Author reply

Sir,

We are thankful to Kounis *et al*. for their keen interest on our recent published topic on amikacin triggered anaphylaxis in peri-operative period.[1] They point out bupivacaine and fentanyl could be a joint forces as antigens to induce anaphylactic shock and Kounis anaphylaxis-associated coronary syndrome.[2] We appreciate their explanation that simultaneous exposure of several allergens have an additive effect on sensitization of mast cells and basophils.[3] Hence, all patients who suffer peri-operative anaphylaxis required a detailed history and examination for drug allergy. If we go back to our case description it is clearly mentioned that anaphylaxis event started just 2 min after intravenous (IV) injection of 1 g amikacin and amikacin was injected 18 min after subarachnoid injection of 2.5 ml of bupivacaine heavy 0.5% with 25 mcg fentanyl for subarachnoid block. Anaphylaxis has rarely been reported as delayed presentation especially after IV exposure and generally occurs within few minutes of IV injection unless otherwise in compromised circulation like cardiac arrest. Delayed presentation generally occurs as a mild allergic reaction not as severe systemic manifestations which occurred in our patient. Some discrete incidence of allergic reactions due to bupivacaine and fentanyl has been published in literature, but mostly they were in combination with some other drugs and mild in presentation. We agree both bupivacaine and fentanyl, which could have combined forces as antigens may produce some allergic reactions without hemodynamic compromise. We used preservative free hyperbaric bupivacaine and fentanyl mixture used in sub arachnoid block and effect of spinal anesthesia came at 4 min after injection with spinal level at T8 without any pruritus, respiratory depression, cutaneous and other cardiovascular or respiratory manifestations. If the drugs rightly act on sub arachnoid block, it is likely that they should cause anaphylaxis earlier if it is the cause at all. Anaphylactic reactions to amide local anesthetics (LA) are extremely uncommon and occurs mainly due to esters. It accounts for only 1% of all to LA reaction.[4] They are usually due to the para-aminobenzoic acid derivatives from esters or methylparaben or due to metabisulfite. Common immune-mediated reaction to LA is a delayed hypersensitivity (type IV) reaction.[5] There is no cross-reactivity between amide and ester LA, except in preservative related allergy. Fentanyl belongs to the phenylpiperidine group of opioid and does not cause histamine release. Very rare report of IgE mediated anaphylaxis to fentanyl is available in literature with IV route,[6] but probably no report available in subarachnoid route. Anaphylaxis due to drug exposure usually occurs in patients with poly-pharmacy in real clinical scenario. However, exact etiology can be assumed from past and present history, drug's onset and nature of action, severity of symptoms. But, our ultimate aim should be early intervention to save the life and proper documentation for future reference.

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