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Brief hypoxic cycles improve uterine contractile function after prolonged hypoxia in term-pregnant but not in nonpregnant rats *in vitro* 

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## ACCEPTED MANUSCRIPT

1	"Revised"
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3	Brief hypoxic cycles improve uterine contractile function after prolonged
4	hypoxia in term-pregnant but not in nonpregnant rats in vitro
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7	During labour, the uterus itself is vulnerable to hypoxia/ischemia that can occur with
8	each strong contraction and this may ultimately cause dysfunctional labour in some
9	women. Periods of Intermittent re-oxygenations are beneficial to tissues subjected to
10	hypoxia to wash out metabolic by-products that have been accumulated during
11	hypoxic stresses which may affect the tissue viability. We proposed that short
12	intermittent hypoxic episodes may protect the uterus from subsequent sustained long
13	hypoxia. To investigate this, two sets of experiments were performed on term-
14	pregnant and nonpregnant rat uterine tissues. In one set of experiment the uterus
15	was subjected to sustained long hypoxia for 40 minutes and then allowed to recover
16	in 100% $O_2$ . In the other set of experiment the uterus was subjected to 3 cycles of 2
17	minutes hypoxia each separated by 20 minutes reoxygenation and followed by a
18	sustained long hypoxia for 40 minutes and then allowed to recover. We found that
19	challenging the uterine tissues with intermittent short hypoxic episodes improved the
20	uterine contractility significantly after the sustained long hypoxia in term-pregnant but
21	not in non-pregnant tissues. These results suggest that a mechanism of uterine
22	tolerance (preconditioning) is confined to uterine tissues very close to labour and it is
23	a protective phenomenon to improve the uterine activity despite the long-lasting
24	paradoxical metabolic challenges that occur during the repeated strong labour
25	contractions.
26	Keywords: hypoxia, contraction, pregnant, uterus
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