Adverse Drug Reaction of Morphine with Monoamine Oxidase Inhibitors

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Monoamine oxidase inhibitors (MAOI) are infamous for their ability to interact with narcotics especially pethidine. A case of hypertensive crisis upon induction of general anaesthesia with morphine, midazolam, pancuronium and thiopentone in a patient taking aurorix (MAOI) is being presented. Patient was scheduled for an elective coronary artery bypass grafting (CABG) surgery. Hypertensive crisis was managed successfully and no morbidity was observed.

Key Words: Morphine, adverse reaction, monoamine oxidase (MAO) Inhibitors

Psychotropic drugs are important in the treatment of severe depression, mania and schizophrenia. They profoundly affect central and peripheral neurotransmitters and ionic mechanisms across cell membrane. Antidepressants include tricyclic antidepressants and monoamine oxidase inhibitors (MAOI.) Prior intake of these drugs is an important consideration in the management of surgical patients.

MAOI have got some important interactions with various drugs used in anaesthetic practice including inhalational agents, barbiturates, sympathomimetics and narcotics.With pethidine MAOI produces a well documented syndrome characterized with agitation, excitement, hypotension, convulsions and hyperpyrexia. We encountered with a patient taking MAOI (Aurorix) in whom acute hypertensive crisis was observed upon administration of morphine. Patient was scheduled for an elective CABG surgery.

Case history

A 60 year old male patient was scheduled for an elective GABG surgery. Pre-anaesthesia history revealed that he was a non diabetic, non hypertensive and non smoker patient. He had a history of recurrent attacks of depression for the last couple of years and according to him, he was taking tab valium 5 mg regularly for this.

In the operation theatre ECG (Lead II V5), oxygen saturation and invasive blood pressure was monitored with the help of an radial cannula (20G, Vasofix) placed in left radial artery under local anaesthesia. General anaesthesia was induced with morphine (0.2mg/kg), midazolam (0.2mg/kg), pancuronium (0.1mg/kg) and thiopentone (2mg/kg). 2% xylocaine (1.5mg/kg) was given for attenuation of pressor response. After 4 minutes of manual ventilation airway was secured with an endotracheal tube (8.5 mm internal diameter). Anaesthesia was maintained with O-2/air/isoflurane. Right internal jugular vein was cannulated and a central venous catheter (Arrow –7F-CV-14703) was threaded in.

During the insertion of central line, there was an acute rise in the blood pressure (250/120 mm Hg). After ruling out any iatrogenic drug administration or any mechanical failure regarding delivery of anasethetic agents to the patient, blood pressure was aggressively managed with isolfurane, glyceryl trinitrate (GTN) and propofol. The blood pressure was brought back to within normal limits in five minutes. There was no obvious cause for this event Surgery was started and upon median sternotomy morphine 3 mg was given and blood pressure again showed a acute rising trend. It was control again with isoflurane, glyceryltrinitrate and propofol.

Rest of the surgical course was uneventful and no more morphine was given either in the theatre or in the postoperative period. He was extubated after seven hours of postoperative elective ventilation. After awakening it was revealed that he was taking (Aurorix) monoamine oxidize inhibitors as self medication, irregularly for several months.

Discussion

Adverse reaction to drugs may be classified into two groups. The most frequent are those that result from the exaggerated but predicated pharmacological action of the drug. The other group comprises of the toxic effects on the cells that result from mechanism unrelated to the intended pharmacological action. These reactions are often unpredictable, frequently severe and result from a number of recognized as well as undiscovered mechanism.

Whenever a drug is being administered the potential for a interaction always exists. Perioperative allergic/ anaphylaxis reaction are also serious and potentially lethal. They occur once in every 5000-25000 anaesthesia experience[1].

Monoamine oxidase (MAO) is an enzyme found principally on the outer mitrochondrial membrane. There are two isoenzymes. MAO-A and MAO-B. Each has got a different substrate specificities. Substrate specificity is relative and is concentration dependent. About 60% of MAO activity in the brain is of the A-type while MAO-B predominates in the liver and lungs[2]. The monoamine oxidase inhibitors were the first effective antidepressants drugs. Their use declined with the introduction of more effective drugs with fewer side effects, but they are still

used in the treatment of atypical and refractory depression and several other disorders e.g. migraine and chronic pain syndromes.

Monoamine oxidase is a major intraneuronal enzyme necessary for the oxidative deamination of many biological amines (serotonin, norepinephrine and dopamine). MAOI inhibits the metabolism of sympathetic amines. The resultant repletion of monoamine stores in the body is responsible for their desired and undesired effect.

MAOI have got some important interactions with sympathetic compounds, barbiturates, and muscle relaxants[3] Several other interactions between MAOI and various agents used in anaesthesia, have been observed including halothane, anticholinergic agents, beta blockers and thiazide diuretics[4,5,6].

MAOI narcotic interaction has two distinct forms. First an excitatory form (Type-I) characterized by sudden agitation, unmanageable behaviour, headache, hypertension, tachycardia, convulsions and coma. It is thought to be attributable to central serotonergic over activity, Second a depressive form (Type-II) consisting of respiratory depression, hypotension and coma as a result of the inhibition of hepatic microsomal enzymes by MAOI leading to accumulation of free narcotics[7]. Pethidine is the only commonly available narcotic to have elicited the excitatory response which is however frequently severe and often fatal[8]

Morphine has not been implicated in the elicitation of type-I response but can cause type-II[9]. However, animal studies did show that pretreatment with MAOI increased the mortality not only from pethidine but also from morphine, pentazocine and phenazone[10]. Case reports exist to support the safe use of alfentanil[11] and remifentanil[12] in patients on MAOI, although a case report has implicated the use of high dose fentanyl during cardiac surgery in the postoperative death of a patient taking MAOI[13].

Our patient was a known case of depressive psychosis and taking various medications including MAOI. Poor evaluation pre-operatively regarding drug intake or hinderance of the facts on the part of the patient were responsible for missing the point regarding intake of MAOI. After about 10-15 minutes of morphine administration the blood pressure showed acute rising trend. Initially we thought that some inadvertent ionotropic agent has been given. Once it was excluded, hypertensive crisis was managed aggressively with propofol. GTN and isolfurane. Fortunately we were working in a well control situation where invasive monitoring and all other pharmacological support was available to control the crisis.

Anaesthesia for patients taking MAOI has been a cause of concern to the anaesthetists for many years. Advice that they should be stopped 10-14 days before anaesthesia is unreasonable for two reasons. First it may compromise patient's underlying psychiatric condition and secondly MAOI forms a stable complex with MAO. Thus further MAO has to be synthesized; this is a long process. The risk of discontinuing the drug and benefits of therapy should be considered on an individual basis[14]. Patients taking MAOI should continue to do so before elective surgery. Anaesthetist should keep in mind the possible drug interactions and look for safe alternatives.

New generation of monoamine inhibitors are emerging which are short acting, receptor specific, and are reversible inhibitors of monoamine oxidase type A enzyme (RIMAs). Moclobemide is the first drug belonging to this class which came into clinical practices[9,15]. These drugs are safer and better tolerated than the conventional MAOI. The safety of moclobemide lies in the fact that it is specific for one type of enzyme, its binding is reversible, it is short acting and rapidly metabolized. Patient taking it can be anaesthetized safely using currently available drugs, apart from pethidine, and theoretically potential for prolongation of analgesics effect or of induction agents does exists.

Case report highlights a possible interaction of morphine and MAOI in patient scheduled for an elective CABG surgery. In patients taking one group of drugs of a certain pathology the attending physician must keep in mind the chances that other groups of drugs for the cure of same pathology have also been taken by the patient.

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