

European Medical Research Group

Meeting held 11 July 1994

The European Medical Research Group met at the Medical Society of London, Lettsom House, London, UK, on 11 July 1994. The guest speaker was Professor TG Dinan of St Bartholomew's Hospital Medical College, London, who gave a lecture on 'Depression and the black humors: new endocrine clues for treatment'.

A poster session was held demonstrating the research in progress of some members of the Group, two of which are published below.

Evaluation of sertraline in overdoses reported in the UK

In the clinical trial development programme of the antidepressant sertraline, a selective serotonin re-uptake inhibitor (SSRI), the drug was shown to have a favourable safety profile. In a database of 1902 patients there were four cases of overdose with sertraline and they were symptomatically managed with no relevant clinical sequelae.¹

In this paper evaluating the post-marketing experience of sertraline, the overdoses reported to the National Poisons Unit, Guy's Hospital, London from December 1990 to December 1992 are reviewed. The safety of sertraline in overdose was classified according to the fatal toxicity index, psychosis, convulsions, cardiotoxicity, orthostatic hypotension, and sedation, as proposed by de Jonghe and Swinkels.²

In this review there were 69 cases where sertraline was taken in combination with at least one other drug or alcohol and 23 reports in which sertraline was taken alone with doses up to 2000 mg. In the latter group drowsiness (n = 5) and vomiting (n = 3) occurred most frequently. In the remainder there were no

symptoms reported. There were no fatalities in patients taking sertraline alone. In contrast to the well known effects of the tricyclic antidepressants, overdose with sertraline did not produce clinically significant reactions such as orthostatic hypotension, cardiotoxicity, psychosis or sedation, or convulsions. This confirms previous experience from the clinical trial development programme,¹ suggesting a reduced pro-convulsant potential compared to tricyclic antidepressants as presented in a recent review on the clinical use and safety of SSRIs.³ These data support the favourable side-effect profile of sertraline, and suggest that it also has a favourable safety margin when taken in overdose.

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1 Doogan DP. Tolerant and safety of sertraline: experience worldwide. *Int Clin Psychopharmacol* 1991; 6 (suppl 2): 47-56.

2 de Jonghe F, Swinkels JA. The safety of antidepressants. *Drugs* 1992; 43 (suppl 2): 40-7.

3 Teicher MH, Glod CA, Cole JO. Antidepressant drugs and the emergence of suicidal tendencies. *Drug Safety* 1993; 8: 186-212.

A pilot study of the effect of hormonal pretreatment during human heart transplantation

A study of serial myocardial biopsies from 230 donor hearts during transplantation showed that 39% of hearts had significant myocardial injury prior to excision. A further 38% deteriorated significantly during the transplant procedure. Assessment was by

quantitative birefringence measurements (QBM). These measure the ability of muscle fibres to respond to adenosine triphosphate (ATP) and calcium and correlate with measurements of cardiac function ($p < 0.001$). Hearts assessed as damaged were worse after transplantation; 51% vs 4% needed inotropic agents; of 35 cardiac deaths (donor organ failure, acute rejection, late coronary occlusive disease), 34 occurred in recipients of damaged donor hearts ($p < 0.001$). Hormonal replacement therapy (T3, cortisol and insulin) has been advocated as a method of preventing myocardial injury following brain death. In a prospective randomised study we tested the effect of pretreating 12 donors with 2 µg/h T3, 1 g methylprednisolone and insulin to normalise serum glucose levels. Free T3 levels were abnormal (2.1 ± 0.3 pmol) and did not normalise (2.6 ± 0.6 pmol) during pretreatment. No effect was observed on the myocardium, QBM 1.35 ± 0.05 compared with 1.32 ± 0.03 in untreated donors. T3 dosage was increased to 4 µg bolus and a continuous infusion 4 µg/h. T3 levels normalised after pretreatment (n = 11 donors) and QBM were improved, mean 1.41 ± 0.06 as compared with 1.31 ± 0.05 in control group ($p < 0.01$). It is concluded that hormonal treatment of brain-dead donors appeared to improve myocardial function. Further studies are needed to ascertain whether pretreatment enhances the long-term survival of the recipients.

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