DRUGS AND LABORATORY TESTS: I. INTERACTION OF PHENAMIN AND ACETYSAL WITH DETERMINATION OF FREE FATTY ACIDS

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Key-words: free fatty acids — Phenamin—Acetysal—hepatic cirrhosis — chronic renal failure

The influence of many drugs on plasma levels of free fatty acids (FFA) (F. P. Kupiecki, 1971; A. Bizzi et al., 1964) presents possibilities as well for imitation or interference with lipid metabolism changes in certain pathological processes as for difficulties and mistakes in their diagnosis or prognosis. The literature data (L. A. Carlson and J. Ostman, 1961; R. Santi and G. Fassina, 1965) about some changes in total plasma FFA after Phenamin or Acetysal application directed us to the comparison of the effects both drugs on total concentration and levels of 7 individual FFA with the changes of the same indexes in 2 patients' groups; with hepatic cirrhosis (HC) and with chronic renal failure (CRF) (3^{rd}—4^{th} degree).

Our attention was paid to Acetysal as a drug belonging to the wide-spread group of non-steroid antiinflammatory agents. Its basic mechanism of action is the inhibition of prostaglandin synthetase (D. Metzler, 1980). The often non-controlled use of Acetysal can lead the physician to false interpretations of laboratory findings. The duration of prostaglandin synthetase inhibition after a single dose Acetysal is 5—7 days long (J. Hirsch, 1977) what is of importance for the clinical practice.

The Phenamin was chosen as a representative of indirect sympathomimetic amines the use of which as regards of their doping and anorexigenic action can be left out of control by physicians.

Material and methods

The study was carried out on 108 persons divided into 5 groups as followed: 1^{st} one — 50 healthy; 2^{nd} — 9 volunteers treated with a single dose of 10 mg Phenamin; 3^{rd} — 9 volunteers given Acetysal (total dose 3,0 g, thrice daily divided in equal 6 hours intervals) 4^{th} — 24 patients with HC, and 5^{th} one — 16 patients with CRF. In any persons the following FFA were determined: myristic $C_{14:0}$; palmitic $C_{16:0}$; palmitoleic $C_{16:1}$; stearic $C_{18:0}$; oleic $C_{18:1}$; linoleic $C_{18:2}$; and arachidic $C_{20:4}$. The changes in both saturated and unsaturated FFA and in the arachidic acid level were followed up and the ratio between the linoleic acid as a precursor of arachidic acid and the arachidic acid itself (index $C_{18:2}/C_{20:4}$) was calculated. The arachidic acid was taken into special consideration because of its importance as an immediate precursor in prostaglandin synthesis for the second series.

The FFA were determined by using gas chromatography with the apparatus Chrom-4. The extraction was perfomed according to Dole's method (1960) and

the methylizing of FFA — by using diazomethane syntesized from acetamide in our laboratory.

The calculations were made according to an intrinsic standard arachinic acid ($C_{20:0}$).

Results and discussion

The received results show that the total amount of FFA is significantly increased, as well after Phenamin and Acetysal treatment as in HC or CRF patients

Fig. 1

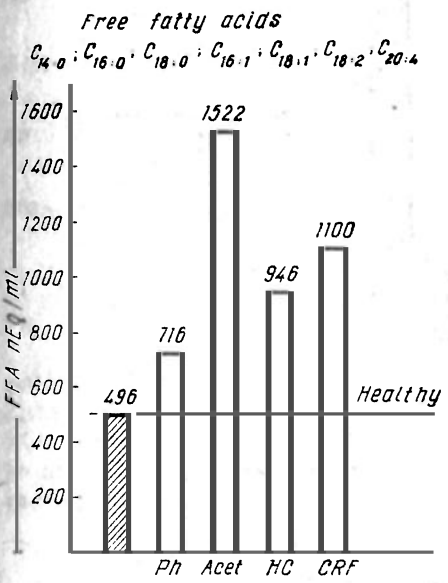
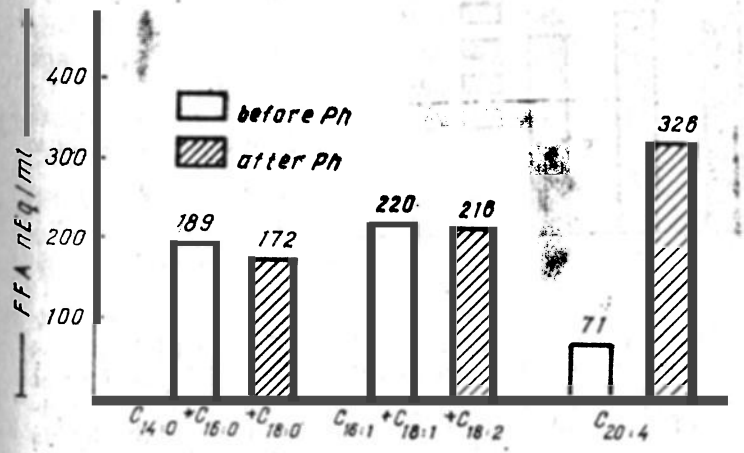


Fig. 2



in comparison with that in healthy individuals (fig. 1). This increase is in both patients' groups within the range of drug-mediated changes. The relative share of saturated and non-saturated FFA and arachidic acid varies in this total in-

crease. After treatment with Phenamin (fig. 2) and Acetysal (fig. 3) the enhancing is due exclusively to the $C_{20:4}$. Probably, the Acetysal inhibition of prostaglandin synthetase blockades the involving of this acid in its further metabolism,

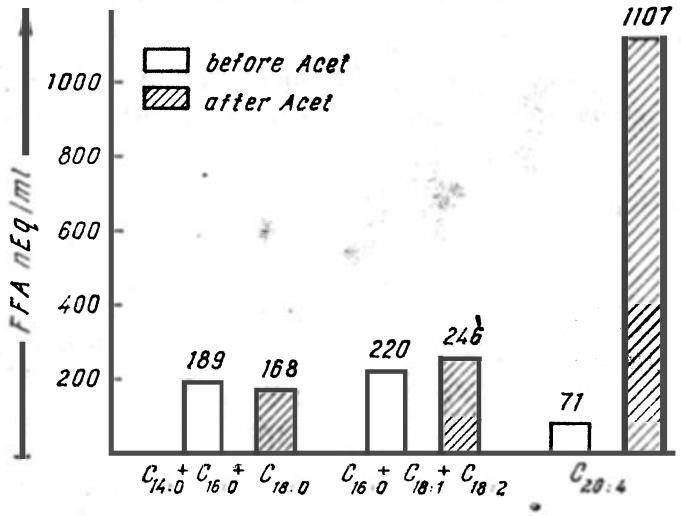


Fig. 3

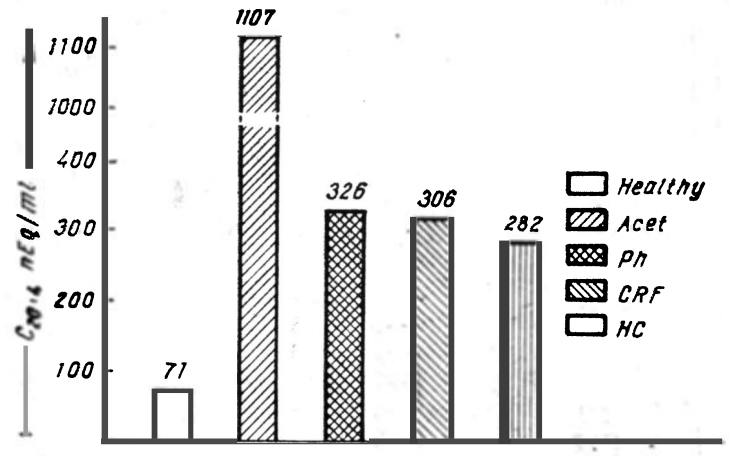


Fig. 4

i. e. in prostaglandin synthesis. In both patients' series the three FFA groups increase. Here, similarly to drug effects, the part of arachidic acid is the largest one. It is fourfold increased in HC patients and even more — in CRF ones. The comparison of absolute amounts of this acid shows a marked similarity of the levels in both patients' groups and Phenamin (fig. 4) treated individuals. In regard to the mechanisms determining the pathological changes of the FFA levels one can presume a larger analogy with the selective adrenergic mediated adipokinesis realized by Phenamin than with the Acetysal action.

The received data demonstrate certain one-way changes of the index $C_{18:2}/C_{20:4}$ (fig. 5) in the series studied. The sharp increase of the relative part of arachidi acid in the group under Acetysal treatment and the similarity of indices in al

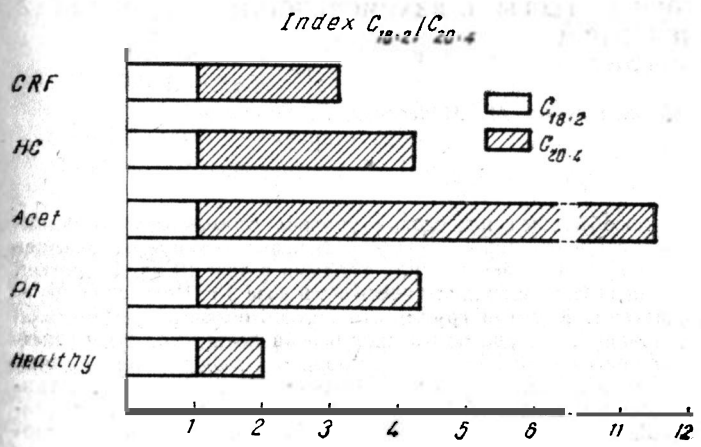


Fig. 5

patients and individuals under Phenamin treatment is clearly outlined. The data showing a significant diminution of the ratio $C_{18:2}/C_{20:4}$ point out that th- liberation of the $C_{20:4}$ and the eventual transformation of the $C_{18:2}$ into $C_{20:4}$ in all groups studied is accomplished considerably more rapidly than the transfor mation of $C_{20:4}$ into prostaglandins.

Conclusions

1. Phenamin which is a representative of catecholamines liberating or ago- nist adrenergic activity carrying drugs, increases the level of plasma FFA, especially of the arachidic acid as an immediate precursor in prostaglandin synthesis.

2. Acetysal which is a prototype of prostaglandin synthetase inhibiting drugs, causes also an increase of the level of plasma FFA by means of selective enhancing of arachidic acid concentration.

3. The interaction between Phenamin and Acetysal with plasma levels of FFA is indirect and it is realized by means of pharmacological mechanisms.

4. The increase of FFA levels and the distribution of FFA after Phenamin or Acetysal application is similar to the changes established in HC and CRF. This circumstance make the interpretation of the results from the studies of FFA by the physician difficult, indeed.

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ЛЕКАРСТВА И ЛАБОРАТОРНЫЕ ТЕСТЫ: I. ВЗАИМОДЕЙСТВИЕ ФЕНАМИНА И АЦЕТИЗАЛА С ОПРЕДЕЛЕНИЕМ СВОБОДНЫХ ЖИРНЫХ КИСЛОТ

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РЕЗЮМЕ

Газово-хроматографическим способом был исследован уровень плазмы семи индивидуальных жирных кислот 108 лиц, распределенных в 5 групп. К первой группе относились здоровые лица. Второй контрольной группе людей вводили фенамин в дозе 10 мг. К третьей контрольной группе относились люди, которым вводили ацетизал в дозе 3 г. Четвертая группа включала больных циррозом печени. К пятой группе относились больные хронической почечной недостаточностью. Установлено, что свободные жирные кислоты лиц, относящихся к II, III, IV и V группам, увеличены по сравнению с их уровнем у людей I-ой группы. Обнаружены различия в распределении индивидуальных свободных жирных кислот, а также и в стоимостях индекса линолевой/арахидоновой кислот. Фенамин вызывает селективный, направленный к арахидоновой кислоте адипокинез. Ацетизал повышает уровень свободных жирных кислот и в особенности арахидоновой кислоты, являющейся ингибитором простогландинсинтетазы. Подобные изменения устанавливаются у больных циррозом печени и хронической почечной недостаточностью, что осложняет интерпретацию результатов исследования свободных жирных кислот у больных, перечисленных к вышеуказанным группам.