



Letter

Oxytocin: A likely underestimated risk for anaphylactic reactions in delivering women sensitized to latex

Oxytocin (Syntocinon) is usually considered an uncommon cause of severe allergic reactions during delivery. Very few documented reports on anaphylactic/anaphylactoid reactions as well as severe airway obstructions have been published.¹ On the contrary, oxytocin may exert several cardiovascular activities, inducing, in some cases, significant side effects during delivery.²

However, some data highlight the possibility that the risk of developing severe systemic reactions after the infusion of oxytocin during delivery could be higher than expected in some allergic women. In this context, allergic sensitization to latex, the second most frequently incriminated substance inducing anaphylaxis during anesthesia,³ which is also a relatively common condition in the female sex,⁴ might constitute an important predisposing risk factor. Moreover, hypersensitivity reactions in the anesthesia setting are significantly higher in adult women than in men.⁴

In this report, we describe 2 life-threatening anaphylactic reactions with onset a few minutes after the infusion of oxytocin in 2 women sensitized to latex allergens. Both patients underwent a detailed interview concerning their clinical history for previous allergic diseases, accurate review of clinical documentation and anesthesiological sheet to evaluate temporal relationship between drug infusion and onset of symptoms, clinical examination, and in vivo and in vitro diagnostic tests to identify the culprit agent/agents.

In Table 1, we reported patients' characteristics and diagnostic results. In both patients the severity of clinical symptoms required resuscitation procedures and successive admission to an intensive care unit.

We have no information on the levels of serum tryptase during reactive events. However, the close relationships between oxytocin infusion and onset, clinical features, and their severity clearly indicate a true anaphylaxis.

Diagnostic procedures confirmed an immunoglobulin E-mediated allergic response to both latex and oxytocin; no allergic response was found to bupivacaine. Sensitization to other agents used before or during Cesarean section such as local antiseptics, proton-pump inhibitors, antihypertensive drugs, low-molecular-weight heparin (enoxaparin sodium), and human albumin can be excluded either for temporal reasons or because these agents have been used after the allergic reaction without any problem.

Five control subjects underwent skin prick tests by using the same Syntocinon solution used in the delivery room for skin prick testings in our patients (Syntocinon *5UI /mL solution in 6 separate vials of 1 mL; Novartis Pharmaceutical, North Ryde, Australia) without any cutaneous response.

Available literature shows that a "true" anaphylaxis after the infusion of oxytocin can be considered, apparently, an uncommon event; more frequently, oxytocin may induce cardiovascular effects mimicking cardiac anaphylaxis.² Some data suggest that the risk of developing anaphylaxis after the infusion of oxytocin during delivery could be much higher in the case of a relationship between oxytocin and latex. Ogata and Minami⁵ demonstrated an homology in the protein sequence of oxytocin and latex allergens Hev b 7.01 and Hev b 7.02 (patatin). These authors suggested that, in their patient sensitized to patatin, subsequent administration of oxytocin could facilitate the antigen recognition, resulting in an anaphylactic response to latex. Draisci et al⁶ showed that latex allergens constitute an important risk in obstetric population. They demonstrated that the prevalence of latex sensitization is 3 times greater in women undergoing cesarean delivery than in nonpregnant women undergoing gynecologic surgery.

The expression of oxytocin receptors plays a role not only in uterine but also in other human tissues, and labor and inflammation increase this expression. Recently oxytocin receptors have been found also in human airway smooth muscle. Moreover, Amrani et al⁷ have shown that asthma-related cytokines (interleukin-13 and tumor necrosis factor alpha) modulate the expression of oxytocin receptors in human airway smooth muscle function, suggesting a potential role of inflammation-induced changes in oxytocin receptor signaling in the regulation of airway hyperresponsiveness in asthma. In other words, in this ex vivo model, oxytocin, under pro-inflammatory cytokine stimulation, may induce contraction of smooth muscle and airway narrowing, suggesting that oxytocin serves as a bronchoconstrictor.⁸ As a confirm of this possibility, a case of exclusive severe airway involvement (bronchospasm and laryngeal stridor) after oxytocin administration has also been reported.⁸

Taken together, these data suggest that inflammatory conditions of airways such as those found in women with asthma might constitute an independent (from anaphylaxis) risk factor for airway obstruction after infusion of oxytocin during delivery. The role of oxytocin receptors could also explain the well-known worsening of asthma control in approximately one third of pregnant women suffering from asthma. Finally, women suffering from severe asthma are at higher risk of anaphylaxis than men.⁹ In our report, we demonstrated 2 life-threatening anaphylactic reactions that occurred a few minutes after the infusion of oxytocin in women sensitized to latex; an immunoglobulin E-mediated mechanism has been shown for both of these agents. Our data suggest that allergic sensitization to latex allergens might constitute a significant risk factor for triggering severe systemic reactions after the infusion of oxytocin in delivering women. This risk could be underestimated if we consider that women show higher

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Table 1
Patients' characteristics and diagnostic results

	Patient 1	Patient 2
Personal data		
Initials	FF	NA
Age (years)	37	42
Family history of allergy	Yes	Yes
Personal history of allergy	Slight itching after the use of latex gloves (No O.E. to latex)	Slight itching after the use of latex gloves Allergic rhinitis from Parietaria pollen. Ranitidine hypersensitivity. (No O.E. to latex)
Previous anesthesiological procedures	Yes, no allergic reactions	Yes, no allergic reactions
Pregnancy characteristics		
No of pregnancies	First	First
Obstetric conditions	Preeclampsia	Oligoamnios, marginal placenta previa
Gestational age	36th week	36th week
Modality of delivering	Cesarean section	Cesarean section
Type of anesthesia	Spinal (subarachnoid route)	Spinal (subarachnoid route)
Drugs used for anesthesia	Atropine 0.4 mg intravenously Hyperbaric bupivacaine 0.5%, 10 mg subarachnoid route Morphine 10 mg intramuscularly	Atropine 0.7 mg intravenously Hyperbaric bupivacaine 0.5%, 10 mg subarachnoid route Morphine 12 mg intramuscularly
Intraoperative plastic devices	Latex-free	Latex-free
Intraoperative anaphylactic reaction		
Onset of allergic symptoms	2–3 minutes after Syntocinon infusion (5 UI intravenously in 10 mL saline solution)	3–4 minutes after Syntocinon infusion (5 UI intravenously in 10 mL saline solution)
Symptoms	Generalized rash and urticaria-angioedema, macroglossia, intraoral and laryngeal angioedema, profound hypotension (60/40 mmHg)	Generalized and facial rash/urticaria-angioedema, dyspnea, hypotension (65/45 mmHg)
Treatment	Tracheal intubation, resuscitation procedures, admission to ICU	Tracheal intubation, resuscitation procedures, sedation, admission to ICU
Diagnostic procedures		
SPT:		
Latex, Oxytocin	+ (w.d. 5 × 6 mm; f.d. 7 × 9 mm), + undiluted (w.d. 4 × 6 mm; f.d. 7 × 8 mm) H. control (w.d. 7 × 9 mm; f.d. 10 × 13 mm)	+ (w.d. 8 × 8 mm; f.d. 10 × 11 mm) + for 1/10 diluted (w.d. 4 × 5 mm ; f.d. 7 × 9 mm) H. control (w.d. 8 × 10 mm; f.d. 13 × 16 mm)
Bupivacaine	No reaction	No reaction
Total IgE evaluation	25.0 Ku/L (n.v. < 100)	117.0 Ku/L (n.v. < 100)
Specific IgE evaluation:		
- Penicilloyl G	0.03 Ku/L (n.v. < 0.1)	0.04 Ku/L (n.v. < 0.1)
- Penicilloyl V	0.04 Ku/L “ “	0.01 Ku/L “ “
- Ampicillin	0.09 Ku/L “ “	0.05 Ku/L “ “
- Amoxycillin	0.02 Ku/L “ “	0.04 Ku/L “ “
- Cefaclor	0.03 Ku/L “ “	0.07 Ku/L “ “
- Latex	0.98 Ku/L “ “	5.70 Ku/L “ “

Abbreviations: SPT = Skin Prick Test; n.v. = normal values; Ku/L = kilounits/liter; ICU = intensive care unit; O.E. = occupational exposure; + = positive; w.d. = wheal diameters; f.d. = flare diameters; H = histamine; IgE = immunoglobulin E.

prevalence of both hypersensitivity reactions in the anesthesia setting and latex allergy than men. Another important finding coming from our case reports is the need to test all of the drugs or substances used intraoperatively,³ because more than 1 sensitization may be present in the same patient. Failing to test oxytocin could have led to an incomplete diagnosis of latex allergy.

In conclusion, our findings suggest the need for particular attention in managing delivering women suffering from latex allergy. An accurate medical history, clinical and diagnostic evaluation, latex-free anesthesiological setting, use of oxytocin-alternative agents and, if the patient suffers from asthma, a drug premedication¹⁰ are likely to reduce the risk of anaphylactic reactions in these women.

Further in vitro studies are necessary to establish the occurrence of an immunologic cross-reaction between latex and oxytocin, and clinical studies are needed for a better understanding of and management of respiratory and cardiac effects of oxytocin administration.

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