EFFECT OF CHRONIC ADMINISTRATION OF ASPIRIN, PHENOBARBITONE AND OXYTETRACYCLINE ON THE PLASMA LEVELS OF VITAMIN A IN ALBINO RATS

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Abstract

Effect of chronic administration of aspirin, phenobarbitone and oxytetracycline under therapeutic doses on the bioavailability of vitamin A was determined in different groups of albino rats. The rats treated with phenobarbitone (group C) showed significantly decreased vitamin A level in plasma whereas the other two groups (B and D) treated with aspirin and oxytetracycline respectively did not exhibit any significant difference as compared to control group (A) (JPMA 40: 89, 1990).

INTRODUCTION

Many drugs and a variety of chemicals are capable of inducing the synthesis of drug metabolizing enzymes, particularly those of hepatic endoplasmic reticulum. Such an enzyme induction can enhance the metabolism not only of the inducing agent but also of a variety of drugs administered concurrently and of some endogenous substances like cortisol, bilirubin and sex steroids\(^1\). Phenobarbitone, a potent inducer of metabolism, has been shown to decrease the plasma levels of several drugs like rifampicin, chlorpromazine, warfarin and vitamins D\(^2\) and A\(^3\). Similarly, chronic use of aspirin, an extensively used analgesic, can cause vitamin C deficiency in the body by inhibiting the transport of ascorbic acid in leukocytes and thus increasing its urinary excretion\(^2\). Likewise, oxytetracycline has been reported to upset the level of vitamin A in different organs of chickens\(^4\). Vitamin A is an important component of diet and its prolonged deficiency in body either due to inadequate intake or to some other reason may manifest itself by scaliness of skin, retarded growth, lack of reproductive abilities and keratinization of cornea\(^5\), and also predisposes the deficient individual to the invasion of some other diseases and increases susceptibility to carcinogenesis\(^6\). This problem is of more significance in infants and young children suffering from Kwashiorkor or marasmus. Accordingly, present project was planned to investigate the effect of chronic administration of phenobarbitone, aspirin and oxytetracycline on the plasma levels of vitamin A in body.

MATERIALS AND METHODS

Animals
Thirty-two, 65-70 days old albino rats of mixed sex were randomly divided into four groups A, B, C and D, kept in a room maintained at 28°C during the experimental period, and fed synthetic diet as shown in Table.
Group A was kept as normal while groups B, C and D, respectively, were fed Aspirin (250 mg/kg), phenobarbitone (1 mg/kg) and oxytetracycline (250 mg/kg) daily for 30 days. Weekly blood samples were drawn from each group by cardiac puncture under anaesthesia for the estimation of plasma vitamin.

**Plasma Vitamin A**

Plasma vitamin A was estimated by modifying the TLC method. TLC glass plates were coated with silica gel G and calcium phosphate (1:1) of 3mm thickness, dried in air, and then activated in an oven. Plasma samples were spotted on these plates which were then developed in cyclohexane and ether (3:1). After air drying these plates were sprayed with molybdophosphoric acid in ethanol and heated at 120 °C for 15-20 minutes until a greyish blue colour developed. The colour spot was scratched and diluted with cyclohexane-ether by centrifugation. The supernatant was then read at 340 nm after setting the spectrophotometer at zero with blank. A standard curve was constructed by plotting the graph between absorbance values against their respective vitamin A concentrations (Figure 1).

**TABLE. Composition of diet given to experimental rats.**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maize starch</td>
<td>52</td>
</tr>
<tr>
<td>Glucose</td>
<td>20</td>
</tr>
<tr>
<td>Potato starch</td>
<td>5</td>
</tr>
<tr>
<td>Casein</td>
<td>12</td>
</tr>
<tr>
<td>Vegetable ghee</td>
<td>10</td>
</tr>
<tr>
<td>Vitamin and mineral premix</td>
<td>1</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION
The average weekly plasma vitamin A level of the treated and normal groups is shown in Figure 2.
The results indicate that the rats in group C fed on phenobarbitone had low plasma vitamin A level whereas the rats of groups B and D treated with aspirin and oxytetracycline respectively did not exhibit such effects, as compared to the normal rats of group A. It can be seen that the phenobarbitone in therapeutic doses, gradually lowers plasma vitamin A level. The phenobarbitone at the end of 1st, 2nd, 3rd and 4th week of the experimental period induced 8, 21, 34 and 50 percent decrease in plasma vitamin A level. The decrease of vitamin level observed by other workers is more evident in rats of younger age at the same dosage level of phenobarbitone. Statistical analysis revealed that phenobarbitone significantly reduced the vitamin A level at the end of 4th week whereas oxytetracycline and aspirin administration did not and it was non-significantly different from that found in the rats of control group A. Our findings are in contrast to that reported by Mingilev in which lowered plasma levels of vitamin A were observed after oxytetracycline administration in chickens, which may be due to species difference. The concentration of vitamin A at the end of 4th week of treatment in group C fed on phenobarbitone was 55 i.u. (16.5 ug) per 10ml of blood, a subnormal level in rats. At this level the signs of vitamin deficiency were not evident. However this much level for longer periods of time is reported to have caused decaying and anatomical deterioration of the rods outer segment in humans. The rats kept in a similar condition for 10 months developed ultrastructural changes leading to blindness. The mechanism by which phenobarbitone affects vitamin level in blood is not completely understood but it probably depletes the liver (storehouse) of vitamin A and enhances

**Figure 2. Average weekly vitamin A level (i.u./100ml of plasma) of rats treated with aspirin, phenobarbitone and oxytetracycline.**
its release, consequently leading to increased excretion from the body\textsuperscript{3}.

\section*{REFERENCES}