Brief Communication

Apnea after reversal of neuromuscular blockade. *A case of rare mix-up*

Mohammad M. Ansari, MD,
Govardhan K. Magaji, DA ,
Annamma Abraham, DA.

Medication error is one of the leading causes of morbidity and mortality in hospitalized patients.[1] Considering the potency, types, and frequency of the drugs administered to patients undergoing anesthesia, the potential exists for errors with disastrous consequences.[2] Several studies indicate that the incidence of medication error associated with anesthesia practice is common. Analysis of critical incidences by Cooper and colleagues[3] showed that drug-related events far exceeded the next most common problem, disconnection of the breathing circuit. The Australian Incident Monitoring Study analyzed adverse events during anesthesia and reported that "The wrong drug" was the most common adverse event.[4] Indeed, anesthetic drug errors have been reported for every aspect of anesthetic–related care, most common being the "Syringe swaps" (70.4%) and misidentification of the label (46.8%).[5] An analysis of closed malpractice claims showed that medication issues are a leading cause of malpractice litigation against Canadian anesthesiologists, totalling 3.5% of claims against all physicians from 1998 to 2002. The most common cause of malpractice action was a medication-related event.[6] Berman[7] reported that errors due to look-alike or sound-alike medication names are common in the United States. Up to 25% of all medication errors are attributed to name confusion, and 33% to packaging or labeling confusion. Systems and recommendations have been developed that may reduce the occurrence of such errors. In our case, an ASA I, male child of 4 years of age and 15 kg body weight was posted for repair of left inguinal hernia under general anesthesia. His routine complete blood count, and biochemistry including urine analysis were within normal limits. The child was premedicated with 5 ml promethazine hydrochloride oral syrup 1 hour before induction of anesthesia. In the operating room, before initiation of anesthesia, his vitals were recorded, his heart rate was 110/minute with normal sinus rhythm, his blood pressure was 106/70 mm Hg and arterial saturation was 99%. An intra-venous cannulation was performed with 22 G cannula without any difficulty and 5% dextrose with one-quarter normal saline started. Anesthesia was induced with 60 mg thiopentone sodium and relaxed with 20 mg suxamethonium, and tracheal intubation was performed with 4.5 mm uncuffed endotracheal tube. Anesthesia was maintained with 25 µgm fentanyl, 50% oxygen with nitrous oxide, 0.6-0.8% sevoflurane and atracurium besylate 0.5 mg/kg as, and when required.

Ayre's T Piece circuit was used for intermittent positive pressure ventilation. Surgery lasted for 45 minutes, and the whole course of anesthesia was uneventful. At the end of surgery, he gained spontaneous respiration, and was kept on 100% oxygen only. Neuromuscular blockade was reversed with 0.75 mg neostigmine and 0.2 mg atropine. After reversal, the heart rate came down from 102/minute to 55/minute and he gradually developed apnea. Heart rate was corrected with the use of atropine. The cause of this fall in heart rate and apnea could not be detected. This unexpected result of reversal alerted us to consider a medication error. A careful check of the syringes loaded with drugs revealed atracurium besylate mixed with neostigmine methyl sulphate instead of atropine. Two syringes kept side-by-side one loaded with atracurium besylate, 5 mg/ml and marked "Atra" and the other syringe loaded with atropine sulphate, 0.1 mg/ml marked "Atro". In this case, 0.75 mg of neostigmine was mixed with 10 mg of atracurium besylate instead of 0.2 mg of atropine sulphate. The manner in which labeling of the syringes was carried out, could have happened with anyone involved in the anesthetic care of the patient. In this patient, this "mix-up" did not cause any undesirable side effect except prolong apnea and bradycardia, which were taken care of appropriately. Later, when the effect of the muscle relaxant wore off, an appropriate dose of reversal was used and tracheal extubation carried out. He was observed for one hour in recovery and then shifted to the ward without any problem. Though this medication error did not cause any deleterious effect on the patient's health, it definitely indicates the need for improved standards for drug labeling.

To conclude, the utmost care is essential while giving drugs during anesthesia care. To improve patient safety, each medical and surgical discipline needs to identify the sources of error and develop evidence based preventative strategies. The incidence of medication error during anesthesia is uncertain, but it is astonishingly low given the millions of drugs administered during anesthesia care.

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From the Prince Saud Bin Jalawi Hospital, Al-Hasa, Kingdom of Saudi Arabia. Address correspondence and reprint requests to: Dr. Mohammad M. Ansari, Prince Saud Bin Jalawi Hospital, Al-Hasa 31982, Kingdom of Saudi Arabia. Tel. +966 (3) 5305094 Mobile. +966 503909361 Fax. +966 (3) 5300070. E-mail: mobarakhussain@hotmail.com

References

1. Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes BA, et al. The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. ***N Engl J Med*** 1991; 324: 377-384.
2. Chopra V, Bovill JG, Spierdijk J, Koornneef F. Reported significance observations during anaesthesia: a prospective analysis over an 18-month period. ***Br J Anaesth*** 1992; 68: 13-17.
3. Cooper JB, Newbower RS, Kitz RJ. An analysis of major errors and equipment failures in anesthesia management: Considerations for prevention and detection. ***Anesthesiology*** 1984; 60: 34-42.
4. Currie M, Mackay P, Morgan C, Runciman WB, Russell WJ, Sellen A, et al. The Australian Incident Monitoring Study. The "wrong drug" problem in anaesthesia: an analysis of 2000 incident reports. ***Anaesth Intensive Care*** 1993; 21: 596-601.
5. Orser BA, Chen RJ, Yee DA. Medication errors in anesthetic practice: a survey of 687 practitioners. ***Can J Anaesth*** 2001; 48: 139-146.
6. Orser BA, Byrick R. Anesthesia-related medication error: time to take action. ***Can J Anaesth*** 2004; 51: 756-760
7. Berman A. Reducing medication errors through naming, labeling and packaging. ***Med Syst*** 2004; 28: 9-29.

Paeonol inhibits the proliferation of human colorectal carcinoma cells and synergic with chemotherapeutic agents

Shiyun Tan, *MD, PhD,* ***Junmei Ye,*** *MD, PhD,*
Cuijuan Qian, *MD, PhD,* ***Chunyan Ji,*** *MD, PhD,*
Changqing Liu, *MD, PhD,* ***Junyu Wang,*** *MD, PhD.*

Colorectal cancer is the third most common cancer in the world and the second leading cause of cancer-related deaths in the United States.[1] Surgical removal of the tumor supplemented with chemotherapeutic agents is a major treatment for it. However, most of the chemotherapeutics for colorectal carcinoma have great aversive effects, so it is indispensable for us to find a proper and natural therapeutic strategy for our patient. Paeonol (Pae) is a Chinese traditional herb, which has been shown to exhibit anti-pyretic, sedative, anti-inflammatory and anti-bacterial[2] activities. It was reported that Pae exhibited anti-tumor activity in multiple cancer cell lines. Gastric lavage with Pae could inhibit liver tumor growth in mice model.[3] Paeonol has been proven to suppress hepatocellular tumourigenesis in vitro.[4] However, little was known on the effect of Pae on colorectal cancer cells. We provided evidence here that Pae inhibited the growth of colorectal carcinoma cell line HT-29, which was also synergistic with certain chemotherapeutic drugs.

The current study was conducted at Renmin Hospital of Wuhan University in China, between September 2003 and September 2004. And the study was approved by our Hospital Ethics Committee. Human colorectal carcinoma cell lines HT-29 were purchased from Oncology Institute of the Zhongnan University. Paeonol was obtained from Shanghai first pharmaceutical factory while 5-fluoro-2,4(1H,3H)pyrimidinedione (5-FU) was from Xu Dong Hai Pu Pharmaceutical Co. Ltd, Shanghai, China, mitomycin C (MMC) from Tokyo Co., and diamminedichloroplatinum (c-DDP) from Qi Lu Pharmaceutical Co., Shandong, China. The in vitro growth rate of HT-29 cells treated with Pae, was measured by the methyl thiazolyl tetrazolium (MTT) method. Briefly, HT-29 cells (1×10^3 cells/well) were seeded in 96-well plates. We added Pae to these cells in the concentration of 0.024, 0.047, 0.094, 0.188, 0.376, 0.752, 1.504 $\mu mol.L^{-1}$, respectively. And one group of cells was added without Pae as blank control. Making sure that each group contained 5 slots. Then the cells were incubated in an incubator for 24, 48, 72 and 96 hours .We added 20 µl MTT to each slot 4 hours ahead of termination, abscised the culture solution, and added 200 µl dimethyl sulphoxide (DMSO) to each slot again. The absorbance value was measured at a wavelength of 570 nm with background subtraction at 650 nm by the use of spectrophotometer. Inhibitory rate = (1-Ae/Ac)×100%. We also observed HT-29 cells at Log phase that had been incubated with different concentrations of Pae under inverted microscope. The cells were also cultured on cover-slip and fixed by 10% formalin and stained with hematoxylin and eosin. Each experiment was performed at least 2 times and results are presented as the mean ± standard deviation. The *p* values were determined by unpaired t test by using the Statistical Program for Social Sciences analysis. We found out that Pae significantly inhibited the growth of the HT-29 cells at a concentration of 7.81- 250 mg/L in a dose-effect and time-effect pattern (**Figure 1**). Microscopically, the control cells proliferated faster with a larger size and brighter field than cells treated with Pae. Hematoxylin and eosin staining of the control cells showed blue nuclear staining without visible apoptotic body. Cells treated with Pae exhibited apoptotic cell in a concentration of 31.25-250 mg/L. Apoptotic cells were distinguished by

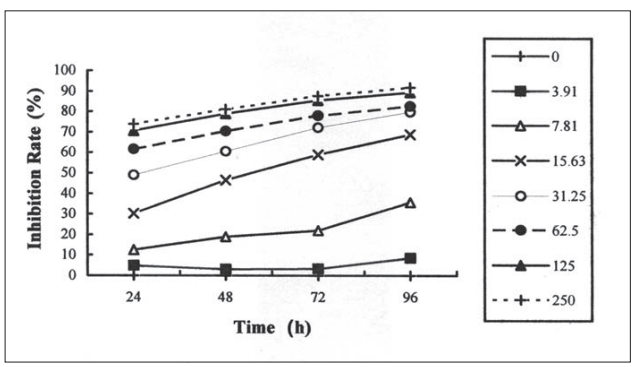

Figure 1 - The effect of paeonol to the proliferation of HT-29 cell.