

ORIGINAL ARTICLE

Anaphylactic reactions during cesarean section

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SUMMARY. Sensitization to latex seems to occur more frequently in women than in men. Obstetric and gynecological surgical procedures have recently been shown to be a common setting for latex anaphylaxis. We analyzed all the cases of anaphylactic reactions during 1240 cesarean sections in 2004; the patients were questioned for risk factors and underwent allergy testing for drugs and latex. Four patients had anaphylaxis under spinal anesthesia and in all cases it was due to latex allergy. Reported symptoms included facial edema, profuse sweating, itching, generalized erythematous rash and hypotension. Only one patient manifested a severe reaction which included bronchospasm, dyspnea, tachypnea and anaphylactic shock, requiring orotracheal intubation and epinephrine. Our data showed a high incidence (1:310) of intraoperative latex anaphylactic reactions in the one-year study period. This may be related to the very specific population (all women) in a very specific setting (obstetrics). To prevent anaphylactic reactions during obstetric surgery it is important to identify potential risk factors to include, for example atopy, adverse reactions to foods and latex items. If latex allergy is confirmed or strongly suspected, patients should be managed in a latex-safe environment. Premedication with antihistamines and steroids might be useful to further reduce the risk. After the delivery, specific desensitization may represent a good therapeutic option.

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INTRODUCTION

The incidence of anaphylactic reactions during general anesthesia ranges from 1:10000 to 1:20000 in the general population.^{1,2} If these reactions are adequately treated, the mortality is less than 6%.^{3,4} A significant female predominance (about 70%) has been observed irrespective of the causal agent.^{5–7}

The most common agents involved in intraoperative anaphylactic reactions are muscle relaxants (61–70%).^{5–8} Natural rubber latex (NRL) is the second most implicated agent and the incidence of latex-related anaphylactic reactions is increasing despite the increasing awareness and the preventive measures undertaken. In a French multicenter epidemiological survey of ana-

phylactic reactions, the rate of latex-related reactions was 0.5% in 1984–89, increased to 12.5% in 1990–92, and had increased to 22.3% in 2001–2002.^{2,5–8}

The incidence of latex sensitization in the general population is about 1:100, and some groups at high risk have been identified: patients with spina bifida and/or urogenital abnormalities, healthcare workers and patients with a history of multiple surgical procedures or allergies to fruits.^{9–14} Sensitization to latex is more frequent in women and a common setting for latex anaphylaxis may be obstetric and gynecological surgery.¹⁵ We analyzed all the cases of anaphylactic reactions in women who underwent cesarean section in 2004.

METHODS

All consecutive patients ($n = 1240$) in 2004 who underwent a caesarean section in the obstetric clinic of the Catholic University Medical School were studied retrospectively. Spinal, epidural or general anesthesia was used as indicated. Patients who were suspected to have intraoperative anaphylactic reactions were questioned

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about previous adverse reactions to latex and drugs, atopic diseases and other risk factors and underwent allergy testing, as is the policy in our department. Reactions were graded from 1 to 4 according to their severity: grade 1 = cutaneous signs; grade 2 = measurable but not life-threatening symptoms; grade 3 = life-threatening reactions; grade 4 = circulatory inefficacy, cardiac and/or respiratory arrest (Table 1).⁶

Anesthesia

In all patients a 16-gauge intravenous cannula (Venflow®) was inserted into the antecubital vein of the left arm. A rapid bolus of lactated Ringer's solution (1000 mL), ranitidine (100 mg) and mezlocillin (2 g) as antibiotic prophylaxis were administered i.v. 30 min before surgery. Bladder catheterization was performed in all patients with catheters containing latex (Rusch Amber silicone-treated) immediately before surgery.

Anesthetic techniques included:

- *Spinal anesthesia* (730 patients, 58.8%) performed with hyperbaric bupivacaine 0.5% plus sufentanil using a 25-gauge pencil-point needle introduced at L2/3 (or L3/4) lumbar interspace. Ephedrine was given i.v. to keep the systolic blood pressure above 100 mmHg. Skin incision was allowed after a T4 level of anesthesia was achieved.
- *Epidural anesthesia* (265 patients, 21.4%) using an 18-gauge epidural catheter (Portex: epidural Minipack®) introduced at L2/3 or L3/4 lumbar interspace, using lidocaine 2% with 1:200000 epinephrine (or ropivacaine 0.75%) plus sufentanil. Skin incision was allowed after a T4 level of anesthesia was reached.
- *General anesthesia* (245 patients, 19.8%) induced with thiopental 5% (4 mg/kg). Tracheal intubation was performed after administration of succinylcholine (1 mg/kg). Anesthesia was maintained with sevoflurane, fentanyl and vecuronium. At the end of surgery, atropine and neostigmine were adminis-

tered to facilitate recovery of normal respiratory function.

After delivery of the infant, oxytocin (20 units) was administered intravenously in 5% glucose. In all cases the surgeons wore surgical latex gloves by the same manufacturer (Ansell's Gammex®).

Allergy testing

Skin prick tests (SPTs) were performed with a standard latex extract (500 µg/mL; ALK Abellø, Madrid, Spain). As cornstarch may be used for glove powder, corn extract was also tested to exclude corn allergy. SPTs and intradermal tests (IDTs) with bupivacaine (1%, diluted 1:100), ranitidine (10 mg/mL, diluted 1:100), sufentanil (1%, diluted 1:100), mezlocillin (250 mg/mL, diluted 1:100) and oxytocin (5 units/mL, diluted 1:10 000) were also performed to exclude drug allergy. SPTs were performed with a Morrow-Brown needle (ALK Abellø) on the volar surface of the forearm. If SPTs were negative, a minimal amount (0.02 mL) of the testing material was injected intradermally.

Glycerin solution and histamine (10 mg/mL) were used as negative and positive controls. Tests, read after 20 min, were considered positive for wheal diameters >4 mm. Serum levels of total and specific anti-NRL immunoglobulin (Ig) E and eosinophilic cationic protein (ECP) were measured by means of fluorescent enzyme immunoassay (UniCAP System; Pharmacia, Uppsala, Sweden). Specific IgE <0.35 kU/L, total IgE <200 kU/L and ECP <20 µg/L were considered normal. ECP is an index of eosinophil activation, which is usually involved in allergic diseases. It has no diagnostic value, but can be helpful to quantify allergic inflammation. Specific anti-NRL IgG4 antibodies were detected *in vitro* with a latex-specific fluorescent enzyme immunoassay (CAP-FEIA; Pharmacia). Blood samples were collected within one hour after the end of surgery. Anaphylaxis was diagnosed on the basis of positive skin test and/or specific IgE results. Otherwise, anaphylactoid reaction was diagnosed.

Table 1. Clinical features and biological findings in the four cases of anaphylaxis at delivery caused by latex

	Age	Grade of severity ^b	Treatment	Evolution	NRL skin prick test	NRL-specific IgE	Atopy ^a	Other risk factors
1	29	2	Ah, CCS, RLD, O ₂	Uneventful	++	1.33 kU/L	Yes	8 VE
2	36	2	Ah, CCS, RLD, O ₂	Uneventful	++	<0.35 kU/L	Yes	6 VE
3	41	3	Epi, Ah, CCS, RLD Intubation	ICU, discharge in 24 h	++	>100 kU/L	Yes	8 VE CD
4	32	2	Ah, CCS, RLD, O ₂	Uneventful	+	11.4 kU/L	No	10 VE CD

Ah: intravenous antihistamine; CCS: intravenous steroids; CD: contact dermatitis; Epi: i.v. epinephrine; ICU: intensive care unit; NRL: natural rubber latex; O₂: oxygen therapy, FiO₂: 1; RLD: removal of all latex devices; VE: vaginal examinations with latex gloves during pregnancy.

^aHistory of any atopic disease (allergic rhinoconjunctivitis, asthma or atopic eczema) and at least one skin prick test reaction to grass pollen, house-dust mite, food allergens or cat allergens.

^bGrade 1: cutaneous signs; grade 2: measurable but not life-threatening symptoms (cutaneous effects, decrease >30% of blood pressure, cough, difficulty in mechanical ventilation); grade 3: life-threatening reactions (cardiovascular collapse, tachycardia, bradycardia, arrhythmias, severe bronchospasm); grade 4: circulatory inefficacy, cardiac and/or respiratory arrest.⁶

RESULTS

During the study period, four patients out of 1240 (1:310), aged 29 to 41 years, manifested anaphylactic reactions during cesarean section. All of the patients had received spinal anesthesia. Demographic data and details about adverse reactions and administered therapy are shown in Table 1.

Case 1

A 29-year-old G1P0 patient, at 41 weeks' gestation developed facial edema, itching and a generalized erythematous rash 30 min after skin incision. Neither hypotension nor bronchospasm were observed. This episode was rapidly managed with medical treatment as shown in Table 1. Complete remission occurred within a few hours after surgery.

Case 2

A 36-year-old G2P1 at 41 weeks' gestation developed a less severe episode of facial edema, erythematous rash, without itching or bronchospasm. No hypotension was observed. Symptoms resolved completely with medical treatment.

Case 3

A 41-year-old G4P2 at 38 weeks' gestation suffered dyspnea and tachypnea with severe bronchospasm and prolonged hypotension. She required tracheal intubation, continuous fluid replacement, administration of vasoactive drugs (epinephrine) and treatment in the intensive care unit (ICU) for anaphylactic shock. Cutaneous symptoms were not observed. Her symptoms resolved within 3 h.

Case 4

A 32-year-old G1P0 at 39 weeks' gestation developed facial edema, itching, urticaria, and profuse sweating. Neither hypotension nor bronchospasm were observed. Symptoms resolved with medical treatment in 120-150 min.

In all cases the reaction occurred about 30 min after the start of the procedure; all patients had received oxytocin at delivery. Three patients were atopic: they suffered from bronchial asthma and two of them were sensitized to grass pollen. They all reported intolerance to rubber material (mainly gloves) but no one was known to be allergic to latex proteins. They had never experienced previous adverse reactions during surgical or medical procedures, nor during pregnancy, despite undergoing obstetric evaluations (once a month) with latex gloves without symptoms. No-one reported

adverse reactions to latex cross-reacting foods. All four patients had a positive SPT to latex extract and/or serum specific IgE to latex (Table 1). All had negative skin tests to corn extract, bupivacaine, ranitidine, mezlocillin and oxytocin. Patients 1 and 3 had total IgE >200 kU/L (325 kU/L and 628 kU/L respectively). Serum levels of ECP were >20 µg/L in patients 1 and 2.

DISCUSSION

These cases suggest a high incidence of intraoperative adverse reactions (1:310) compared with other reports,^{1,2} although in fact our cases are from a short period of time (1 year) and a relatively small number of patients (1240). It is difficult to interpret such a high incidence of anaphylactic reactions. Our data concern a very specific patient population in a very specific surgical setting.

Our patients reacted during spinal anesthesia, perhaps because of the high rate of spinal anesthesia for cesarean delivery compared with other clinical settings. Since epidemiologic data from the literature mainly concern anaphylactic reactions during general anesthesia, it is difficult to make a comparison, and our numbers are too small to estimate whether spinal anesthesia is less safe than epidural or general.

In our report an immediate type IgE-mediated allergy to latex was diagnosed in all cases. Although some authors have reported an increasing incidence of latex anaphylaxis, the high rate of latex-related reactions in our patient group is likely because regional anesthesia is most often used for cesarean delivery, reducing the rate of exposure to muscle relaxants.⁵⁻⁸

All our patients were adult women. A significant female predominance has been observed irrespective of the causal agent and particularly for latex-related reactions.^{5-7,15} It may be related to the higher predisposition in women to allergic diseases, their more frequent exposure to NRL items during everyday life and working time, and a greater mucosal contact with latex through barrier contraceptives.^{12,16} Furthermore, according to the literature, the obstetric population seems to have additional risk factors. Many episodes of anaphylactic reactions induced by latex gloves have been reported after normal vaginal delivery or vaginal exploration, most likely provoked by the extensive contact of surgical gloves with highly absorptive membranes.¹⁷⁻²³ Thus, the most common setting for latex anaphylaxis during surgery may be obstetric and gynecologic procedures, which have been reported to account for approximately 50% of all reactions caused by latex.¹⁵

Latex reactions occur during maintenance anesthesia, usually exhibiting a delay of 30 to 60 min. Our patients manifested symptoms during maintenance anesthesia,

30-50 min after the beginning of surgery, although they were exposed to latex items (such as catheters and latex gloves) from the start. The injection of oxytocin may have a fundamental role in triggering the reactions, by inducing sudden uterine contraction, which may provoke the release of latex particles from the uterus into the bloodstream.¹⁵

Since cesarean section represents a surgical procedure at high risk for latex-related anaphylaxis, a policy to identify high-risk patients during the preanesthetic visit is needed and the history is the most important tool (see box). All our patients had risk factors, such as history of previous allergic diseases. At first they all denied allergy to latex, but when more carefully questioned they reported intolerance (hand itching) after wearing gloves. This problem was ignored because all the patients had previously undergone several gynecological examinations during pregnancy without symptoms or adverse reactions. Other authors reported that thorough questioning after the reaction revealed the presence of symptoms suggestive of latex sensitization before the anaphylactic reaction in 34% of cases.⁶ Chen et al. identified some risk factors: known immediate allergic reactions to latex, atopy, previous abdominal surgery and regular use of condoms.²³ They suggested that patients with atopy and other risk factors should be treated in a latex-free environment. The increased risk of latex allergy in patients with allergies to several cross-reacting fruits and vegetables (potato, avocado, banana and kiwi fruit, for example) has also been reported.^{13,14} Latex precautions are indicated if latex allergy is confirmed or suspected.

If elective surgery is needed during pregnancy, patients who are members of high-risk groups should be referred to an allergist for skin test and measurement of serum specific IgE to exclude latex allergy.²⁴ If emergency cesarean section is required, or if allergy tests are not warranted and one or more risk factors are present, latex-safety procedures are advisable.

Avoidance is clearly the main prophylactic measure to prevent adverse reactions. The operating room should be free of latex items and the patient should be the first case of the day in order to reduce the risk. It is not always possible to avoid latex completely; some authors report anaphylaxis due to unintentional exposure to airborne latex particles, which may endanger fetal life.²¹

Premedication regimens, usually including corticosteroids and antihistamines, may be useful to reduce the severity of reactions. Although they have not proven to be effective at preventing anaphylactic reactions, there is still a theoretic rationale for their use and they should be considered in the presence of risk factors (see box).²⁵⁻²⁹

After delivery, latex specific immunotherapy may represent an interesting new therapeutic approach to manage latex-allergic patients.^{30,31} It may lead to a

relatively rapid tolerance to latex exposure and allow patients to undergo surgical procedures without symptoms. In particular, a case was reported of a patient who became pregnant after desensitizing treatment and successfully delivered a baby in a latex-containing delivery room. However, these encouraging results should be further confirmed by double-blind placebo-controlled studies.

This is only a preliminary report. Further prospective studies need to be performed, involving large centers and therefore a larger group of patients to better assess risk and to provide more precise data about the incidence of reactions to latex during obstetric surgery and the measures to prevent them.

Risk factors

- Allergic reactions to latex
- Intolerance to latex condoms
- Allergic reactions to cross-reacting foods (pine-apple, melon, chestnut, nuts, kiwi fruit, banana, avocado, potato, tomato, and others^{13,14})
- Adverse reactions during surgical or invasive diagnostic procedures
- Multiple operations
- Operations within the 1st year of life
- Atopy
- Professional exposure

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