Selçuk Üniversitesi Vet. Fak. Dergisi
1. Sayı (65-69), 1985

HYPERGLYCEMIC EFFECT OF N - METHYLGLUCAMINE ANTIMONITE (GLUCANTIME) IN MICE

N - Methylglucamine antimonite (Glucantime)'in farelerde hiperglisemik etkisi

Murat YURDAKÖK[1]
Erol KINIK[2]
Serdar DİKER[3]
Hüdaverdi ERER[4]
Uğur DİLMEN[5]
Mehmet CEYHAN[6]
Osman KUTSAL[7]

Summary: N - methylglucamine antimonite (Glucantime) was injected intramuscularly to ten albino mice in a dose of 15 - 30 mg/kg for the first three days and then 60 mg/kg for twelve days. Glucantime was also injected in the same manner but in double doses to another ten mice. No drug was administred to ten mice that were used as a control group. In the sixteenth day, there were hyperglycemia, parenchymatous and vacuolar degeneration, hepatocellular necrosis and inflammation in the livers of the experimental mice which were marked as a double dose group. The frequent monitoring of blood glucose of the patients with Kala-azar receiving Glucantime was suggested.

Özet: N - methyglucamine antimonite (Glucantime)'in glukoz metabolizması ve karaciğer morfolojisi üzerindeki etkilerini araştırmak

(1) Pediatri Uzmanı, H. Ü. Halk Sağlığı Enstitüsü, Ankara, Türkiye.
(2) Prof. Dr., H. Ü. Tıp Fakültesi Pediatri Anabilim Dalı, Ankara, Türkiye.
(3) Araşt. Gör. Dr., A. Ü. Veteriner Fakültesi Mikrobiyoloji Anabilim Dalı, Ankara, Türkiye.
(4) Yard. Doç. Dr., S. Ü. Veteriner Fakültesi Patoloji Anabilim Dalı, Konya, Türkiye.
(5) Pediatri Uzmanı, Türkiye Sağlık ve Tedavi Vakfı Ahmet Örs Hastanesi, Ankara, Türkiye.
(6) Pediatri Başasistanı, H. Ü. Tıp Fakültesi Pediatri Anabilim Dalı, Ankara, Türkiye.
(7) Araşt. Gör., A. Ü. Veteriner Fakültesi Patoloji Anabilim Dalı, Ankara, Türkiye.

(F.: 5)

amacıyla 10 albino fareye ilk üç gün 15 - 30 mg/kg, sonraki 12 gün, günde 60 mg/kg olmak üzere intramüsküler olarak Glucantime ve 10 fareye de aynı ilaç iki misli dozda verildi. Hiç bir ilaç verilmeyen 10 fare ise kontrol grubu olarak kullanıldı. Onaltıncı gün yapılan incelemelerde, yüksek doz alanlarda daha belirgin olmak üzere, Glucantime uygulanan faralerde hiperglisemi ile karaciğerlerin histolojik muayenesinde, hepatositlerde parankim ve vakuoler dejenerasyon, yer yer nekrotik değişiklikler ve portal bölgelerde mononükleer hücre ve daha az sayıda nötrofil lökosit infiltrasyonları görüldü. Glucantime alan Leishmaniasis'li hastaların kan şekerlerinin sık aralıklarla izlenmesi önerildi.

Introduction

N - methylglucamine antimonite (Glucantime) is one of the populaı drugs used in the therapy of Leishmaniasis (4). During the therapy of a two - year - old boy with Kala - azar, hyperglycemia (391 mg/dl) was seen after the fifteenth dose of Glucantime (each dose 60 mg/kg) infected intramuscularly. Therefore, a study concerning hyperglycemic effects oi Glucantime in mice was carried.

Materials and Methods

In this study male albino mice were used which were supplied by the Ankara University, Faculty of Veterinary Medicine, Department oi Bacteriology, Laboratory Animals Breeding Unit. All of the mice were at fous weeks of age and weighed 46 - 57 grams. They were fed in individual cages with food (Turkish Standart Rodent Food) and water *ad libitum*.

Thirty mice were divided into three equal groups. The first group was separated as a control and recevied no drug. Ten mice in the second group were given Glucantime as a single daily doses of 15 mg/kg per day intramuscularyl for the first day, 30 mg/kg for the second day, and threafter it was continued with the injection of 60 mg/kg per day for twelve days. Glucantime was given to other ten mice in the third group in the same manner, but in double doses.

On the sixteenth day blood samples from the heart were taken to determine the blood glucose level by Somogyi - Nelson Method (1) and the livers for histological examination were fixed in 10 per cent formalin, processed by routine methods, cut 5 micron thick and stained with haematoxylin and eosin.

Results

Blood glucose levels were significantly higher in the experimental group than the control group. It was however the highest in the double dose group (third group) (Table 1). The difference between the blood glucose level in the three groups were found to be statistically significant ($p<0.05$).

In histological examination of livers in the experimental group hepatocellular degeneration (parenchymatous and vacuolar) in varying degrees and scattered small foci of hepatocellular necrosis and mononuclear cells and polymorphonuclear leucocytes infiltration were observed (Fig. 1). No changes were seen in the control group. In the double-dose group all these changes were much more severe (Fig. 2, 3).

Tablo 1. Blood glucose levels in the control and experiment groups.

Groups	Blood glucose level (mg/dl)
Control group (n:10)	58.9∓ 4.7
Glucantime standart dose group (n:10)	101.0∓10.3
Glucantime double dose group (n:10)	124.8∓10.7

Discussion

Various kinds of side effects of Glucantime (such as, fever, rush, xerostomia, hypersalivation, cough, bradycardia, ECG changes, abdominal pain, vomiting, diarrhea, toxic hepatitis, hemolytic anemia, agranulocytosis, bleedings, nephrotoxicity, convulsions, cardiovascular collaps anaphylactoid schock) have been reported in the literature (2, 3, 5, 6, 7). But there is no report concerning the hyperglycemic effect of Glucantime. We have showed that Glucantime caused hyperglycemia which is dose dependent. Although we don't know the mecanism of hyperglycemia due to Glucantime, it might be related toxic pancreatitis just as the toxic hepatitis which was seen in this study. Further experiments are needed to be investigated on this subject.

We therefore suggest that blood glucose level should be determined during the Glucantime therapy.

References

1 - Bauer, J. P., Ackerman, P. G. and Toro, G. (1974): Clinical Laboratory Methods. St. Louis: C. V. Mosby, Co. p. 383.

2 - Bourée, P. et Dulac, O. (1977): Agranulocytose, au cours d'une leishmaniose viscerale traitee par le Glucantime. Arch. Franc. Péd., 34:659.

3 - Cahill, K. M. (1964): Leishmaniasis in the Sudan Republic, infection in American Personnel. Am. J. Trop. Med. Hyg., 13 : 794.

4 - Giraud, P., Bernard, R., Orsini, A. and Coignet, J. (1962): New data on the treatment of Kala-azar. Turk. J. Pediatr., 4 : 157.

5 - Goth, A. (1970): Medical Pharmacology. St. Louis, C. V. Mosby Co., p. 572.

6 - Hashash, M., Serafy, A. and State, F. (1981): Histopathological cochlear changes induced by antimonial antibilharzial drugs. J. Laryngol. Otolog., 95 : 455.

7 - Rollo, I. (1975): The Pharmalogical Basis of Therapeutics. New York McMillan Publ. Co., p. 929 - 930, 1034 - 1037.

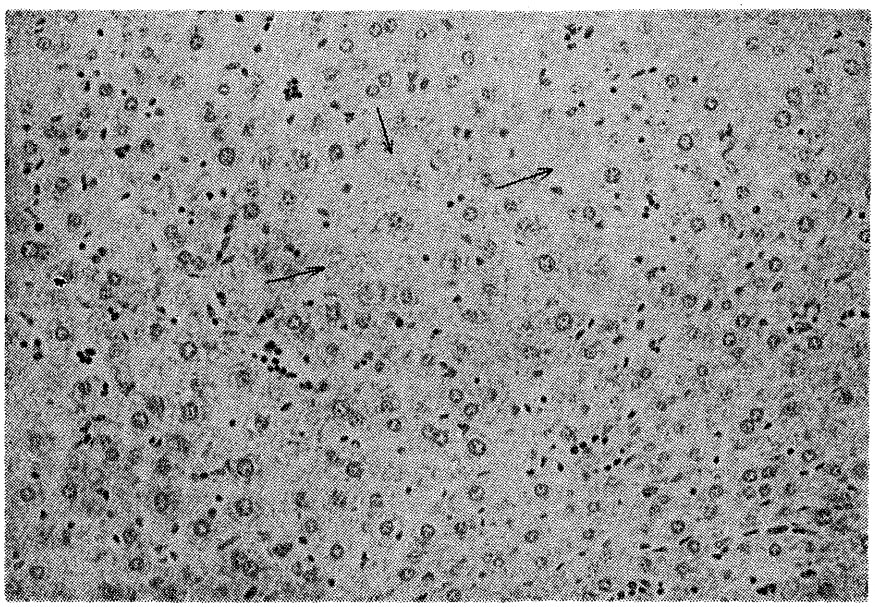

Fig. 1. Glucantime standart dose group. Parenchymatous degeneration and necrosis (arrows) in hepatocytes (Karaciğer epitel hücrelerinde parenkim dejenerasyonu ve nekroz). H. E. X 236.

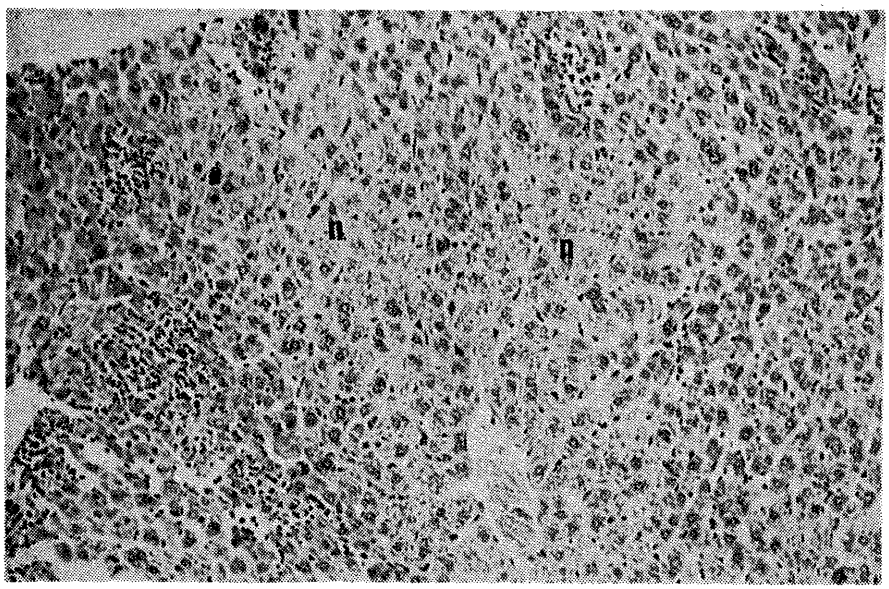

Fig. 2. Glucatime double dose group. Focal necrosis (n) and mononuclear cells infiltration in the portal areas (Fokal nekroz ve portal bölgelerde mononükleer hücre infiltrasyonu). H. E. X 132.

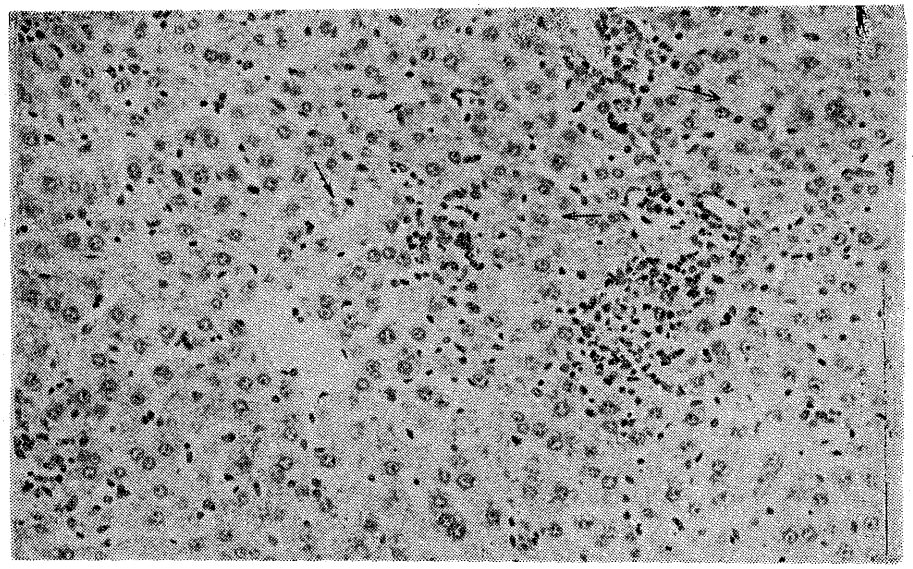

Fig. 3. Glucantime double dose group. Vacuolar degeneration in hepatocytes (arrows) and mononuclear cells infiltration in the portal areas (Karaciğer epitel hücrelerinde vakuoler dejenerasyon ve portal bölgelerde mononükleer hücre infiltrasyonu). H. E. X 186.