Effects of physical training on plasma levels of thromboxane (TXB₂) in patients on hemodialysis

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ABSTRACT: Thromboxane (TXA₂) is a catabolic product of arachidonic acid which is produced mainly in the cellular membranes of human cells activated by phospholipase A₂. Thromboxane is also produced in small quantities non-enzymatically via rearrangement of isoprostanate endoperoxide atoms. TXA₂ is an unstable, yet very active biomolecule. It induces platelets accumulation and incorporation and has a vasoconstrictive action on the smooth muscle fibers of the vessels. Very soon after its production, thromboxane is hydrolysed in TXB₂, which is a stable but inactive biomolecule.

The levels of TXB₂ in the plasma are increased in patients with a variety of diseases, including patients with chronic renal failure who are under chronic periodic hemodialysis. However, there is no information about plasma changes of TXB₂ in hemodialysed patients who exercise mildly (on a special biodynamic bicycle) during the hemodialysis session.

We have studied 20 normal subjects (NS), 13 men and 7 women, aged 47.4 ± 7.2 years and 34 patients with chronic renal failure who were on hemodialysis. Our subjects were divided into two groups, TN and TN/ERG. The TN group consisted of 20 patients, 13 men and 7 women, aged 55.8 ± 10.5 years; group TN/ERG consisted of 14 patients, 9 men and 5 women, aged 56.1 ± 7.9 years. The TN/ERG group patients participated for a period of 6 months in a physical exercise program of 30-60 min, using an ergonomic bicycle during hemodialysis. In normal subjects and hemodialysed patients, before and after hemodialysis, plasma levels of TXB₂ were measured by a sensitive modern enzyme immunoassay method.

According to our measurements, the TXB₂ levels in the plasma of patients on hemodialysis, before and after hemodialysis, who were following a physical training program, were lower than the equivalent values of hemodialysed patients who were not following this physical training program. This result constitutes an additional evidence that controlled physical activity induces beneficial biochemical changes in the hemodialysed patients.

Key words: Thromboxane, Hemodialysis, Exercise.

INTRODUCTION

Thromboxane A₂ (TXA₂) is a catabolic product of Arachidonic Acid (A.A.). A.A. is released from the cellular membranes of human cells (platelets, macrophages, glomerular mesangial cells e.t.c.) by phospholipase A₂. It is converted to prostaglandin endoperoxides under the effect of cyclo-oxygenase (endoperoxide synthase). Endoperoxides are then converted to prostaglandins (PGs), prostacyclin (PGI₂) and thromboxane A₂ (TXA₂). Besides that, TXA₂ is produced in vivo and non-enzymatically by free radical - catalyzed lipid peroxidation via isoprostane endoperoxides rearrangement¹-⁴. Being a potent platelet aggregating and very efficient vasoconstrictor agent, TXA₂ is an antagonist to prostacyclin. It is believed that physiological balance between the two components plays an important regulatory role in the maintenance of normal vascular tone and in the pathogenesis of various cardiovascular disorders. In the kidney, TXA₂ causes marked renal vasostriction and thus enhanced renal TXA₂ production reduces renal blood flow and glomerular filtration rate. Enhanced TXA2 production has been described in a number of kidney diseases. Furthermore, TXA₂ has

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been implicated in various inflammatory or immunological renal diseases. Since TXA₂ is rapidly converted to thromboxane B₂ (TXB₂), a chemically stable but biologically inactive hydration product, thromboxane synthesis of biological tissues has been monitored by measuring TXB₂.²⁻²³

In vitro and in vivo experiments have demonstrated thromboxane production by kidney cells, lung cells, skin cells, liver cells, connective tissue cells, etc. The measurement of the plasma levels of TXB₂ gives useful information on: a) the evaluation of the effects of pharmacologically active substances capable of decreasing TXA₂ synthesis, b) the hemorrhagic or thrombo-embolic conditions and their follow up during treatment, c) blood abnormalities, either congenital or acquired and d) the disturbance of platelet function in the course of atherosclerosis, diabetes, chronic renal failure and vascular diseases associated or not to inflammatory states.⁶⁻¹³

The plasma levels of TXA₂ are increased in patients with Chronic Renal Failure (CRF), but there is no information about the plasma levels of TXB₂ in CRF patients on hemodialysis (HD), who were following a physical training program during the hemodialysis.

Purpose

The purpose of this study was to evaluate the plasma levels of TXB₂ in CRF patients on hemodialysis who were following a physical training program during the hemodialysis.

MATERIAL AND METHOD

We monitored 20 normal humans, 13 males and 7 females, aged 47.4 ± 7.2 years old (N.H. group) and 34 CRF patients on hemodialysis, who were separated into two groups: HD and HD/EXER. The HD group consisted of 20 patients on hemodialysis, 13 males and 7 females, aged 55.8 ± 10.5 years old; the HD/EXER group consisted of 14 patients, 9 males and 5 females, aged 56.1 ± 7.9 years old who followed a program of physical training during hemodialysis. TXB₂ levels were measured in the plasma of the healthy individuals and the CRF patients on HD (before and after HD) by the sensitive enzymoimmunoassay method (EIA) with KITTS from R and D systems (www.randd-systems.com). The performance characteristics of this EIA method are as follows:

a) Sensitivity: The sensitivity was 8 pg/ml.
b) Precision: The intra and inter assay coefficient of variation (CV) was 3.6% and 7.7% respectively.
c) Specificity: The TXB₂ antiserum, which is used in this assay, was quite good, bound to: TXB₂ 100%, 2.3 dinor TXB₂ 7.5% and of the A.A. metabolites under 2%.

Exercise training rehabilitation program during hemodialysis

Group HD/EXER patients followed a 6-month rehabilitation program during the first two hours of their hemodialysis sessions under the supervision of two physical therapists. The training sessions took place 3 times a week for 60 minutes each time. Special stationary bicycles were moved up to the dialysis chairs or beds. Patients were cycling for 30 to 60 min and afterwards performed exercises for strength and flexibility for 15 to 30 minutes. The first 5 minutes consisted of warm-up, the second period consisted of physical training at desired workload (cycling and exercises), and the last 5 minutes consisted of cooldown. Exercise intensity was constantly corresponding to 13 (somewhat hard) of the Borg perceived exertion scale.

RESULTS

According to our measurements, the plasma levels of TXB₂ were as follows: a) In healthy individuals 87.5 ± 15.1 pg/ml. b) In patients before hemodialysis 606.0 ± 80.1 pg/ml with a statistically significant difference from the levels of healthy individuals (control group) (p < 0.001). c) In patients after hemodialysis, 438.8 ± 62.0 pg/ml with statistical significant difference from the levels of the healthy individuals, d) In patients before hemodialysis, who were on the physical training program, 498.8 ± 67.6 pg/ml, with statistical difference from the patients before hemodialysis who had not followed the physical training program (p < 0.05). e) In patients after hemodialysis, who were on the physical training program, 363.5 ± 52.5 pg/ml, with statistically significant difference than before hemodialysis (p < 0.01).

DISCUSSION

The plasma levels of TXB₂ of patients before hemodialysis were increased about 7 times above that of
Η επίδραση της ήπιας άσκησης στα επίπεδα του θρομβοξάνιον (TXB₂) αιμοκαθαρισμένων ασθενών

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ΠΕΡΙΛΗΨΗ: Το θρομβοξάνιον (TXA₂) είναι ένα καταβολικό προϊόν του αραχιδονικού οξέος, το οποίο παράγεται χωρίς στις καταρακτικές μεμβράνες των κατάρους του ανθρώπινου οργανισμού με τη δράση της ήπιας άσκησης. Το θρομβοξάνιον επίσης παράγεται σε μικρά ποσά, μη ενζιματικά, με αναδιάταξη των ατόμων των εναπόσπαστων του οσφυοστανίου. Το TXA₂ είναι ένα ασταθές, αλλά πολύ ενεργό βιομορφό. Προκαλεί συσσώρευση και συσσώματοποίηση των αιμοποιών και επιδεικνύει υψηλή δραστικότητα στις λείες μυών υπό τους ενζυμοι. Πολύ γρήγορα μετά την παραγωγή του υδρολύεται στο TXB₂, το οποίο είναι ένα σταθερό, αλλά ανενεργό βιομορφό.

Τα επίπεδα του TXB₂ στο πλάσμα είναι αυξημένα στους ασθενείς με ένα μεγάλο αριθμό παθολογικών καταστάσεων μεταξύ των οποίων συγκεκριμένα στους ασθενείς με χρόνια νεφρική ενδείξεια που κάνουν χρήση συνεχιζόμενων αιμοκαθαριστών. Ωστόσο, δεν υπάρχουν πληροφορίες για τις μεταβολές του TXB₂ στους αιμοκαθαριστέους ασθενείς που κάνουν ήπια άσκηση (σε εγκυτταρικό κατά τη διάρκεια της αιμοκαθαριστής).
Το υλικό μας το αποτέλεσαν 20 φυσιολογικά άτομα (Φ.Α.) 13 άνδρες και 7 γυναίκες ηλικίας 47,4 ± 7,2 χρόνων και 34 χρόνια αμικαθαρσμένοι ασθενείς, οι οποίοι χωρίζονταν σε δύο ομάδες ΤΝ και ΤΝ/ΕΡΓ. Την ημέρα ΤΝ την αποτέλεσαν 20 ασθενείς, 13 άνδρες και 7 γυναίκες, ηλικίας 55,8 ± 10,5 χρόνων και την ημέρα ΤΝ/ΕΡΓ 14 ασθενείς, 9 άνδρες και 5 γυναίκες, ηλικίας 56,1 ± 7,9 χρόνων. Οι ασθενείς της ομάδας ΤΝ/ΕΡΓ συμμετείχαν ακόμη και σε πρόγραμμα φυσικής άσκησης για 30-60 με ευθεία εργοδοτικά κατά τη διάρκεια της αμικαθάρτωσης τους. Στα φυσιολογικά άτομα και στους αμικαθαρσμένους ασθενείς (πριν και μετά την αμικαθάρτωση) μετρήθηκαν τα επίπεδα του TXB₂ στο πλάσμα με εναλλακτική σύγχρονη ενζυμοαναλυτική μέθοδο (ELA).

Από τις μεταβολές μας πρόσκεψε ότι τα επίπεδα του TXB₂ στο πλάσμα των αμικαθαρσμένων ασθενών πριν και μετά την αμικαθάρτωση ήταν σε πρόγραμμα φυσικής άσκησης βρέθηκαν χαμηλότερα από τα αντίστοιχα των αμικαθαρσμένων ασθενών που δεν ήταν σε πρόγραμμα φυσικής άσκησης. Αυτό αποτελεί μια επιπλέον αποδείξη ότι η επεξεργασία φυσικής άσκησης προκαλεί ενυδάτωση μεταβολών στα ασθενή άτομα.

Δέξεις Κλειδιά: Θρομβοβάθμιο, Αμικαθάρτωση, Φυσική Άσκηση.

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