

Availability of essential drugs in Pakistan

The anaesthetists are probably the only specialists in the practice of medicine who administer drugs (almost always intravenously) and observe its effects on different physiological or pathological phenomena in a patient. The art of administering anaesthesia is really an induction of an unnatural state to facilitate surgical procedures and in itself involves many systemic changes in the body of the recipient. Hence, induction of general anaesthesia as well as spinal analgesia is usually associated with hypotension and intubation and is usually followed by tachycardia and hypertension, especially in susceptible patients. The adverse effects observed during anaesthesia are not only limited to the drug actions, but the surgical patients may either have deranged physiology due to the surgical disease itself or the patient might have concurrent systemic ailments like diabetes mellitus, hypertension, cardiac insufficiency or hormone disturbances etc. Although all efforts are usually made to optimise the patients' general condition before operative procedure, it is sometimes not possible to bring the abnormalities in physical parameters back to normal even with the most sincere discourse by the treating physicians. The anaesthetist depends upon ready availability of a variety of therapeutic agents to facilitate as smooth a sailing as possible, and to counteract the foreseeable side effects of the drugs used as well as systemic dysfunction.

The readers of this journal are quite familiar with an acute and potentially life threatening condition precipitated by many anaesthetic agents malignant hyperpyrexia. Only the luckiest patients will manage to survive. The factors favouring survival are the anticipation, the early recognition of the onset of the condition and aggressive symptomatic treatment. The specific drug indicated in this condition, dantrolene^{1,2}, is not available even in the advanced

healthcare facilities in this country. The drug might well have to be used only a few times in the life time of a professional anaesthetist, but its presence in his armamentarium will ensure that no patient will ever die just because of its non-availability.

Almost all textbooks of anaesthesia advocate ephedrine as the drug of choice to counter the postspinal hypotension. Yet only select centres manage to procure this important vasoconstrictor; the drug is not available in the open market. Similarly phenylephrine, another peripheral vasoconstrictor, is not available anywhere. Noradrenaline (norepinephrine in USA), a very useful ionotropic drug introduced only a few years back, is at risk of being discontinued due to its restricted use in intensive care centres and emergency medical care, and thus has a low business profile for the marketing company^{3,4}.

Adequate analgesia is the hallmark of the anaesthetic technique; rather it constitutes an important component of the anaesthetic triad, namely sleep, pain relief and relaxation. Pain relief is essential to counter the effects of the sympathetic stimulation associated with unrelieved pain during and after the surgery. Unfortunately in this country, all what is available to us for intraoperative and postoperative pain relief is NSAID's or second line narcotic analgesics, e.g., diclofenac, nalbuphine, tramadol and ketorolac. Morphine and even pethidine are not marketed openly and are tightly controlled by the health authorities, for fear of illegal use. These drugs are sometimes made available to military hospitals, but civil hospitals are exempt from this favour. Same is the case with fentanyl. Fentanyl is one of the most potent analgesic drugs (80 times as compared to morphine), which remained available round the globe

for institutional use⁵. It has since been followed by salts with even better analgesic and safety profile, namely sufentanyl and remifentanyl. None of these is within reach of anaesthetists and pain specialists of this country. Health authorities are probably reluctant to register these for the fear of abuse. Ironically, charas and heroin (diamorphine) are available in this country at the corner of any street of a city, yet the patients are deprived of potent analgesics for their severest pains. Military hospitals have a well-defined system to register and account for the use of morphine and pethidine. Strict vigilance is exercised to control the use; hence these are termed as 'controlled drugs'. The procurement and supply to hospitals and field units is the responsibility of Armed Forces Medical Stores Depot. One wonders why same type of a system can not be implemented in civil medical institutions. Something has to be done at an appropriate level to deal with this humanitarian crisis and urgently, as pain relief is one of the basic human rights.

Two other drugs merit special mention in the context of pain relief. EMLA (eutectic mixture of local anaesthetics, e.g. lignocaine and prilocaine) has been in wide use in different forms in the developed countries for many years, but has yet to be introduced in Pakistan. EMLA patches in bright colours and famous cartoon shapes applied to the dorsum of a child's hand render it painless to cannulate in a few minutes. In cream form it is used for small procedures, for example cyst or ganglion removal. Drug company Astra Zeneca, and some local pharmaceutical companies have been repeatedly approached and persuaded by the author for its local marketing, but the positive results are yet to be seen. The other drug is the local anaesthetic ropivacaine. It is associated with less motor block as compared to lignocaine and bupivacaine in equipotent doses, yet has a better safety profile and has virtually replaced bupivacaine, wherever long duration of pain relief is required⁶. It remains to be introduced in our local

market. Even Astra Zeneca, its parent manufacturing company has declined to market it here for unspecified reasons. Some local pharma companies have been persuaded to manufacture and/or market these very useful drugs locally (one argument offered for EMLA cream was its anticipated extensive use by local beauty clinics in waxing and threading practices, and hence its high profitability to the manufacturing company - author).

Some anaesthetists have voiced the occasional non-availability of halothane and thiopentone. Both these drugs have been mainstay of general anaesthesia and were widely used throughout the world. Halothane has been incriminated with the increased incidence of liver dysfunction and hepatitis; so its manufacture has since been discontinued by the parent company ICI. It is still being manufactured by some Korean drug companies mostly for consumption in the third world countries for reason of its low cost as compared to its successors with heightened safety profile, e.g., isoflurane and sevoflurane. Most of the private hospitals and clinics in Pakistan have anaesthesia machines fitted with halothane vaporisers and continue its use due to its low cost. These clinics disregard its hepatic, renal and cardiac toxicity⁷⁻⁸. This practice can not be approved on any account, keeping in view that the saving accrued by halothane use is not transferred to the patient. Further, the manufacturing companies of halothane lack assurances of strict quality control measures. Thiopentone has been in use for many years and remained as the main induction agent, despite introduction of many rivals, e.g., etomidate, etc. This drug is known to have some side effects including increased hemodynamic effects and precipitation of porphyria in susceptible patients. Propofol, on the other hand has a better recovery profile and can be safely used in case of suspected or known porphyria susceptibility. For this reason it has mostly replaced thiopentone as induction agent in the developed countries as well as better health institutions in the developing countries like Pakistan.

Propofol is four times costly as compared to thiopentone. For this reason most of the public sector hospitals and private clinics continue to use it. In the present scenario of financial crisis leading to healthcare budget cuts, perhaps it is prudent to ensure its continued availability.

The sympathetic blockers, e.g., propranolol and esmolol have long been withdrawn from the local market. These two intravenous drugs were favourite with the anaesthetists for control of intubation related stress and intraoperative hypertension. The list goes on and on, but it suffices to mention that although all sensible anaesthetists are alive to this issue, only a concerted effort from all quarters of the country could redress the situation. Our patients deserve the best as they are the axis around which all our universe revolves.

Pakistan Society of Anesthesiologists (PSA) has repeatedly raised her voice in national as well as international anaesthesia conferences, but to no avail. A better option is perhaps a direct approach to legislators and concerned health authorities by eminent anaesthesia scholars of this country for discussing this very important and vital issue. Fellow anaesthetists throughout the country can be persuaded to write letters to legislators and higher authorities to come into action, to pass relevant bills and have a constant vigilance over steps taken by health ministry to comply with. Only persistence can bear fruits.

The open market policy without strict realisation of the healthcare needs is a dilemma. Our health authorities need to rise to the problem of drug availability in this country for the benefit of sixty

million inhabitants. The local pharmaceutical industry too, is urged to step their foot into and adopt marketing policies according to the needs of the patients. Low profit but essential products should not be withdrawn or discontinued, and new and useful but limited-use products must be introduced even when the expected profit margin might be a major discouraging factor.

REFERENCES:

1. Harrison GG. "Control of the malignant hyperpyrexia syndrome in MHS swine by dantrolene sodium". *Br J Anaesth* 1975;47 (1): 625.
2. Kolb ME, Horne ML, Martz R. "Dantrolene in human malignant hyperthermia". *Anesthesiology* 1982;56 (4): 25462.
3. Budavari S, editor. *The Merck Index: An encyclopedia of chemicals, drugs, and biologicals*, 12th edition. Whitehouse Station: Merck.
4. Reynolds JEF, ed. *Martindale: The complete drug reference* (29th ed.). 1989 London: Pharmaceutical Press.
5. Ogawa J, Nakamura K, Iizuka K, Sekizuka M, Yamamoto K, Horiuchi R. Optimal conversion ratio of oral morphine to transdermal fentanyl patches to the cancer pain. *Yakugaku Zasshi* 2009;129(3):335-40.
6. Xu HW, Zhang L, Cao W, Zhang X, Zhang WS. Clinical efficacy and pharmacokinetics of different concentrations of ropivacaine with the same dosage on blocking lumbar plexus with sciatic nerves. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2009;40(3):495-8..
7. Irwin MG, Trinh T, Yao CL. Occupational exposure to anaesthetic gases: a role for TIVA. *Expert Opin Drug Saf*. 2009;8(4):473-83.
8. Antoine DJ, Williams DP, Park BK. Understanding the role of reactive metabolites in drug-induced hepatotoxicity: state of the scienc. *Expert Opin Drug Metab Toxicol* 2008;4(11):1415-27.

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