

Three patients with lead poisoning following use of a Chinese herbal pill

To the Editor—It was certainly not a surprise to us that traditional Chinese medication gave rise to the complication described in the paper by Auyeung et al.¹ In Hong Kong, the public often assume that these ‘non-western’ remedies are safe because they are termed ‘traditional’ and ‘herbal’, and are plant-derived products, but as many researchers have revealed, these traditional remedies can pose a significant health threat. Like western medicines, traditional Chinese medicine (TCM) may produce both predictable and unpredictable side-effects. Predictable effects may include direct toxicity, toxicity related to overdose of a preparation, and interaction with western pharmaceuticals. Unpredictable effects may include allergic and anaphylactic reactions, and idiosyncratic reactions. Many well-documented herbal drugs such as Aconitum (附子), known to cause toxic reactions, are available to practitioners for use in prescriptions. Drug-related side-effects may also be associated with the inappropriate handling or manufacture of these TCMs, for example, misidentification, lack of standardisation, substitution of one herb for another, contamination of the herbal preparations, and adulteration with western pharmaceuticals.^{2,3}

Lead poisoning associated with traditional remedies or herbal medicine has been reported before. Lead intoxication from traditional Chinese remedies stems from two sources: the mineral drugs and contaminated herbal medicine.^{4,5} Mineral drugs, such as Cinnabaria (硃砂), are commonly used for sedative purposes, and for systemic and skin infections given orally or topically like sulphur (硫磺), Realgar (雄黃), Calomelas (輕粉), and Chalcantithum (膽礬). Contaminants of herbal medicines such as micro-organisms, microbial toxins, pesticides, fumigation agents, radioactivity, and heavy metals have been identified. This highlights the need for good control of the starting materials and finished product, and the importance of good manufacturing practice in controlling the purity of herbal medications.

It is nearly impossible to estimate the incidence of adverse effects for traditional Chinese herbal medicine from

case reports and case series alone, since the total exposure to a particular medicinal substance is unknown. There are currently insufficient data to fully quantify the risks presented by TCM. In order to improve the safety of TCM, more research must be undertaken. This should include the identification and characterisation of active constituents, in vitro laboratory studies on pharmacological activity and mechanism of action, identification of toxicological parameters such as LD50, and clinical trials on either the individual herb alone or in combination formulas.

At present there is no established mechanism for ensuring the safety of TCM, and no rapid system to warn the public against taking those remedies identified as dangerous. The Government should speed up legislation to improve the regulatory framework for TCM, eg setting up a regulatory body controlling the ingredients, purity and distribution, providing a proper channel to ensure that appropriate information is available to the public when they buy unlicensed herbal remedies, and restricting potentially toxic Chinese remedies to qualified TCM practitioners.

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Safety and comfort during sedation for diagnostic or therapeutic procedures

To the Editor—Having read a seminar paper by Hung et al¹ in the April 2002 issue of the *Hong Kong Medical Journal*, I would like to make the following comments. The paper, discussing safety and comfort during sedation for

diagnostic or therapeutic procedures,¹ is concise and well presented, given the scope and confines of publication. However, I would like to add some of my thoughts and cautionary notes on the use of midazolam. As a sedative

agent, it certainly is widely used but I do not consider it as safe as most people think for the following reasons. Roche Pharmaceuticals, the manufacturer of midazolam, has stated clearly that "it should be used for intravenous sedation only with caution and must not be administered by single bolus or rapid [intravenous] i.v. administration. Patients should be continuously monitored for early signs of hypoventilation or apnoea. Patients should continue to be monitored during the recovery period."²

Litman et al,³ University of Pennsylvania School of Medicine, reported in a study of healthy volunteers aged 26 to 41 years that all study subjects exhibited complete upper airway obstruction during sedation with midazolam when dynamic negative airway pressure (DNAP) from as low as minus 2 cm H₂O was applied. The dose of midazolam was well within the 'average' dose used. When DNAP was at minus 14 cm H₂O all subjects had complete upper airway obstruction. When flumazenil (Anexate) was given to reverse the effect of midazolam, the tendency to upper airway obstruction was also reversed. Thus midazolam can cause respiratory depression as well as upper airway

obstruction when the patient makes inspiratory efforts (thus generating negative airway pressure). This combination can be very hazardous and I absolutely endorse every word of caution Hung et al¹ have written in their seminar paper.

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Authors' reply

To the Editor—Thank you for giving us the opportunity to respond to comments raised on the safety of midazolam. As deliberated in our article, midazolam can cause hypoxaemia and desaturation.¹ The conjunctive use of opioids provides analgesia in addition to sedation but increases the risks of hypoxaemia and other adverse respiratory events.² Recent work by Litman et al³ demonstrated the occurrence of upper airway obstruction during deep sedation with midazolam and its reversibility with flumazenil. In contrast with conscious sedation, deep sedation is an area of controversy as airway obstruction often occurs irrespective of the sedative agent used. The progression from conscious sedation to deep sedation is often subtle. Litman et al's work³ highlighted the risks of deep sedation and reinforced our call for adequate staff training and facilities. Certainly midazolam has been associated with some fatalities related to respiratory depression and cardiac arrest particularly in the elderly even when appropriate doses were used.⁴ We are also aware of a local patient who developed airway obstruction after receiving 5 mg of midazolam intravenously for sedation and died subsequently. Even though midazolam is recommended as the sedative of choice for use by a non-anaesthesiologist,⁵ its safety rests with proper usage in conscious sedation only. The physician using sedation has to be aware of its potential risks including cardiac arrest. We emphasise again the careful, slow, or stepwise titration needed when using sedatives, and the importance of appropriate monitoring to detect potential life-threatening complications. Flumazenil, a specific antagonist of benzodiazepines, should be available to counteract any unintended overdose

whenever midazolam is administered.⁶ The fact that flumazenil has a shorter duration of action than midazolam must also be borne in mind during use.

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