

## MINI REVIEW

# Narrative minireview of the current status of hyperbaric oxygen therapy for pregnant women

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**Abstract**

We performed a narrative minireview for a PubMed search on March 31, 2023, using the keywords “pregnant” and “hyperbaric oxygen” to identify any related articles. Most reports have described pregnant women with carbon monoxide (CO) poisoning being treated by hyperbaric oxygen therapy (HBOT). HBOT helped improve the maternal condition and ensure normal fetal development. Some pregnant women with CO poisoning treated by HBOT suffered abortions or gave premature birth to low-weight babies or with congenital malformations. However, these results were considered sequelae of CO poisoning, not HBOT. We hypothesized that for pregnant women facing a life-threatening situation, for which the effectiveness of HBOT has previously been suggested, prioritizing the stabilization of the mother may also be beneficial for normal fetal development.

**KEYWORDS**

hyperbaric oxygen therapy, neonate, pregnant women

## INTRODUCTION

Hyperbaric oxygen therapy (HBOT) consists of using pure oxygen at increased pressure (in general, 2–3 atmosphere absolute [ATA]) to augment oxygen levels in the blood (hyperoxemia) and tissue (hyperoxia). This results in a major supply of reactive oxygen species and reactive nitrite species, with a consequent increased expression of growth factors, promotion of neovascularization, and enhanced immunomodulatory properties.<sup>1</sup>

HBOT is typically delivered in hyperbaric chambers to a single patient at a time (monoplaced) or in a room accommodating multiple patients at the same pressure (multiplace chambers). The commonly accepted indications for HBOT are air or gas arterial or venous emboli, decompression sickness (DCS), carbon monoxide (CO) poisoning, gas gangrene, selected crush injuries, selected arterial insufficiencies, severe otherwise untreatable anemias, certain intracranial abscesses, necrotizing soft tissue infections, chronic refractory

osteomyelitis, delayed radiation-induced injury, compromised skin grafts, acute thermal burn injuries, and sudden sensorineural hearing loss.<sup>2</sup>

However, a number of major adverse effects induced by HBOT have been reported. The two most common complications during HBOT are claustrophobia and barotrauma. In addition, as a result of the hyperoxic and hyperbaric environment, seizures might be induced due to the toxic properties of oxygen at high concentrations. In addition, retinopathy due to premature delivery in pregnant women might develop.<sup>2,3</sup>

HBOT may also be teratogenic for fetuses when pregnant women receive HBOT.<sup>4,5</sup> We previously experienced a case wherein a pregnant woman suffering from nonobstructive ileus consulted our facility for HBOT. HBOT has been reported to be indicated for ileus.<sup>6,7</sup> However, the indications of HBOT for pregnant women remain unclear, except for cases of CO poisoning, and we therefore canceled this consultation.

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**TABLE 1** Summary of previous reports concerning HBOT for pregnant women before delivery, abortion, or cesarean section.

Ref. no.	First author	Type	N	Maternal age (years)	Fetal age (weeks of gestation)	Disease	Cause	Maternal CO-Hb	HBOT ATA	Duration (min)
15	Kosaki	Case	1	30	31	CO	Accident (camp)	28.6	2	60
16	Gabrielli	Case	1	14	37	CO	Accident (heater)	5.3	3	180
17	Greingor	Case	1	31	21	CO	Accident (heater)	24.6	2.5	90
18	Brown	Case	1	27	32	CO	Accident (fire)	25.1	3+2	46+50
19	Van Hoesen	Case	1	17	37	CO	Accident (car)	47.2	2.4	90
20	Mandal	Case	1	31	35	CO	Accident (heater)	25.3	2.8	100
21	Santos	Case series	2/37	?	?	CO	Wildfire	3.7	2.5	90
22	Tchirikov	Case 1	2	22	30	Severe placental insufficiency	N/A	N/A	1.4	50
22	Tchirikov	Case 2	2	30	25	Severe placental insufficiency	N/A	N/A	1.4	50

Number of times	Side effects	Indication or subject	Delivery outcome	Neonate follow-up	Key message
3	No	High CO Hb	At 41 weeks, she delivered a healthy infant weighing 2862 g	After 3 months' follow-up, both the infant and mother are doing well	During pregnancy, CO negatively affects both the fetus and mother, so it is critical for emergency physicians to promptly recognize and manage such poisoning cases
1	No	Headache, vomiting	At 24 h after HBOT, she vaginally delivered a healthy infant weighing 3035 g	Normal after 4 weeks	CO intoxication in late pregnancy was treated with HBOT without adverse consequences
1	No	High CO Hb	She was discharged in good health 1 day after exposure and delivered a healthy male infant at term weighing 3800 g	No description	Despite maternal well-being, fetal morbidity or mortality can still occur. HBOT seems to be the treatment of choice, and all pregnant women suffering from CO intoxication should be referred for HBOT
	No	High CO Hb, syncope attack	A healthy 3200 g male by vaginal delivery	No description	Both mother and fetus are doing fine. No negative effects from the HBOT were observed
1	No	High CO Hb and consciousness disturbance of mother with fetal distress syndrome	A healthy 3600 g female by vaginal delivery	Follow-up examinations at 2 and 6 months old revealed normal growth and development with normal findings from a fundoscopic examination	Acute CO poisoning during pregnancy was successfully treated with HBOT. Recommendations are suggested for the use of HBOT during pregnancy
2	No	Fetal distress	A healthy male by vaginal delivery	Normal development after 1 year	HBOT appears to be safe and effective for maternal body and fetus with CO intoxication
?	No description	Two of 37 were pregnant. No detailed information was available.	?	No description	Wildfires can cause clinically relevant CO poisoning, with typical signs and symptoms
7	No	Severe placental insufficiency	At 31 + 4 weeks' gestation, the patient gave birth spontaneously to a preterm newborn weighing 1378 g.	At 5 years old, the boy is doing well, but the speech development was delayed without any neurological disturbance	Fetal nutrition combined with HBOT is technically possible and may allow the prolongation of the pregnancy
7	No	Severe placental insufficiency	During HBOT, the patient complained of uterine contractions. One day later, her child was delivered by cesarean section because of fetal late decelerations. The newborn weighed 420 g, Apgar 3/8/8	The newborn unfortunately developed pulmonary bleeding on day 4 of life with subsequent hypotonia, anuria, leucopenia, and thrombocytopenia, and died 6 days later	Fetal nutrition combined with HBOT is technically possible and may allow the prolongation of the pregnancy

Continues

TABLE 1 Continued

Ref. no.	First author	Type	N	Maternal age (years)	Fetal age (weeks of gestation)	Disease	Cause	Maternal CO-Hb	HBOT ATA	Duration (min)
23	Ozgok-Kangal	Original	27	26.8	18	CO	No description	27.9	2 or 2.5	30, 75 or 90
24	Arslan	Original	32	25	23	CO	Three patients were poisoned at work, and 29 were poisoned by stoves at home or in tents in which they were living	24.9	2.4	120
25	Elkharrat	Original	44	27.5	21	CO	No description	19	2	120

Abbreviations: ATA, atmosphere absolute; CO, carbon monoxide; Hb, hemoglobin; HBOT, hyperbaric oxygen therapy; N/A, not applicable; ?, no description.

Given the above, we reviewed reports concerning the clinical usefulness, safety, and adverse effects of HBOT for pregnant women and summarized the essential data.

## METHODS

We performed a narrative minireview for a PubMed search on March 31, 2023, to identify any related articles using the keywords “pregnant” and “hyperbaric oxygen”. The inclusion criterion was pregnant women who had actually received HBOT before delivery, abortion, or caesarean section. The exclusion criterion was reports written in languages other than English.

## RESULTS

We found 288 articles after the PubMed search. Of these, 35 reports described pregnant women actually treated by HBOT before delivery, abortion, or caesarean section. After excluding 17 reports written in languages other than English

and 7 that were review articles and did not include original clinical data,<sup>8–14</sup> the remaining 11 reports were summarized (Table 1).<sup>15–25</sup> There were eight case reports<sup>15–22</sup> and three original reports.<sup>23–25</sup> The number of pregnant women who were treated by HBOT before delivery, abortion, or caesarean section was 113 in total. The average age of pregnant women, whose ages were described in the reports, was 26.4 years. The average gestational week, when the weeks were described in the reports, was 21.5 weeks. Ten of the eleven reports involved pregnant women with CO poisoning treated by HBOT.<sup>15–21,23–25</sup> All 10 reports showed the efficacy of HBOT for improving the maternal condition and enabling normal fetal development. Some pregnant women with CO poisoning treated by HBOT had abortions or gave birth to low-weight babies prematurely or with congenital malformations.<sup>25</sup> However, these results were considered sequelae of CO poisoning rather than HBOT.<sup>23–25</sup> Based on this clinical evidence, standard HBOT in pregnancy appears to be safe and is considered beneficial, reducing the severity of maternal and fetal injuries and fetal deformities.<sup>14</sup> In addition, HBOT may improve long-term fetal outcomes even after birth.<sup>23</sup>

Number of times	Side effects	Indication or subject	Delivery outcome	Neonate follow-up	Key message
1 (3 in 30 min)	No description		Vaginal (66.6%), caesarean (29.6%), abortion (3.7%); Infant weight $\geq$ 2500 g (95.7%), <2500 g (4.3%); 3 of 28 had abortion, premature birth, or limb malformation	The median infant age was 34 (8–44) months at the last interview. Only 1 child (43 months old) could not speak	There was no definite evidence of fetal morbidity or mortality after HBOT. HBOT may improve long-term fetal outcomes after <i>in utero</i> CO poisoning without complications
1 (81.8%) 2 (15.2%) 3 (3.0%)	No description		Four patients had premature births (32–34 weeks). Two neonates died after birth: one from congenital cyanotic heart disease, and the other from a twin pregnancy at 33rd week with a birth weight of 1800 g and respiratory distress. The others were healthy.	No description	HBOT is not advisable for pregnant patients except in cases of CO poisoning. HBOT under 2.4 ATA pressure for 120 min has no harmful effects on the mother or fetus
1	No description	Ten patients sustained a loss of consciousness for a few seconds, two were in a coma, and the remainder had headaches, gastrointestinal dysfunction, and dizziness	Obstetric follow-up data were available for 38 women. Normal delivery of normal infants in 32 (85%), spontaneous abortion in 12 (5%), medical abortion (10 weeks' gestation) in 1 (2%), premature delivery of a normal baby in 1 (2%), induction of labor (36 weeks' gestation) in 1 (2%), and baby with Down syndrome in 1 (2%)	The infant was born with major cardiopulmonary defects and died 6 days later	There is no evidence that HBOT was involved with either abortion in our study. HBOT may be performed in pregnant women acutely intoxicated with CO

The remaining article described two pregnant women with severe placental insufficiency treated by HBOT.<sup>22</sup> The first patient gave birth spontaneously to a newborn weighing 1378 g at 31 weeks' gestation. In a follow-up examination at 5 years of age, the boy was doing well without any developmental delay. In the second case, the patient gave birth to a hypotrophic newborn weighing 420 g at 25 weeks' gestation; unfortunately, the extremely preterm newborn died 6 days later. The authors concluded that adequate fetal nutrition combined with HBOT was technically possible and facilitated the prolongation of the pregnancy.<sup>22</sup>

One article described a 2-hour-old neonate with CO poisoning who underwent HBOT.<sup>26</sup> His 41-year-old mother had accidentally suffered CO poisoning at 38 weeks' gestation by a heater. Given the decreased fetal movement and biophysical profile score, the obstetrics team decided to perform emergency caesarean section. After delivery, the patient's carboxyhemoglobin value was 11.9%, and the maternal value was 7.4%. Both mother and neonate underwent HBOT at 2.4 atmosphere absolutes (ATA) for 90 min starting 2.5 h after delivery. The infant was discharged

in good condition 3 days after delivery but later lost to follow-up.

Another article described a case of residual severe neurological deficits and stillbirth due to delayed HBOT for a pregnant woman suffering from air embolism.<sup>27</sup> A 36-year-old woman in her 30th week of pregnancy developed convulsion and fell unconscious due to air embolism induced by orogenital sex. She underwent tracheal intubation and 100% oxygenation and magnesium sulfate administration. She spontaneously suffered stillbirth 3 h after the incident. She received delayed HBOT at 39 h after the incident but sustained severe sequelae from it. The author insisted that emergency HBOT was still required to obtain favorable outcomes for both the mother and fetus.

## DISCUSSION

This review indicated that standard HBOT for pregnant women suffering from CO poisoning is safe and considered beneficial, reducing the severity of maternal and fetal injury.

Concerning the safety of HBOT for pregnant women, HBOT ranging from 1.4 to 3 ATA with a duration of 30 to 180 min was found to be safe based on the results from Table 1. Typical side effects of HBOT are barotrauma for the middle ear, sinus, or oxygen toxicity.<sup>28,29</sup> However, such problems for pregnant women have not been documented in the previous reports as noted in Table 1. Strict operational protocols and in-chamber monitoring might result in an improvement of maternal safety.<sup>28</sup>

Fetal hemoglobin binds to CO as maternal hemoglobin does but with 2.5–3 times greater affinity.<sup>14</sup> A shift to the left of the dissociation curve is also expected in the fetal compartment. Furthermore, fetal carboxyhemoglobin has a half-life approximately 4 times longer than maternal carboxyhemoglobin.<sup>14</sup> As such, even in cases where the mother is doing well, fetal morbidity or mortality can still occur. Accordingly, even in asymptomatic cases of maternal CO exposure, HBOT might be necessary to minimize fetal injuries and ensure normal fetal development.<sup>14</sup> Normal fetal development requires the stabilization of vital signs of the maternal body.<sup>30–32</sup> Accordingly, for pregnant women facing a life-threatening situation for which HBOT has proven effective, prioritizing stabilizing the mother would also be beneficial for normal fetal development. At least a single episode of hypoxia from CO poisoning can be teratogenic for a fetus; however, there has so far been no report of a single HBOT being teratogenic for a fetus based on experimental studies.<sup>33</sup> Accordingly, fetal teratogenic complications are likely to be related to CO poisoning, but they are not related to HBOT.<sup>23</sup>

No previous report has described the benefits and adverse effects of HBOT for healthy pregnant women and, in particular, their fetuses. Sapunar et al.<sup>34</sup> reported the effects of HBOT on rat embryos. They found that HBOT did not induce malformations at either 3.3 or 4.3 ATA and that the largest embryotoxic effects involved decreasing the fetal body weight and increasing the placental weight. Gilman et al.<sup>35</sup> reported the effects of DCS and treatment for fetal development using pregnant hamsters. They induced DCS by exposing hamsters to 7.1 ATA of compressed air breathing for 40 min. Comparisons were then made between three groups of pregnant hamsters: (1) those that developed DCS; (2) those that did not; and (3) a control (nondivided) group. Maternal DCS left untreated resulted in frequent and severe teratogenic effects. Furthermore, fetuses from females that did not develop DCS were significantly smaller at term than those from control animals. However, fetuses from females with DCS that were treated with HBOT did not differ markedly from controls. Accordingly, these experimental results support our hypothesis that prioritizing the stabilization of critically ill mothers with HBOT would also be beneficial for normal fetal development.

One limitation associated with the present study was that no report investigated the effects of HBOT on all stages of pregnancy, and none evaluated the condition and development of the neonate after birth. In addition, experimental

animals are not equal to humans, especially with regard to high cortical and visual functions. Moreover, only successful cases might have been previously reported. Furthermore, there have been no clinical reports of HBOT being applied to pregnant woman in a life-threatening situation except for CO poisoning. Accordingly, further accumulation of clinical evidence concerning the effects of HBOT on pregnant women, fetuses, and development after birth is needed.

## CONCLUSION

Standard HBOT for pregnant women suffering from CO poisoning has been proven to be safe and is considered beneficial, reducing the severity of both maternal and fetal injury. For pregnant women facing a life-threatening situation, for which the effectiveness of HBOT has previously been suggested, prioritizing the stabilization of the mother may also be beneficial for normal fetal development.

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## CONFLICT OF INTEREST STATEMENT

We do not have conflict interest to declare.

## DATA AVAILABILITY STATEMENT

We do not have data are available.

## ETHICS STATEMENT

Approval of the research protocol: Juntendo University review board (298).

Informed consent: N/A.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

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