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Increased Glycosylated Haemoglobin A_1 in Opiate Addicts: Evidence for a Hyperglycaemic Effect of Morphine

Dear Sir

The hyperglycaemic effect of morphine has been a well recognized phenomenon throughout this century [1], but the mechanism of its action still remains unclear. Recent studies in the dog [2] and in man [3] suggest that both morphine and beta-endorphin increase the plasma levels of glucose, insulin and glucagon. These observations have led to the suggestion that the interference of the opioid peptides on carbohydrate metabolism may be through modifications of pancreatic hormone release.

We have studied the effect of protracted morphine administration on carbohydrate metabolism in 27 male addicts (age range: 18–34 years, mean ± SEM: 24 ± 2.2 years) before narcotic withdrawal. The results were compared with those obtained in 46 healthy males matched for age (mean ± SEM: 25 ± 1.8 years) and weight. Carbohydrate metabolism was assessed by determining fasting plasma glucose (mean of three samples on three consecutive days) and glycosylated haemoglobin A_1 (HbA_1) (mean of two samples) which represents a very useful index of the glycaemic control of the last 3–4 weeks [4]. Glycosylated haemoglobin A_1 was determined according to the method of Welch and Boucher [5]. The intra- and inter-assay coefficients of variation for this method are 1.5% and 3%, respectively. The mean ± SEM HbA_1 level was 7.18 ± 0.17% in addicts and 6.11 ± 0.06% in control subjects, a difference which is statistically significant ($p < 0.001$). No significant difference was found in fasting plasma glucose (5.08 ± 0.13 mmol/l in addicts versus 4.72 ± 0.19 mmol/l in control subjects). No significant correlation was found between fasting plasma glucose and HbA_1 in addicts. Total haemoglobin was 15 ± 0.2 g/dl in addicts and 14.3 ± 0.4 g/dl in controls (NS) (Fig. 1).

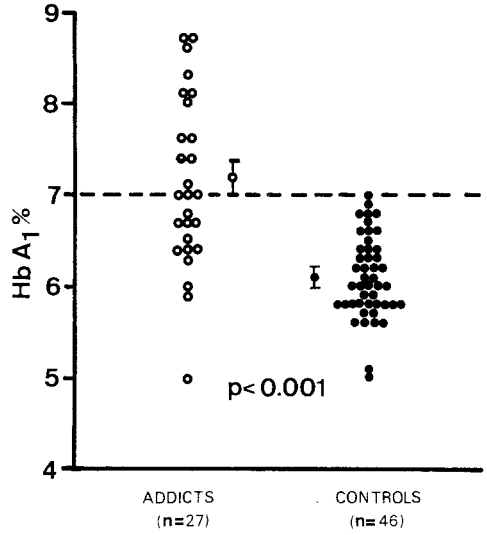

Fig. 1. HbA_1 levels in addicts and control healthy subjects

Our results seem to indicate that addicts have, in the course of their usual life, intolerance to ingested carbohydrates, which is reflected by the increased HbA_1 levels. To our knowledge, this is the first demonstration that chronic morphine administration interferes adversely with carbohydrate metabolism. If that is due to a direct effect of morphine (at the liver or the periphery) or to alterated pancreatic hormone secretion, we cannot say. Interestingly, Reed and Ghodse [6] found an increased and delayed insulin response to oral glucose tolerance tests in addicts; a similar type of response may be found in the early stages of glucose intolerance. On the other hand, the non-physiological nature of the oral glucose tolerance test and its poor prognostic value are now emphasized [7].

Yours sincerely

A. Ceriello, D. Giugliano, P. Dello Russo, S. Sgambato and F. D'Onofrio

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Dr. D. Giugliano
Institute of Medical Pathology
Faculty of Medicine I
University of Naples
80138 Naples, Italy