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Effects of dietary poly-unsaturated fatty acids on the β-adrenergic receptor reactivity in the guinea pig respiratory system

C. Loesberg, G. Folkerts, F. M. A. Woutersen-van Nijnanten and F. P. Nijkamp

Institute of Veterinary Pharmacology, Pharmacy and Toxicology, Dept. of Pharmacology, State University of Utrecht, P.O. Box 80176, 3508 TD Utrecht, The Netherlands

Introduction

Dietary poly-unsaturated fatty acids (PUFA's) are able to influence fatty acid profiles in guinea pig lung membranes [1]. Modulations of membrane fatty acids may affect β-adrenergic receptor adenylate cyclase coupling, probably by altering membrane micro-viscosity [2]. Moreover, modulations in membrane fatty acids may lead to alterations in the production of their metabolites, the prostanoids. These prostanoids (prostaglandins, leukotrienes) in their turn may interfere in β-adrenergic receptor regulation.

In the first series of experiments it was investigated whether variations in dietary linoleic acid contents were able to affect the β-adrenergic receptor function of guinea pig tracheal spirals, *in vitro*. Deliberately a very moderate variance in dietary regimen under strictly controlled experimental conditions was chosen. Next it was investigated if the effects observed in the first experiments were due to linoleic acid itself or to effects of PUFA's in general.

Methods

60 Male guinea pigs weighing between 195 and 210 gram were divided randomly into three dietary groups immediately after weaning. Each group was fed a semi-synthetic diet (35 energy%) that slightly differed in the amount of linoleic acid being present (6, 12 and 22% respectively). Fats were added as vegetable oils. Water and food were given *ad libitum*. After a six week period cumulative dose response curves for the β-adrenergic receptor agonist isoprenaline were made on isolated tracheal spirals, *in vitro*. Animals were given (i.p.) a lethal dose of 0.5 ml/100 g body weight of pentobarbital sodium (Nembutal). Subsequently tracheas were removed, cut in a spiral fashion and mounted into an organ bath [3]. After an equilibrium period isoprenaline was added to the organ bath and relaxations were measured using an isotonic transducer.

Results and discussion

The cumulative dose response curves for isoprenaline showed a maximal relaxation in the dietary group receiving 12% linoleic acid. Dose response curves of the other two groups (3% and 22% linoleic acid respectively) showed a significantly diminished response ($P < 0.01$; two way ANOVA). Maximal relaxation was significantly ($P < 0.01$) decreased (18% and 19% respectively as compared to the 12% linoleic acid group). To analyse whether the observed differences were due to a specific linoleic acid effect, five alternative diets (35 en%) were selected that all consisted of a minimal amount of 3% linoleic acid, but differed in the amount of other PUFA's being present (Table 1).

Maximal relaxation was observed again in the dietary group with 12% linoleic acid (group 3). In the dietary groups 1 and 2 receiving less linoleic acid (3 and 6% respectively) dose response curves

Table 1
Isoprenaline induced (maximal) relaxation of guinea pig isolated tracheal spirals in 5 dietary groups.

Group	Dietary Pufa's			Max. relaxation (% of group 3)
	Linoleic acid 18:2 (n–6)	Linolenic acid 18:3 (n–3)	Fish oil (20+22):>3	
1	3	–	–	76
2	6	–	–	75
3	12	–	–	100
4	3	3	–	87
5	3	–	3	84

were significant diminished ($P < 0.01$, two way ANOVA) relative to that of the 12% linoleic acid group. Maximal relaxation being decreased 24% and 25% respectively. No differences were observed between dietary groups 1 and 2, indicating that administration of 3% additional linoleic acid to a diet already containing 3% linoleic acid had no effect. Administration of 3% linolenic acid or 3% fish oil (fatty acids that have more double bonds than linoleic acid) however, resulted in a significant ($P < 0.05$; two way ANOVA) increase in relaxing capacity, as compared to the 3% linoleic acid group. Dose response curves of these dietary groups (groups 4 and 5) however, were still significantly ($P < 0.05$, two way ANOVA) below that of the dietary group with 12% linoleic acid. Maximal relaxations of groups 4 and 5 were decreased 13% and 16% respectively, as compared to group 3. In both experiments no effect of the different dietary regimens on weight gain or food intake could be detected.

In conclusion:

1. Slight modifications of dietary PUFA's exerted profound effects on β-adrenergic receptor function in guinea pig trachea.
2. An optimal β-adrenergic receptor function requires an optimal amount of dietary fatty acid.
3. The effect of PUFA's on the β-adrenergic receptor response is dependent on the amount of dietary PUFA as well as on the degree of unsaturation of the fatty acids present in the diet.

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