

Anaphylaxis during anaesthesia: Indian scenario

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ABSTRACT

Background and Aims: Anaphylaxis during anaesthesia is a rare but serious problem. In contrast to the developed countries where databases of perianaesthetic anaphylaxis are preserved, none exist in India. We conducted a survey amongst Indian anaesthesiologists to study the incidence and aetiology of anaphylaxis during anaesthesia in India. **Methods:** A written questionnaire comprising 20 items was mailed electronically or distributed personally to 600 randomly selected Indian anaesthesiologists. The responses were compiled and analysed. **Results:** We received responses from 242 anaesthesiologists. One hundred and sixty-two (67%) anaesthesiologists had encountered anaphylaxis during anaesthesia. Anaesthetic drugs led to 40% of reactions, and 60% of reactions were attributed to non-anaesthetic drugs. Opioids were the most common anaesthetic drugs implicated in anaphylaxis during anaesthesia, and non-depolarising muscle relaxants were the second most commonly implicated agents. Colloids, antibiotics and blood transfusion were the common non-anaesthetic agents thought to be responsible for anaphylactic reactions during anaesthesia. There were five deaths due to anaphylaxis during anaesthesia. Only 10% of anaesthesiologists ordered for allergy testing subsequently though 38% of anaesthesiologists had access to allergy testing facilities. **Conclusions:** Our survey reveals that two-thirds of participating Indian anaesthesiologists had witnessed anaphylaxis during anaesthesia. Commonly implicated anaesthetic drugs were opioids and non-depolarising muscle relaxants while colloids, antibiotics and blood transfusion were the common non-anaesthetic agents causing anaphylactic reactions during anaesthesia. Further, our survey reveals low utilisation and paucity of referral allergy centres to investigate suspected cases of anaphylaxis during anaesthesia.

Key words: Anaesthesia, anaphylaxis, survey

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INTRODUCTION

Perianaesthetic anaphylaxis is a rare but serious problem. Reported incidence of perianaesthetic anaphylaxis varies from 1 in 3500 to 1 in 25,000 anaesthetics with a mortality rate of 4%, and an additional 2% surviving with severe brain damage.^[1,2] Understanding perianaesthetic anaphylaxis is important because patients under anaesthesia are at greater risk for adverse outcomes as a result of systemic effects of anaesthesia.^[3] Serious anaphylactic reactions during anaesthesia and in the peri-operative period can rapidly evolve into life-threatening situations if not recognised and managed promptly. Underreporting of cases has led to lack of awareness about the magnitude of the problem in India. The aim of this study was to describe the epidemiology of anaphylaxis during anaesthesia

through a survey amongst Indian anaesthesiologists. In addition, this study provides an opportunity to identify areas of concern in the Indian context and postulate possible solutions.

METHODS

Institutional Review Board's approval was obtained. A questionnaire comprising twenty

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items pertaining to anaphylaxis under anaesthesia was prepared and mailed electronically or distributed personally to 600 randomly selected Indian anaesthesiologists [Appendix 1]. It was electronically mailed to 300 randomly selected Indian anaesthesiologists from a list of national conference delegates along with a covering letter stating the purpose of the study soliciting them to send back the questionnaire after filling their responses by electronic mail. The questionnaire was also distributed personally to 300 randomly selected anaesthesiologists at various anaesthesia conferences over an 18-month period requesting them to fill up the questionnaire. The filled questionnaires were duly collected and the responses were compiled. Data were entered into Microsoft Office Suite 2007 Excel (Microsoft Corp., Redmond, WA, USA) and analysed by descriptive statistics using the Statistical Packages for Social Science version 17.0 (SPSS Inc., Chicago, IL, USA). Data were presented as frequency (numbers) or percentage and mean with standard deviation.

RESULTS

Out of the 600 questionnaires distributed, we received responses from 242 (40.3%) anaesthesiologists. Twenty-five anaesthesiologists (8%) out of 300 responded to the electronically mailed questionnaire while 217 out of 300 (74.3%) responded to the personally distributed questionnaires. Thus, data from 242 respondents were analysed. On analysing the geographical distribution of respondents in India, 140 (58%) were from northern states, 34 (14%) were from western and central states, 58 (24%) were from southern states and 10 (4%) were from eastern states. One hundred and fourteen (47%) respondents in our survey were working in private hospitals, 94 (39%) in government hospitals while 34 (14%) were working in autonomous institutes. About 44 (18%) respondents were designated as faculty, 101 (42%)

were consultants, 24 (10%) were specialists, 40 (17%) were senior residents and 33 (13%) were postgraduate students. Mean years of experience of respondent anaesthesiologists were 12.8 ± 10.7 years.

One hundred and sixty-two (67%) respondents had encountered an anaphylactic reaction during anaesthesia. Ninety-eight (60.5%) had encountered it on more than one occasion, 50 (31%) had encountered it only once while the remaining 14 (8.5%) did not remember on how many occasions they had encountered an anaphylactic reaction during anaesthesia. One hundred and forty-five (89%) out of 162 anaesthesiologists who had encountered an anaphylactic reaction during anaesthesia mentioned the type of anaesthesia during which they experienced anaphylaxis. Eighty-five anaesthesiologists (58.6%) had encountered an anaphylactic reaction during general anaesthesia, 23 (15.9%) during central neuraxial blockade, 3 (2.1%) during peripheral nerve blockade, 3 (2.1%) during monitored anaesthesia care and 2 (1.4%) during local anaesthesia alone. Twenty-nine (20%) anaesthesiologists had encountered anaphylaxis during more than one kind of anaesthesia. Overall, 114 (78.6%) anaesthesiologists had encountered an anaphylactic reaction during general anaesthesia, 45 (31%) during central neuraxial blockade, 10 (6.9%) during peripheral nerve blockade, 6 (4.1%) during monitored anaesthesia care and 4 (2.8%) during local anaesthesia. Responses to other questions in the questionnaire are mentioned in Table 1.

Anaesthetic drugs contributed to 40% of reactions while non-anaesthetic drugs were involved in 60% of reactions. The most common anaesthetic drug implicated was an opioid ($n = 25$) while non-depolarising muscle relaxant was the second ($n = 20$) most commonly implicated agent. Colloids ($n = 36$), antibiotics ($n = 34$) and blood transfusion ($n = 25$) were the common

Table 1: Response to different questions

Questions	Number of anaesthesiologists	
	Yes, <i>n</i> (%)	No, <i>n</i> (%)
Have you ever encountered an anaphylactic reaction under anaesthesia?	162/242 (67)	80/242 (33)
Could you pinpoint a specific agent for anaphylactic reaction under anaesthesia?	131/162 (81)	31/162 (19)
Did you perform allergy testing subsequently?	23/162 (14)	139/162 (86)
Did allergy testing results match with the clinical suspicion?	17/23 (74)	6/23 (26)
Did you warn your patient against further exposures?	136/162 (84)	26/162 (16)
Does your hospital have allergy testing facilities?*	62/162 (38)	50/162 (31)
Are you aware of guidelines of anaphylaxis management?	191/242 (79)	51/242 (21)
Do you take elaborate history of allergy during pre-anaesthetic evaluation?	235/242 (97)	7/242 (3)

Data are represented as number and percentage. *50/162 (31) respondents did not know whether their hospital have allergy testing facilities

non-anaesthetic agents causing anaphylactic reactions during anaesthesia. Table 2 shows the agent suspected to be implicated in anaphylactic reactions during anaesthesia. Anaesthesiologists diagnosed anaphylaxis during anaesthesia by the presence of cutaneous, cardiovascular, respiratory and other manifestations of anaphylaxis [Table 3]. Agents used in the management of anaphylactic reaction during anaesthesia by anaesthesiologists in our survey are shown in Table 4. Eighty-seven (54.8%) anaesthesiologists used adrenaline while managing anaphylaxis during anaesthesia. Three (1.9%) respondents did not mention as to how they managed anaphylactic reaction during anaesthesia. One hundred and eleven out of 159 (70%) anaesthesiologists did not mention the order of administration of these agents. Amongst the anaesthesiologists who mentioned the order of administration of drugs used for the management of anaphylactic reaction during anaesthesia, adrenaline was the first drug to be used by 40% of anaesthesiologists, while 35% used antihistaminic first, 21% used steroid and 4% used vasopressor first. One hundred and thirty-six anaesthesiologists (84%) warned their patients against future exposure after suspected anaphylactic reaction during anaesthesia. However, only 28 (20.6%) anaesthesiologists who warned their patients against future exposure specified as to how they did so. A written account of an anaphylactic reaction during anaesthesia was issued to patients by ten anaesthesiologists, verbal and written account was given by nine anaesthesiologists, verbal account alone was mentioned by six anaesthesiologists while one anaesthesiologist each issued an allergy card, collar and bracelet for warning against further exposure.

In our survey, five deaths were reported as a result of anaphylactic reaction during anaesthesia, two each as a result of bone cement and blood transfusion, and one due to ceftriaxone. Two hundred and twenty-eight (94.2%) Indian anaesthesiologists in our survey had mentioned what they thought as the common agents leading to anaphylactic reaction during anaesthesia practice as shown in Table 5 while 14 (5.8%) anaesthesiologists did not mention these agents.

DISCUSSION

The findings of a survey based on random sampling technique, if representative of particular population under study, can be extrapolated to a wider population.

Table 2: Agent implicated in anaphylactic reaction during anaesthesia (as per survey)

Agent	Number of anaesthesiologists, n (%) (out of 162)
Colloids	36 (22.2)
Antibiotics	34 (21)
Muscle relaxants	25 (15.4)
Non-depolarising muscle relaxants/succinylcholine	20/5 (12.3/3.1)
Opioids	25 (15.4)
Induction agents	17 (10.5)
Thiopentone/propofol	12/5 (7.4/3.1)
Local anaesthetics	16 (9.9)
Blood transfusion	25 (15.4)
Ranitidine	12 (7.4)
Radiocontrast dye	6 (3.7)
Protamine	5 (3.1)
Diclofenac sodium	6 (3.7)
Neostigmine/aprotinin	4/4 (2.5/2.5)
Oxytocin/bone cement	2/2 (1.2/1.2)
Other agents* (one time each)	9 (5.6)

Data are represented as number and percentage. *Betadine, hydatid cyst, latex, intravenous fluid, anti-tetanus serum, ondansetron, NSAID, paracetamol, heparin - 1 (0.6). NSAID – Non-steroidal anti-inflammatory drug

Table 3: Diagnosis of anaphylactic reaction during anaesthesia (as per survey)

Clinical manifestations	Number of anaesthesiologists, n (%) (out of 162)
Cardiovascular + respiratory + cutaneous	37 (22.8)
Cutaneous	37 (22.8)
Cutaneous + cardiovascular	32 (19.8)
Cardiovascular + respiratory	19 (11.7)
Cardiovascular	18 (11.1)
Cutaneous + respiratory	11 (6.8)
Respiratory	3 (1.9)
Vocal cord oedema	1 (0.6)
Convulsions + cardiovascular + respiratory + cutaneous	1 (0.6)
Did not specify	3 (1.9)

Data are represented as number and percentage

Table 4: Management of anaphylactic reaction during anaesthesia (as per survey)

Drug used	Number of anaesthesiologists, n (%) (out of 162)
Adrenaline + vasopressor + antihistaminic + steroid	50 (30.9)
Antihistaminic + steroid	40 (24.7)
Antihistaminic + steroid + adrenaline	18 (11.1)
Vasopressor + antihistaminic + steroid	16 (9.9)
Vasopressor + steroid + adrenaline	7 (4.3)
Steroid + adrenaline	6 (3.7)
Steroid/antihistaminic/adrenaline	5 (3.1)/5 (3.1)/4 (2.5)
Vasopressor + antihistaminic	3 (1.9)
Other combinations/did not specify	5 (3.1)/3 (1.9)

Data are represented as number and percentage

Table 5: Common agents for anaphylaxis in anaesthesia practice (response to question 20)

Agent	Number of anaesthesiologists, n (%) (out of 228)
Blood transfusion	160 (70.2)
Radiocontrast agent	144 (63.2)
Colloids	132 (57.9)
Muscle relaxant	102 (44.7)
Thiopentone	67 (28.4)
Propofol	59 (25.9)
Ranitidine	56 (24.6)
Antibiotic	37 (16.2)
Others*	31 (13.6)

Data are represented as number and percentage. *Opioid 6 (2.6), local anaesthetic 8 (3.5), ondansetron 3 (1.3), NSAID 3 (1.3), bone cement 2 (0.87), atropine, aprotinin, heparin, protamine, paracetamol, latex, neostigmine, hydatid cyst, intralipid - 1 (0.44) each. NSAID – Non-steroidal anti-inflammatory drug

To increase the response rate to our survey, a letter stating the purpose of survey accompanied the electronic mail.

The response rate to our electronically sent questionnaire was low probably because of lack of interest of the anaesthesiologists in the survey topic, poor internet access, reluctance to use this medium of communication or it might have gone to spam mail which they failed to check. Our questions were short, simple and were in logical order. Most of the questions were close-ended questions and only two were open-ended questions. The response rate to the latter (order of administration of agents used to manage anaphylaxis under anaesthesia and how did you warn your patient against further exposures) was lower. The dropouts in personally distributed questionnaires may be because of lack of interest in the survey topic, failure on the part of investigator to collect the questionnaire and consideration of filling the questionnaire as waste of time. Anaesthesiologists who have experienced an anaphylactic reaction during anaesthesia may have been more likely to respond to our survey. Despite the limitations of written questionnaire-based survey, we managed to get responses from anaesthesiologists all over India from government, private as well as autonomous institutes working in different capacities.

Although any drug or biologic agent can cause anaphylaxis, the literature suggests that neuromuscular blocking agents, latex, antibiotics, hypnotics, colloids and opioids are the common causes of anaphylaxis in the perioperative period.^[4-13] Most of these data are from Australia, European countries, New Zealand and the United States, where centres have been established to investigate the occurrences of perioperative anaphylaxis.^[4-13] Our survey reveals that colloids,

antibiotics and blood transfusion were the common non-anaesthetic agents causing anaphylaxis during anaesthesia. Opioids, followed by non-depolarising muscle relaxants, were the commonly implicated anaesthetic agents [Table 2]. Latex was not much implicated as an agent causing anaphylaxis during anaesthesia in our survey though it has been much implicated in French and the United States survey.^[11,12] Antibiotics are the primary cause of perioperative anaphylaxis.^[2,10,12-17] Any patient presenting with hypersensitive reaction during anaesthesia must undergo an immediate and secondary investigation for the causal agent.^[17,18] Testing is important to prevent recurrences during subsequent anaesthetics by avoiding the offending agent as well as labelling patients with wrong allergy, leading to unnecessary warnings against harmless substances.^[18] Our survey reveals that this aspect was missing in the Indian context. This is partly because of lack of testing facilities and referral allergy centres. Even when allergy testing facilities exist, they are underutilised.

The strength of our survey is that to our knowledge it is the first Indian epidemiologic study on anaphylaxis during anaesthesia. It also helps us identify that this problem exists in the Indian context. The sample population (anaesthesiologists in India) was representative of the whole country and the gaps in the management and knowledge of anaphylaxis amongst anaesthesiologists were identified. To assess the incidence rate of anaphylactic reaction during anaesthesia in India, one would need the annual number of anaphylactic reactions during anaesthesia and the number of anaesthetics performed during that period. We propose that all major hospitals in India should strive to keep track of the number of anaphylactic reactions during anaesthesia over a year and thus deduce their incidence rate. Data from different hospitals nationwide can then be pooled by a central agency to have a national database in India. Till then, anaesthesiologists should report these events to the adverse drug reaction monitoring centres run by Pharmacovigilance Programme of India to help create our national database.

France, the United Kingdom and many Scandinavian countries such as Denmark, Finland, Iceland, Norway and Sweden have clinical practice guidelines for the management of patients undergoing anaphylaxis under anaesthesia.^[19-24] Likewise, there is a need to formulate national guidelines for management of anaphylaxis during anaesthesia in the Indian setting with the goal of improving patient safety. We recommend

creation of a central agency in India for reporting of suspected cases of peri-anaesthetic anaphylaxis, zonal allergological centres dedicated towards their investigation and for maintaining a national database. Uniform warning alerts along with a detailed written and verbal account should be issued to patients undergoing anaphylaxis during anaesthesia. There should be a standardised protocol for management of these cases. Practice sessions of simulation-based scenario of anaphylaxis during anaesthesia for both trainees as well as practising anaesthesiologists will improve patient management and promote safety under anaesthesia.

The limitations of our study are that we did not quantify the severity of anaphylaxis and the response rate was low with web-based survey. As 86% of anaesthesiologists did not perform allergy testing after suspected anaphylactic reactions during anaesthesia, one cannot differentiate between immune-mediated and nonimmune-mediated reactions from our survey.

CONCLUSIONS

Our survey reveals that two-third of participating Indian anaesthesiologists had witnessed anaphylaxis during anaesthesia. Commonly implicated anaesthetic drugs were opioids and non-depolarising muscle relaxants while colloids, antibiotics and blood transfusion were the common non-anaesthetic agents causing anaphylactic reactions during anaesthesia. Further, our survey reveals low utilisation and paucity of referral allergy centres to investigate suspected cases of anaphylaxis during anaesthesia. The findings of our survey also highlight the need to create more referral allergy centres to investigate suspected cases of anaphylaxis during anaesthesia, a national database, standardised patient management protocols and incident reporting in India.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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APPENDIX 1

Questionnaire

1. Name (Optional):
E-mail id:
2. Designation: Faculty/Consultant/Specialist/Senior Resident/PG student
3. Present place of work: Government Hospital/Private Hospital/Autonomous Institute/Others
4. Name of city:
5. Years of experience: Post M.D./D.A./D.N.B.
6. Do you take comprehensive history of allergy during PAC? Yes/No
7. Have you ever encountered an anaphylactic reaction under anaesthesia? Yes/No
8. If yes, on how many occasions? Once/>Once/Don't remember
9. Could you pinpoint it to a specific agent? Yes/No
10. If yes, what was the agent?
11. Type of anaesthesia: GA/Neuraxial/Peripheral Nerve block/Local/MAC
12. How did you diagnose? Cutaneous manifestations/Cardiovascular/Respiratory/Others/Combination
13. How did you manage? Vasopressor/Antihistaminic/Steroids/Adrenaline/Combination (order of administration)
14. Did the patient survive? Yes/No
15. Did you do any allergy testing subsequently? Yes/No
16. Did the clinical suspicion and allergy testing match? Yes/No/NA
17. Did you warn your patient against further exposures? Yes/No (specify how?)
18. Does your hospital have any allergy testing facilities? Yes/No/Don't know
19. Are you aware of guidelines of anaphylaxis management? Yes/No
20. What are the common agents for anaphylaxis in anaesthesia practice? Muscle relaxant/Thiopentone/Propofol/Ranitidine/Colloids/Blood transfusion/Radiocontrast agent/Others (specify)

Announcement

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