Letters to the Editor

HALOPERIDOL DECANOATE: ROUTE OF ADMINISTRATION

Sir,

Haloperidol decanoate (HPL-D) is a useful depot neuroleptic on several counts: it has a duration of action of 4-6 weeks, there is no dumping effect associated with its administration, and the adverse effects milligram for milligram are fewer and milder than those observed with the oral form of haloperidol (Beresford and Ward, 1987; Glazer and Kane, 1992).

HPL-D requires to be administered by deep intramuscular injection; subcutaneous administration may be associated with the development of injection site reactions (Hamann et al., 1990). In low doses, intramuscular administration into the deltoid is feasible and convenient. In high doses, however, the larger volume of drug to be administered necessitates injection into the gluteus.

This is where the problem arises. Disposable syringes in India usually have an approximately one inch needle length. Disposable 21 gauge needles, required for use with HPL-D, are generally of the same length. Constitutional and behavioural factors, more in women than in men, usually result in the presence of gluteal fat that is over an inch or two in thickness in the average Indian patient. In consequence, it is likely that despite gluteal compression during injection, few Indian patients truly receive deep intramuscular HPL-D when the drug is injected into the buttock, in fact, it is possible that many patients are actually receiving the injection in subcutaneous fat.

No reports of injection site reaction with HPL-D have appeared in the Indian scientific press. Is this because of under-reporting or might subcutaneous HPL-D be less harmful than earlier believed?

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STRESS, DEPRESSION AND GENOMIC CHANGE

Sir,

Dysregulation of hypothalamo-pituitary adrenal axis (HPA) is one of the oldest and most consistent findings in depression. It is now generally accepted that stressful life events and chronic difficulties can trigger the onset of depression in predisposed individuals. Enough is known about the central control of HPA function and its response to stress in the neurobiology of triggering the depression. The stress induces hypercortisolaemia which triggers depression by inducing genomic change. There are two types of corticoid receptors in brain tissue - type I and type II receptors (Reul & De Kloet, 1986). Under basal conditions cortisol has very high affinity with 80% occupancy of type I receptors whereas type II receptors are occupied and activated only during stress (Ratka, 1989). Further, hippocampus is the most vulnerable site for the neurotoxic action of glucocorticoids. The glucocorticoid receptors are predominantly present in hippocampal area. Of late, in vivo hippocampal atrophy assessed using magnetic resonance imaging has been correlated with plasma cortisol levels in depression (Axelson et al., 1993). A related but astonishing fact is that all hormones with well defined effects on mood (estrogen, progesterone, glucocorticoids and thyroxine) have intracellular receptors whereas most other hormones act through membrane receptors. More surprising than this is that these intracellular receptors have two
aminoacid sequences in common which are thought to bind hormones to specific sequences of DNA and modify the gene transcription (Beato, 1989). The complex formed by the binding of a steroid with a receptor is translocated into the cell nucleus where it binds to DNA and influences the expression of genes. So the activation in depression of the HPA axis involves various steps in producing excess cortisol and then inducing genomic change. The blockade at each one of them is being targeted to antagonise the effects of stressful life events in producing depression or in the treatment of depression. The therapeutic potential of antiglucocorticoid drugs especially type II receptor antagonists and steroid synthesis inhibitors have been explored with encouraging results in patients with mood disorders (Mitchell & O'Keeane, 1998).

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