhibitors since their effectiveness needs at least a minimal NO drive.
- A valuable approach to bypass the need for a sufficient NO drive would be the activation of cGMP production by sGC in a NO-independent manner by the use of a sGC stimulator.

Therefore the aims of the present study were:
1. to test the effects of a new therapeutic strategy: the use of a NO-independent home-dependent sGC stimulator, BAY 60-4552, and to compare them to the effects of a PDE5 inhibitor, vardenafil, and
2. to evaluate the possible additional benefits offered by a combined treatment with BAY 60-4552 and vardenafil on the erectile responses to electrical stimulation of the cavernous nerve (ES CN) in anesthetized rats with bilateral CN crush injury.

RESULTS

Effects of iv treatments on mean arterial pressure

- In CN crushed anesthetized rats, while iv BAY 60-4552 0.03mg/kg iv did not change MAP, BAY 60-4552 0.3mg/kg significantly lowered MAP.
- Intravenous BAY 60-4552 (0.03 mg/kg)/ vardenafil (0.03 mg/kg) combination decreased MAP similarly to iv vardenafil alone.

CONCLUSIONS

To conclude, the present study supports the hypothesis that:

- stimulation of sGC by BAY 60-4552 could ameliorate ED following CN injury,
- a combined administration of the sGC stimulator BAY 60-4552 and the PDE5 inhibitor vardenafil constitutes a valuable approach in treating ED in situations in which PDE5 inhibitors alone are not fully efficacious, and in which NO release is impaired as it is the case in men post-RP.