ORIGINAL ARTICLE

STUDY OF ADVERSE DRUG REACTION IN ANAESTHESIA PRACTICE

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ABSTRACT

Introduction: Adverse drug reaction generally occurs on re-exposure to a specific antigen and requires the release of pro-inflammatory mediators, but it can also occur on first exposure, because there is cross-reactivity among many commercial products and drugs. Thus present study was aimed to study the incidence of adverse drug reactions, and to identify common drugs, that causes adverse drug reaction.

Methodology: Patients included in study were all age groups undergoing different types of surgery under anaesthesia from June 2006 to October 2008 at civil hospital, Ahmedabad. Total 77 patients included in the study were examined preoperatively and history noted in proforma. Perioperatively any type of localized or generalized reactions of any organ system involved also noted.

Results: Majority of the patients had reactions due to muscle relaxants (20.77%) followed by colloids (19.48%). Haemacele was most common 9.09%, among all colloids causing ADR. Among IV induction agent thiopental (6.49%) was most common followed by Propofol (5.19%). Bronchospasm was the most common reaction occurring about (37.66%) of the patients. Urticaria (23.37%), Rigors (12.98%), Hypotension (9.09%) and others like rash, itching, collapse, convulsion etc, occur in (16.78%).

Conclusion: Drugs involved in adverse drug reactions were Muscle relaxants, Colloids, I.V induction agents, Antibiotics, BT, Rantac, Emset and other drugs like local anesthetics, methyl methacrylate cement used in replacement surgeries causes reaction. Muscle relaxants, IV induction agents, colloids are the most common anesthetic drugs or substances that may lead to anaphylaxis.

Keywords: Adverse Drug Reaction, Haemacele, Bronchospasm, Urticaria, Convulsion

INTRODUCTION

Adverse drug reaction generally occurs on re-exposure to a specific antigen and requires the release of pro-inflammatory mediators, but it can also occur on first exposure, because there is cross-reactivity among many commercial products and drugs. Anaphylaxis is generally an unanticipated severe allergic reaction, often explosive in onset that can occur perioperatively, especially during a surgical procedure when multiple drugs are administered during the conduction of an anesthetic.

A survey of drug reaction during anesthesia demonstrated that cardiovascular symptoms (73.6%), cutaneous symptoms (69.6%) and bronchospasm (44.2%) were the most common clinical features. [1] Incidence of anaphylaxis and anaphylactoid reaction during anesthesia has been calculated to range from 1 in 3,500 to 1 in 13,000 cases.

Muscle relaxants are associated with the most frequent incidence of anaphylaxis, and over the two decades, natural rubber latex has emerged as the second most common cause of anaphylaxis. Incidence of cause of latex anaphylaxis is decreasing as a result of identification of at-risk patients and prevention measures. Antibiotics and induction drugs account for the next group of drugs more likely to lead to anaphylactic reactions. Muscle relaxants (69.1%) and latex (12.1%) were the most frequently involved drugs according to the most recent French epidemiological survey.

Pre and postoperative investigation must be performed to confirm the nature of the reaction, the responsibility of the suspected drugs and to provide precise recommendations for future anesthetic procedures. These include plasma histamine, tryptase and specific IgE concentration determination at the time of the reaction and at skin tests 6 weeks later. Treatment of anaphylaxis is aimed at interrupting contact with the responsible antigen, inhibiting mediator production and release, and modulating the effects of released mediators. It must be initiated as quickly as possible and relies on widely accepted principles.

Thus present study was aimed to study the incidence of adverse drug reactions, and to identify common drugs, that causes adverse drug reaction.

METHODOLOGY

This Study was conducted at B.J.Medical College, Civil Hospital, Ahmedabad, after taking Ethical Committee clearance.

Selection of Patients: Patients included in study were all age groups undergoing different types of surgery under anaesthesia from June 2006 to October 2008 at civil hospital, Ahmedabad.

Inclusion Criteria: Patients fulfilling all of the below criteria were included in the study.

1) Patients with no previous anesthesia exposure.
2) Patients with no history of previous adverse drug reactions.
3) ASA Risk category I AND II patients.
4) Adverse event appear after the suspected drug was administrated.
5) Adverse reaction improves when the drug was discontinued or a specific antagonist was administered.
6) Patients willing to participate in the study and agree to give informed written consent.

Exclusion Criteria: Patients fulfilling any of the below criteria were excluded from the study.

1) Patients with previous anesthesia exposure.
2) Patients with previous history of drug reactions.
3) ASA Risk category III and IV patients.
4) Patients not willing to participate in the study and not agree to give informed written consent.

Patients included in the study were examined preoperatively and history noted in proforma. Perioperatively any type of localized or generalized reactions of any organ system involved also noted.

Reactions if any were observed were: Cutaneous Lesions: Rash/ erythema, urticaria, itching, burning, pain at site, pigmentation; Respiratory system: Bronchospasm, pulmonary oedema, respiratory depression, hypoxia, cyanosis; Cardiovascular system: Hypotension, bradycardia, collapse, cardiac dysrhythmias; Gastro-intestinal system: Nausea, vomiting; Central nervous system: Delirium, disorientation, convulsion; Renal system: Decreased urine output (oliguria / anuria).

According to the type of drug reaction, treatment was given in the form of anti-histaminic, corticosteroid drugs and IV fluids. Treatment given was recorded in proforma. Recorded data was analyzed statistically and Mean as well as S.D, was analyzed with the help of computer software.

RESULTS

This study was conducted at B.J.Medical College, Civil Hospital, Ahmedabad. Total number of the patients operated was 57,605. Out of those 77 patients were observed having adverse drug reaction. Following observation and results were recorded from patients having drug reactions.

Table 1: Distribution of drugs causing adverse drug reaction (N=77)

Name of drug	No. (%)
Muscle relaxant	**16 (20.77)**
Depolarizing (Scoline)	6 (7.79)
Non depolarizing (Nor + Atra)	10 (12.98)
Colloids	**15 (19.48)**
Haemacele	7 (9.09)
Microspan	5 (6.49)
Dextran-40	3 (3.89)
IV induction agent	**11 (14.28)**
Thiopental	5 (6.49)
Propofol	4 (5.19)
Ketamine	2 (2.59)
Antibiotics	**10 (12.98)**
Blood Transfusion	**7 (9.09)**
Rantac	**6 (7.79)**
Emset	**3 (3.89)**
Others	**9 (11.68)**

Majority of the patients had reactions due to muscle relaxants (20.77%) followed by colloids (19.48%). Only three muscle relaxants were used named Scoline, Atracurium, and Norqurone. Other drugs have been not used. Haemacele was most common 9.09%, among all colloids causing ADR. Among IV induction agent thiopental (6.49%) was most common followed by propofol (5.19%) for causing ADR.

Table 2: Type of reaction (N=77)

Type of reaction	No. (%)
Bronchospasm	29 (37.66)
Urticaria	18 (23.37)
Rigors	18 (12.98)
Hypotension	7 (9.09)
Others	13 (16.78)

Bronchospasm was the most common reaction occurring about (37.66%) of the patients. Urticaria (23.37%), Rigors (12.98%), Hypotension (9.09%) and others like rash, itching, collapse, convulsion etc, occur in (16.78%).

DISCUSSION

An adverse drug reaction generally occurs on re-exposure to a specific antigen and requires the release of pro inflammatory mediators, but it can also occur on

first exposure because there is cross reactivity among many commercial products and drugs. By definition, Any noxious change which is suspected to be due to a drug occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in future use of same drug is called adverse drug reaction.

One study was conducted In France with repeated inquiries by the perioperative anaphylactic reactions study group. Laxenaire MC.[1] had done survey. The survey concerned 1,750 patients tested in 27 diagnostic centers, from January 1992 to June 1994. The reactions occurred at all ages, predominantly between 10 and 50 years, the sex-ratio (F/M) was 2.4. IgE dependent anaphylaxis--was diagnosed in 1,000 patients (57.8%) and due to 1,030 agents muscle relaxants (59.2%), latex (19%), hypnotics (5.9%), benzodiazepines (2.1%), Opioids (3.5%), plasma substitutes (5%), antibiotics (3.1%) and other drugs given during anaesthesia such as aprotinine and protamine (2.2%). Suxamethonium was responsible for 39.3% of muscle relaxant anaphylaxis, vecuronium for 36%, atracurium for 14.5%, pancuronium for 4.8%, gallamine for 3.1% and alcuronium for 2.3%.

Another study done by Paul Michel.[7] Anaphylactic and anaphylactoid reactions were diagnosed in 518 cases (66%) and 271 cases (34%), respectively. The most common causes of anaphylaxis were neuromuscular blocking agents (NMBAs) (n = 306, 58.2%), latex (n = 88, 16.7%), and antibiotics (n= 79, 15.1%). Rocuronium (n = 132, 43.1%) and succinylcholine (n = 69, 22.6%) were the most frequently incriminated NMBAs.

In our study reactions were also most common between 10 to 50 years and female are more prone as compared to males. Mean age of the patients is 40.13 ± 13.31. in years. Sex difference include females (56%) more common then males (44%). Drugs involved in adverse drug reactions were Muscle relaxants (20.77%), Colloids (19.48%), I.V induction agents (14.28%), Antibiotics (12.98%) BT (9.09%), Rantac (7.79%), Emset (3.89%) and other drugs like local anesthetics, methyl methacrylate cement used in replacement surgeries causes (11.68%) reactions. So our study correlates with above two studies.

Study done by Laxenaire MC.[2] anaphylactic reactions to anesthetic and associated agents used during the perioperative period have been reported with increasing frequency in most developed countries. Most published reports on the incidence of anaphylaxis come from France, Australia, the UK and New Zealand. The estimated incidence of anaphylaxis ranges from 1:10,000 to 1:20,000. Muscle relaxants (69.1%) and latex (12.1%) were the most frequently involved drugs according to the most recent French epidemiological survey. The present study also showed that muscle relaxants were most common among drugs causing adverse drug reactions.

One study done by Laxenaire MC.[1] Study was carried out in 49 public and private hospitals spread through out France. A series of albumin and 95% of dextrans, 43 anaphylactoid reactions were recorded, giving an overall frequency of 0.219%, or one reaction for 456 patients. The frequency differed according to the substitute considered: 0.345% for gelatins, 0.273% for dextrans, 0.099% for albumin and 0.058% for HES.

In our study reaction due to Colloids was 19.48%. Difference in result of colloid study may be due to that, in our institution we used more colloid agents instead of blood.

Regarding anaphylactic reactions due to antibiotics, one study done by Soupramanien Sivagnanam.[6] the study was done on Vancomycin. Vancomycin can cause two types of hypersensitivity reactions, the red man syndrome and anaphylaxis.

Red man syndrome has often been associated with rapid infusion of the first dose of the drug and was initially attributed to impurities found in vancomycin preparations. Even after improvement in vancomycin purity, however, reports of the syndrome persist. Other antibiotics (e.g. ciprofloxacin, amphotericinB, rifampicin and teicoplanin) or other drugs that stimulate histamine release can result in red man syndrome.

Other study done by T.Ayyappan Pillai et al.[3] Case report on, drug reaction due to i.v cefotaxime in burn patient.

In our study antibiotics were responsible for 12.98% reactions. Most common antibiotics were cefotaxime and other include vancomycin because we had used vancomycin in only patients of open heart surgeries.

Regarding IV induction agents one study done by Nishiyama. T, Hanaoka. K.[4] at France on propofol induced bronchoconstriction. According to their study about 1.2% of cases of perioperative anaphylactic shock were attributable to propofol. According to our study reaction due to propofol was 5.19%, which correlates with above study.

According to our study the most common drug causing adverse drug reactions was muscle relaxants, followed by colloids. Other common being i.v induction agents, blood, benzodiazepines, opioids, and antibiotics. These results were comparable with above studies.

According to our study most common type of reaction was Bronchospasm in (37.66%). Other reactions include Urticaria (23.37%), Hypotension (9.09%), Rigors (12.98%) and other like rash, itching, etc. in (16.78%).

There were some variation in results because of those studies were carried out wide spread across multiple centers and thousands of patients, but our study was single institution based involvement.

CONCLUSION

Drugs involved in adverse drug reactions were Muscle relaxants, Colloids, I.V induction agents, Antibiotics, BT, Rantac, Emset and other drugs like local anesthetics, methyl methacrylate cement used in replacement surgeries causes reaction. Muscle relaxants, IV induction agents, colloids are the most common anesthetic drugs or substances that may lead to anaphylaxis.

Most common type of reaction was bronchospasm. Other reactions include Urticaria, Hypotension, Rigors and other like rash, itching, etc.

Drug reactions can occur to any of patient coming for surgery with any of drug and sometimes these reactions are fatal so prevention is the most important component to decrease the incidence of anaphylaxis.

REFERENCE

1. Laxenaire MC, Feldman L. Anaphylactoid reactions to colloid plasma substitutes. Ann Fr Anesth Reanim. 1994; 13: 301-310.
2. Laxenaire MC. Substances responsible for peranesthetic anaphylactic shock. A third French multicenter study. Ann Fr Anesth Reanim.1996; 18: 796-809.
3. T. Ayyappan Pillai, Ashwani Kumar Jalewab, Indu A Chadha. Antibiotic prophylaxis- Hobson's choice in burns management. Journal of international society for burns injuries. 1998; 24: 760-762.
4. Nishiyama.T, Hanaoka.K. Propofol induced bronchoconstriction; two case reports. Aneasth Analg. 2001; 93: 645-646.
5. S. Moorthy. Anaphylactoid Reaction to Etomidate: Report of a Case. Journal of Clinical Anesthesia. 2003; 13: 582 – 584.
6. Soupramanien Sivagnanam and Dirk Deleu. Red man syndrome. Crit Care. 2003; 7: 119–120.
7. Paul Michel, Laxenaire, Marie-Claire; Anaphylactoid reactions during anesthesia, anesthesiology. 2003; 99: 536-545.
8. Paul Michel, Laxenaire, Marie-Claire; Anaphylactoid reactions during anesthesia, anesthesiology. 2003; 99: 536-545.
9. Amir-Ali Sohrabpour, Mehdi Saberi-Firooz; Halothane hepatitis in Iran: A review of 59 cases World J Gastroenterol 2008; 14: 5322-5326.
10. Daghfous R, el Aidli S, Sfaxi M, Daghfous M, Kastall S. Halothane-induced hepatitis. 8 case reports. Tunis Med 2003; 81: 874-878
11. Laxenaire MC, Moneret- Vaytrin, et al. Anaesthetic drugs responsible for anaphylactic shock. Ann Fr Anesth Reanim. 1990; 9: 501-6.
12. Boston Collababorative Drug Surveillance Survey. Drug induced anaphylaxis. JAMA. 1973; 224: 613-15.
13. Fisher M, Munro L. Life threatening anaphylactoid reaction to muscle relaxants. Anesth Analg. 1983; 62: 559-64.
14. Beamish D, Brown DT. Adverse response to iv anesthetics. Br J Anesth.1981; 53: 55-7.