

Botulinum toxin type A in pregnancy

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Abstract

Question My patient received 62 units of botulinum toxin type A (BTX-A) for facial lines. Two weeks later, she found out that she was pregnant. Will this cause any harm to her fetus?

Answer Botulinum toxin is not expected to be present in systemic circulation following proper intramuscular or intradermal injection. Moreover, BTX-A, which has a high molecular weight, does not appear to cross the placenta. From the 38 pregnancies reported in the literature, including women who had botulism poisoning during pregnancy, exposure to BTX-A does not appear to increase the risk of adverse outcome in the fetus.

Toxine botulinique de type A durant la grossesse

Résumé

Question L'une de mes patientes a reçu 62 unités de toxine botulinique de type A (BTX-A) pour réduire les rides du visage. Deux semaines plus tard, elle s'est rendu compte qu'elle était enceinte. Cette injection peut-elle nuire au fœtus?

Réponse On ne s'attendrait pas à ce que la toxine botulinique soit présente dans la circulation systémique à la suite d'une injection intramusculaire ou intradermique effectuée de manière appropriée. De plus, la BTX-A, qui a un poids moléculaire élevé, ne semble pas traverser le placenta. Dans les 38 grossesses semblables signalées dans les ouvrages scientifiques, même chez des femmes qui ont eu un empoisonnement botulinique durant la grossesse, l'exposition au BTX-A ne semble pas augmenter le risque d'issues défavorables chez le fœtus.


Botulinum toxin type A (BTX-A) is a purified neurotoxin from the bacterium *Clostridium botulinum*. It has numerous medical applications such as treatment of cervical dystonia, focal spasticity, strabismus, achalasia, blepharospasm, hyperhidrosis, migraine, and tension headache.¹ It has also become popular among dermatologists and plastic surgeons for its cosmetic indications to temporarily paralyze facial muscles and diminish wrinkles in the skin.² With more women delaying pregnancy until later in life, inadvertent exposure of pregnant women to BTX-A is likely to occur at a greater frequency.

Botulinum toxin is a large protein with a high molecular weight (150 kD).² When injected intramuscularly in recommended doses, BTX-A is not expected to enter systemic circulation.² Therefore, BTX-A is unlikely to be present at the maternal-fetal interface.

In rabbits, botulinum toxin was not detectable in the placenta or in the fetuses when given intravenously in highly lethal doses.³ However, fetal malformations and abortions were reported in rabbits with daily injections of BTX-A (doses of 0.125 U/kg and 0.5 U/kg daily, and 2 U/kg, 4 U/kg, and 6 U/kg).² Similar adverse fetal outcomes were not found in pregnant mice.²

Information about exposure to botulinum toxin in human pregnancy is limited to case reports and a survey.⁴⁻¹⁸ Seven cases of women with botulism poisoning in either their second or third trimester have been reported.⁴⁻¹⁰ No evidence of birth defects or infantile botulism in the neonates was noted in any case. In one case, when maternal paralysis was severe, fetal movements were the only visible movements in her body.⁶ In 2 of the above cases, infant serum was taken and no botulinum toxin was detected.^{4,10} An additional 28 pregnancies with exposure to BTX-A therapy (at least 18 of 28 had first-trimester exposure) reported 25 normal live pregnancies, 1 therapeutic abortion, and 2 spontaneous abortions.¹¹⁻¹⁶ Both women who had spontaneous abortions had histories of spontaneous abortions. There are also 3 reports of first-trimester use of BTX-A for cosmetic indications.^{17,18} Two healthy babies were delivered, and no details were provided for the third case.

With proper administration of BTX-A, it is not expected to enter systemic circulation. Therefore, based on its local action and on the existing data, administering BTX-A to a pregnant woman is not expected to cause any fetal harm. However, until more data are available, benefits and potential risks to both the mother

and the infant should be considered when recommending BTX-A injection to a pregnant patient. 

Competing interests

None declared

References

1. *Botox* [product monograph]. Irvine, CA: Allergan Inc; 2011.
2. *Botox Cosmetic* [product monograph]. Irvine, CA: Allergan Inc; 2011.
3. Hildebrandt GJ, Lamanna C, Heckly RJ. Distribution and particle size of type A botulinum toxin in body fluids of intravenously injected rabbits. *Proc Soc Exp Biol Med* 1961;107(284):284-9.
4. St Clair EH, DiLiberti JH, O'Brien ML. Observations of an infant born to a mother with botulism [Letter]. *J Pediatr* 1975;87(4):658.
5. Centers for Disease Control and Prevention. Wound botulism—California, 1995. *MMWR Morb Mortal Wkly Rep* 1995;44(48):889-92.
6. Polo JM, Martin J, Berciano J. Botulism and pregnancy. *Lancet* 1996;348(9021):195.
7. Robin L, Herman D, Redett R. Botulism in a pregnant woman. *N Engl J Med* 1996;335(11):823-4.
8. Morrison GA, Lang C, Huda S. Botulism in a pregnant intravenous drug abuser. *Anaesthesia* 2006;61(1):57-60.
9. Magri K, Bresson V, Barbier C. Botulisme et grossesse. *J Gynecol Obstet Biol Reprod (Paris)* 2006;35(6):624-6.
10. Centers for Disease Control and Prevention. Type A botulism—Oregon. *MMWR* 1973;22(26):218-23.
11. Newman WJ, Davis TL, Padaliya BB, Covington CD, Gill CE, Abramovitch AI, et al. Botulinum toxin type A therapy during pregnancy. *Mov Disord* 2004;19(11):1384-5.
12. Bodkin CL, Maurer KB, Wszolek ZK. Botulinum toxin type A therapy during pregnancy. *Mov Disord* 2005;20(8):1081-2.
13. Morgan JC, Iyer SS, Moser ET, Singer C, Sethi KD. Botulism toxin A during pregnancy: a survey of treating physicians. *J Neurol Neurosurg Psychiatry* 2006;77(1):117-9.
14. Wataganara T, Leelakusolvong S, Sunsaneevithayakul P, Vantanasiri C. Treatment of severe achalasia during pregnancy with esophagoscopy injection of botulinum toxin A: a case report. *J Perinatol* 2009;29(9):637-9.
15. Li Yim JF, Weir CR. Botulinum toxin and pregnancy—a cautionary tale. *Strabismus* 2010;18(2):65-6.
16. Aranda MA, Herranz A, del Val J, Bellido S, Garcia-Ruiz P. Botulinum toxin A during pregnancy, still a debate. *Eur J Neurol* 2012;19(8):e81-2.
17. De Oliveira Monteiro E. Botulinum toxin and pregnancy. *Skinmed* 2006;5(6):308.
18. Kuczkowski KM. Anesthetic implications of botulinum toxin type A (Botox) injections for the treatment of 'the aging face' in the parturient. *Acta Anaesthesiol Scand* 2007;51(4):515-6.

MOTHERISK

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Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future Motherisk Updates. Published Motherisk Updates are available on the *Canadian Family Physician* website (www.cfp.ca) and also on the Motherisk website (www.motherisk.org).

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