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Title: NO IN-VIVO CONSTRICTION OF THE FETAL DUCTUS ARTERIOSUS BY PROSTANOID PGF2A-RECEPTOR ANTAGONIST OBE002 IN RATS

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Abstract:

Prostaglandins play an essential role in term and preterm labour. Tocolysis with non-steroidal anti-inflammatory drugs (NSAID), which inhibit prostaglandin synthesis, is an effective treatment for preterm labor (PTL). However, use of NSAIDs is limited to 48 hours and complicated by in utero constriction of the ductus arteriosus (DA). OBE002 is a new, orally-active, selective prostaglandin F2α (PGF2α) receptor antagonist which is being developed to delay PTL. To clarify the potential of OBE002 to constrict the ductus, we administered vehicle, OBE002 or the NSAID indomethacin to near-term rats on gestation day 21. Four hours after treatment cesarean section was performed, neonates were euthanized and direct examination of the ductus arteriosus (DA) was performed using a dissecting microscope. Constriction of the DA was graded from “no constriction (0)” to “DA fully constricted (3)”. OBE002 (20mg/kg) or vehicle (PEG400), administered intravenously to the rat, did not constrict the fetal ductus, whereas indomethacin treated rats had constricted DAs; litter mean scores were 0.03±0.18, 0.00±0.00 and 0.83±0.19, respectively. These results indicate that PGF2α modulation does not play a major role in the fetal and neonatal ductus and show that a PGF2α antagonist such as OBE002 may be devoid of the limitations of NSAIDs for the treatment of PTL.