CASE REPORT

ATROPINE TOXICITY IN ACUTE CERVICAL SPINAL INJURY

By J. H. E. BAKER, B.Sc., M.B., B.S., M.R.C.P.,¹ and J. R. SILVER, M.B., B.S., F.R.C.P.²

¹Senior Registrar, Midlands Spinal Unit, Robert Jones & Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire. ²Consultant in Spinal Injuries, National Spinal Injuries Centre, Stoke Mandeville Hospital, Aylesbury, Bucks.

Summary. A patient with a C.3/C.4 fracture dislocation resulting in an incomplete tetraplegia was treated with Cimetidine 400 mg bd to prevent gastrointestinal bleeding and 0.6 mg of atropine 6 hourly. He developed symptoms of atropine poisoning in the form of hallucinations, confusion and dilated pupils when the total dosage of atropine was 2.8 mg. This is far below the toxic levels normally considered necessary to produce atropine poisoning. The patient recovered.

In view of the fact that this combination of drugs may be used in spinal units to prevent gastrointestinal bleeding and bradycardia, this experience is reported.

Introduction

Bradycardia is a recognised feature of acute cervical cord injury. In extreme cases it can lead to cardiac arrest. Atropine has been used as a prophylactic to prevent this during manipulation causing vagal stimulation, such as tracheal suction. This use of atropine is not without hazard, as the following case history indicates.

Case Report

ON the 17th September 1981, a 20-year-old medical student, while practising rugby football, sustained a mild head injury and a C.3/4 fracture dislocation resulting in incomplete tetraplegia below C.5. At the receiving hospital he was placed on skull traction, given dexamethasone 24 mg and placed on cimetidine 400 mg bd. He was intubated and required transient ventilation.

He was transferred to this centre 2 days after injury ventilating spontaneously. He was rational, giving an accurate account of his accident. Minor adjustments were made to his skull traction; his pulse rate was 48 and he was given 0.6 mg of atropine intra-muscularly which was to be repeated as required but not more frequently than six-hourly. Three days later he became agitated and confused at night with formed hallucinations; these were visual, monochromic and microsmic. His pupils, hitherto reactant, had become fixed and dilated, he developed tachycardia. In this period he had received 2.8 mg of atropine overall and at one point 2.1 mg in a period of 17 hours. He had also been given Parenterovite I and II high potency in the course of intravenous infusion. The atropine was

discontinued and his mental state improved dramatically overnight and was normal within 18 hours, 36 hours later his Cimetidine was stopped but there was no change in his mental state. His level and degree of paralysis did not change, at all times his vital capacity did not fall below 900 ml and his arterial blood gases remained satisfactory. His systolic arterial blood pressure did not fall below 90 mm/Hg.

Discussion

Confusion within the first week of a cervical injury usually derives from hypoxia, shock, head injury or multiple injuries: either abdominal causing splinting of the diaphragm, or thoracic causing lung contusion, haemo-pneumothorax, flail segment or atelectasis. (Silver, 1968, Frankel, 1968, Harris, 1968 and Silver, Morris and Otfinowski, 1980). Untoward reaction to drugs can also lead to confusion as can withdrawal from alcohol, narcotic analgesics or psychotropic preparations. (Frankel, 1968).

In this boy ventilation, gaseous exchange and perfusion were adequate and no additional injuries were present; his head injury was mild. His liver function tests were normal and there was no history of alcohol or drug abuse.

He was on two drugs (Cimetidine and atropine) that could give rise to confusion. Cimetidine had been administered at the receiving hospital because of the risk of gastro-intestinal bleeding, possibly compounded by steroids. Cimetidine has been reported as inducing a toxic confusional state (Kendall, 1979, Johnson, 1979, Basvasajai, 1980, Sharpe, 1980, Ng, 1981, Russell *et al.*, 1981, Evans, 1981 and Brier, 1980). This includes agitation, and formed hallucinations (Yundofsky, 1980 and Adler *et al.*, 1980) similar to those seen in atropine intoxication. It has also been known to masquerade as delirium tremens (Waddington, 1981). His improvement was not related to removal of Cimetidine.

We concluded that he was suffering from atropine poisoning, he had persistent features of muscarine blockade, and his clinical improvement was related to its withdrawal. The rationale of its use is that in the acute stages of cervical spinal injury asystole may either occur spontaneously or as the result of vagal stimulation, particularly endotracheal suction (Dollfus and Frankel, 1965, Frankel, Mathias and Spalding, 1975, Angell-James and Daly, 1969 and Frankel and Mathias, 1974). Atropine has been used prophylactically in the management. Repeated doses of atropine have been given without significant side effects.

The time for the metabolism and excretion of atropine is not well documented. A time of 12 hours as a serum half life has been cited (Goodman and Gillman, 1980 and Martindale, 1977), other workers (Gosselin, 1960, Kalser 1971 and Kalser and McLaine, 1970), believe that the time course is 24 hours or up to 88 (Avery, 1980). On the data given in Martindale (1977) and Goodman and Gilman (1980), this young man did not receive a toxic dose. The symptom complex of agitation, tachycardia, fixed mydriasis and confusion all point to atropine intoxication and its withdrawal produced dramatic improvement. The drug combination of cimetidine and atropine has hitherto been used without ill effect on this unit as part of routine management to combat the hazards of gastric erosion on one hand and vagal arrest on the other. The role of cimetidine

is secondary. It is known to induce bradycardia (Fry, 1979, Ahmed, 1979 and Kurch, 1980). As such it may have slowed his pulse even further. There is no evidence that the Cimetidine impaired his liver function or that it interacted with the Atropine directly. The withdrawal of the atropine caused the remission of all the symptoms.

Conclusion

The value of the use of atropine in sustaining the heart rate in acute tetraplegia is recognised. However, those who treat acute spinal injuries should add the risk of atropine toxicity to other causes of confusion developing in patients with acute spinal injury, particularly where other drugs are simultaneously administered and it should be further recognised that this can occur at levels lower than those recognised as toxic.

REFERENCES

- ADLER E. *et al.* (1980). Cimetidine toxicity manifested in paranoia and hallucinations. *American Journal of Psychiatry*, **137**, 1112-1113.
- AHMED S. (1979). Cimetidine and cardiovascular complications (letter). *British Medical Journal*, **2**, 1369.
- ANGELL-JAMES J. & DALY M. de B. 1969. Cardiovascular responses in apnoeic asphyxia. *Journal of Physiol (Lond)*. **201**, 87-104.
- BASAVARAJU, N. C. *et al.* (1980). Cimetidine-induced mental confusion in the elderly. *New York State Journal of Medicine*, **80**, 1287-1288.
- BRIER, K. L. *et al.* 1980. Cimetidine and mental confusion. *Critical Care Medicine*, **8**, 760-761.
- DOLLFUS, P. A. & FRANKEL, H. L. (1965). Cardiovascular reflexes in tracheostomised tetraplegics. *Paraplegia*, **2**, 227-235.
- EVANS, A. L. (1981). Cimetidine and toxic psychosis (letter). *American Journal of Psychiatry*, **138**, 1262.
- FRANKEL, H. L. (1968). Associated chest injuries. *Paraplegia*, **5**, 221-225.
- FRANKEL, H. L., MATHIAS, C. J. & SPALDING, M. R. (1975). Mechanisms of reflex cardiac arrest in tetraplegic patients. *Lancet*, **2**, 1183-1185.
- FRANKEL, H. L. & MATHIAS, C. J. (1974). In: P. J. Vinken and G. Bruin (eds) *Handbook of Clinical Neurology*, **26**, 313-338.
- FRY, E. N. (1979). Life threatening arrhythmias and intravenous cimetidine. (letter). *British Medical Journal*, **2**, 1075.
- GILMAN, A. G., GOODMAN, L. S. & GILMAN, A. (Eds). (1980). *Goodman and Gilman's Pharmacological Basis of Therapeutics*, New York, MacMillan.
- GOSSELIN, R. E. *et al.* (1960). The fate of atropine in man. *Clinical Pharmacology and Therapeutics*, **1**, 597-603.
- HARRIS, P. (1968). Associated injuries in traumatic paraplegia and tetraplegia. *Paraplegia*, **5**, 215-220.
- JOHNSON, J. & BAILEY, S. (1979). Cimetidine and psychiatric complications. *British Journal of Psychiatry*, **134**, 315-316.
- KALSER, S. C. (1971). The fate of atropine in man. *Annals of the New York Academy of Sciences*, **179**, 667-83.
- KALSER, S. C. & MCLAIN, P. L. (1970). Atropine metabolism in man. *Clinical Pharmacology and Therapeutics*, **11**, 214-27.
- KARCH, F. E. *et al.* (1980). Bradycardia associated with cimetidine. *Journal of Family Practice*, **11**, 319-320.
- KINNELL, H. G. & WEBB, A. (1979). Confusion associated with cimetidine (letter). *British Medical Journal*, **2**, 1438.
- MARTINDALE. (1977). In: E. Wade (Ed). *The Extra Pharmacopoeia*, 27th Edition. 225-226.

- NG, J. Y., JONES, T. E., DISNEY, A. P. & MATHEW, T. H. (1981). Prolonged confusion after cimetidine (letter). *Medical Journal of Australia*, **1**, 656-7.
- RUSSELL, W. L. & LOPEZ, L. M. (1981). Cimetidine-induced mental status changes, case report and literature review. *American Journal of Hospital Pharmacology*, **37**, 1166-71.
- SHARPE, P. L. & BURLAND, W. L. (1980). Mental confusion and H₂ receptor blockers (letter). *Lancet*, **2**, 924.
- SILVER, J. R. (1968). Chest injuries and complications in the early stages of spinal cord injury. *Paraplegia*, **5**, 226-243.
- SILVER, J. R., MORRIS, W. R. & OTFINOWSKI, J. S. (1980). Associated injuries in patients with spinal injury. *Injury*, **12**, 219-224.
- WEDDINGTON, W. W. (1981). Cimetidine toxic reactions masquerading as D.T.s. *Journal of American Medical Association*, **245**, 1058-1059.
- YUDOFKY, S. C. (1980). Agitation, dementia and hallucinations in patients on cimetidine. *General Hospital Psychiatry*, **2**, 233-236.