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Nongenomic Effects of Aldosterone on Renal Protein Expressions of pEGFR and pERK1/2 in Rat Kidney

Kittisak Sinphitukkul[a] Somchit Eiam-Ong[b] Krissanapong Manotham[d]
Somchai Eiam-Ong[c]

[a]Inter-Department of Physiology, Graduate School, [b]Department of Physiology, and [c]Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, and [d]Department of Medicine, Lerdsin General Hospital, Bangkok, Thailand

Key Words
Aldosterone · Nongenomic action · pEGFR-pERK1/2 · Protein abundance · Immunohistochemistry · Rat kidney

Abstract
Background: In vitro studies have demonstrated that aldosterone elicits nongenomic actions by enhancing protein expressions of phosphorylated epidermal growth factor receptor (pEGFR) and phosphorylated extracellular signal-regulated kinases 1/2 (pERK1/2). There are no available in vivo investigations regarding this action of aldosterone on renal pEGFR-pERK1/2 protein expressions. ***Methods:*** Male Wistar rats received normal saline solution, low-dose (LA: 150 μg/kg BW) or high-dose aldosterone (HA: 500 μg/kg BW) by intraperitoneal injection. After 30 min, protein abundances and localizations of renal pEGFR and pERK1/2 were determined by Western blot and immunohistochemistry. ***Results:*** Plasma aldosterone levels were increased in LA and HA groups ($p < 0.001$). Aldosterone enhanced renal pEGFR and pERK1/2 protein abundances ($p < 0.001$). HA showed a greater stimulation on pEGFR immunoreactivity than LA in the glomerulus, vasa recta, and thin limb of Henle's loop in the inner medulla area. LA provided more reactivity of pERK1/2 in the thick ascending limb of Henle's loop, outer medullary collecting duct, and proximal straight tubule, whereas HA illustrated more pERK1/2 activation in the glomerulus, peritubular capillary, and inner medulla region. ***Conclusion:*** This is the first in vivo study which demonstrates that aldosterone, via the nongenomic pathway, could elevate pEGFR and pERK1/2 protein abundances and expressions in the rat kidney. These results indicate that aldosterone induces phosphorylation of EGFR upstream of ERK1/2.

Introduction

Aldosterone exhibits a major role in maintaining electrolyte balance via classical genomic actions by stimulation of sodium reabsorption, and potassium and hydrogen secretion by distal nephron, mediated through binding to the mineralocorticoid receptor [1, 2]. Following studies in kidney cell lines, native renal tubule, and whole animal clearly demonstrated the nongenomic effects of aldosterone on several ion transports along the renal tubule and renal vasculature function [3–5].

Recent studies in several tissues including kidney have indicated that the nongenomic actions of aldosterone involve the generation of various intracellular secondary

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Assoc. Prof. Somchit Eiam-Ong, PhD
Department of Physiology, Faculty of Medicine
Chulalongkorn University
Bangkok 10330 (Thailand)
Tel./Fax +66 2 256 4267, E-Mail EiamOng@netscape.net

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Short communication

Efficacy of tenofovir disoproxil fumarate/emtricitabine compared with emtricitabine alone in antiretroviral-naive HIV–HBV coinfection in Thailand

Anchalee Avihingsanon[1,2], Sharon R Lewin[3,4,5], Stephen Kerr[1,6], Judy J Chang[4], Komolmit Piyawat[7], Nounpen Napissanant[1], Gail V Matthews[6], Gregory J Dore[6], Scott Bowden[8], Joep Lange[9], Kiat Ruxrungtham[1,2]*

[1]HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand
[2]Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3]Infectious Diseases Unit, Alfred Hospital, Melbourne, Australia
[4]Department of Medicine, Monash University, Melbourne, Australia
[5]Centre for Virology, Burnet Institute, Melbourne, Australia
[6]National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, Australia
[7]Division of Gastroenterology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[8]Victorian Infectious Diseases Reference Laboratory, Melbourne, Australia
[9]Centre for Poverty-Related and Communicable Diseases, Amsterdam, the Netherlands

*Corresponding author e-mail: Anchalee.A@hivnat.org

Background: Therapy for chronic hepatitis B with tenofovir disoproxil fumarate (TDF) and lamivudine (3TC) or emtricitabine (FTC) is currently recommended for HIV–HBV coinfection. However, there is limited randomized data on the efficacy of combined therapy with TDF and FTC, especially in antiretroviral (ARV)-naive patients.

Methods: This was a prospective randomized clinical trial comparing the efficacy of HBV monotherapy with FTC versus TDF/FTC combination therapy in ARV-naive HIV–HBV coinfection. HIV–HBV-coinfected patients initiating ARV were randomized to either FTC/zidovudine/efavirenz (EFV; *n*=6) or TDF/FTC/EFV (*n*=10). The primary end point was the time-weighted area under the curve (TWAUC) of HBV DNA at 48 weeks.

Results: The median baseline CD4$^+$ T-cell count was 64 cells/μl (interquartile range [IQR] 36–172), plasma HIV type-1 RNA was 4.90 $\log_{10}$ copies/ml (IQR 4.58–5.44) and plasma HBV DNA was 8.76 $\log_{10}$ copies/ml (IQR 8.45–8.82). A total of 11/16 (69%) patients were hepatitis B e antigen (HBeAg)-positive. The median TWAUC decrease in HBV DNA was -5.32 $\log_{10}$ copies/ml in the TDF/FTC group compared with -3.25 $\log_{10}$ copies/ml in the FTC group (*P*=0.03). At week 48, 90% of the TDF/FTC group and 33% of the FTC group had plasma HBV DNA<170 copies/ml (*P*=0.036, intention-to-treat analysis). HBeAg loss was observed in 4/11 (36%) HBeAg-positive patients. Hepatic flares were observed in 3/16 (19%) of patients.

Conclusions: TDF/FTC combination therapy resulted in a significantly greater decrease in HBV DNA than FTC monotherapy, with a greater proportion of patients with undetectable HBV DNA at week 48. Our study supports the current recommendation of ARV containing TDF/FTC as the treatment of choice for patients with HIV–HBV coinfection.

Introduction

Chronic HBV is a major coinfection in HIV-infected patients in Africa and Asia, where both HIV and HBV are prevalent. HIV infection modifies the natural course of HBV leading to accelerated liver disease progression, increased liver-related morbidity [1] and increased rates of antiretroviral (ARV)-related hepatotoxicity [2]. Treatment for both HIV and HBV are usually initiated simultaneously and treatment is generally life-long. Current HIV treatment guidelines recommend the use of combination therapy, including two HBV-active nucleoside/nucleotide analogues for any HIV–HBV-coinfected patient initiating antiretroviral therapy (ART). The most commonly used HBV-active nucleoside/nucleotide analogues that are also active against

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ORIGINAL ARTICLE

Randomized trial of two different doses of pyridoxine in the prevention of capecitabine-associated palmar-plantar erythrodysesthesia

T CHALERMCHAI,[1] K TANTIPHLACHIVA,[2] H SUWANRUSME,[1] N VORAVUD[1] and V SRIURANPONG[1]

[1]*Medical Oncology Unit, Department of Medicine and* [2]*Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Abstract

***Aim*:** The aim of the present study was to compare the efficacy of 200 mg versus 400 mg daily of pyridoxine in preventing or delaying the onset of palmar-plantar erythrodysesthesia (PPE) in capecitabine-treated patients.

***Methods*:** Patients with histologically confirmed breast cancer or colorectal cancer receiving single agent capecitabine started at 2000 to 2500 mg/m^2 daily from day 1 to 14 every 3 weeks were randomly assigned to receive 200 mg or 400 mg daily of pyridoxine for PPE prophylaxis. The primary endpoint was the reduction of incidence of grade 2 or greater PPE. Secondary endpoints were reduction of severe PPE and prolongation of time to development of grade 2 or greater PPE.

***Results*:** There were 56 patients in this study. The baseline characteristics were generally similar in both groups. The high dose arm had less PPE than the low dose arm (11 of 28 or 39% *vs* 20 of 28 or 71%, relative risk = 0.26 [0.08, 0.79], $P = 0.031$). Grade III PPE developed in 3 of 28 (10.7%) versus none in patients receiving 200 mg versus 400 mg pyridoxine, respectively (relative risk 2.12 [1.594, 2.819], $P = 0.24$). High dose pyridoxine had a longer time to development of grade 2 or greater PPE compared to the low dose arm, 87 days versus 62 days. The 400 mg pyridoxine group had, however, a worsened tumor response and tended to have greater tumor treatment failure and shorter time to treatment failure.

***Conclusion*:** With the limitation of sample size in this study, there was a trend to improve PPE incidence and time to event with a higher dose of pyridoxine. Further validation of these results in a larger population is warranted.

Key words: capecitabine, palmar-plantar erythrodysesthesia, pyridoxine.

INTRODUCTION

Palmar-plantar erythrodysesthesia (PPE) is a distinctive cutaneous reaction that is most commonly induced by cytotoxic chemotherapy.[1–4] The first report of PPE caused by mitotane treatment was described by Zuehlke in 1974.[5] PPE was subsequently reported in various publications using different terms, such as hand-foot syndrome, acral erythema, and Burgdorf's reaction.[6,7] Many drugs have been implicated as a cause of PPE. Doxorubicin, liposomal doxorubicin, docetaxel and fluoropyrimidine are common PPE-associated chemotherapeutic agents.[1–3,8] The clinical presenting symptoms usually begin with dysesthesia and tingling sensation of both palms and soles. After a few days, swelling and erythema of the skin occurs with some burning sensation or pain. Some patients develop severe cutaneous reactions, such as bullous

Correspondence: Dr Narin N Voravud MD, Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
Email: dr.narin@hotmail.com

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Low vegetable intake is strongly associated with venous thromboembolism in Thai population

Lantarima Bhoopat[a], Ponlapat Rojnuckarin[a], Narin Hiransuthikul[b] and Tanin Intragumtornchai[a]

Recent studies have demonstrated a much higher incidence of venous thromboembolism (VTE) among Asian patients compared with previous studies. This study aims to determine dietary and behavioral factors that may have contributed to this increase. A case-control study was conducted. Cases were objectively confirmed VTE between 2006 and 2009 at King Chulalongkorn Memorial Hospital. Patients with underlying cancer, antiphospholipid syndrome and arterial thrombosis were excluded. Controls were age and sex-matched healthy volunteers. Food consumption was assessed using a food frequency questionnaire modified from the Thailand National Health Examination Survey III previously validated in the Thai population. There were 97 cases and 195 controls. The mean age was 54.6 years and 70% were women. VTE patients consumed significantly less vegetable, fish and spicy food compared with normal individuals with an odds ratio (OR) for venous thrombosis of 3.74 [95% confidence interval (CI) 2.24–6.26, $P<0.001$], 2.05 (95% CI 1.24–3.41, $P=0.005$) and 2.30 (95% CI 1.29–4.11, $P=0.01$), respectively. Additionally, thrombosis was associated with overweight (OR 2.1, 95% CI 1.21–3.62, $P=0.002$), obesity (OR 3.1, 95% CI 1.46–6.74, $P=0.001$) and estrogen uses (OR 3.7, 95% CI 1.05–13.2, $P=0.02$), but not with smoking or lack of exercise. A multivariate analysis showed that low vegetable consumption (OR 3.74, 95% CI 1.85–7.55, $P<0.001$), female hormones (OR 5.80, 95% CI 1.51–22.22, $P=0.011$) and body mass index (BMI, $P=0.048$) were independently associated with VTE. Low vegetable intake, hormonal use and high BMI are the risk factors for noncancer-related VTE in Thai population. *Blood Coagul Fibrinolysis* 21:758–763 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: deep vein thrombosis, diet, estrogen, obesity, venous thromboembolism

[a]Department of Medicine and [b]Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Correspondence to Ponlapat Rojnuckarin, MD, PhD, Department of Medicine, King Chulalongkorn Memorial Hospital, Rama IV Rd, Patumwan, Bangkok 10330, Thailand
E-mail: rojnuckarinp@gmail.com

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Introduction

Two large objective studies in the past demonstrated that the incidence of perioperative venous thromboembolism (VTE) among Thais was 10 times less than that of the Western population [1,2]. More recent data in Asian patients, however, clearly indicate that VTE is currently very common and approaching the rate in Caucasians [3,4]. A combination of multiple factors, both genetic and environmental, contributes to the pathogenesis of venous thrombosis [5]. Hereditary factors are likely to be unchanged and, therefore, acquired risk factors including cancer, immobilization and estrogen use have been implicated. For instance, studies in Thai VTE patients revealed that active cancer was the most important risk factors contributing to 19–40% of cases [6,7]. Nevertheless, the causes of thrombosis in the majority of patients remain to be determined. The aim of this study is to investigate the basis of the marked epidemiological change in our country.

Diet and lifestyle are the prime suspects. During the past decades, there has been an apparent transformation of behavior. A recent survey discovered a low fruit and vegetable consumption, below the daily recommended levels, in the Thai population [8]. Furthermore, the prevalence of obesity has greatly increased among Thais [9]. The role of behavioral factors has been extensively studied in Western populations. A prospective cohort of 14 962 Western people over 12 years found that a greater fish, fruit and vegetable, as well as lower red meat consumption, was related to a lower incidence of VTE [10]. This may partly be due to high blood homocysteine levels from excessive methionine-containing food, such as eggs and meat, and deficiency in vitamin B_6 and folate. Hyperhomocysteinemia is responsible for both arterial and venous thrombosis [11–15]. In addition to food composition, regular exercise could potentially prevent VTE [16,17]. In the same direction as these studies, high body mass index (BMI) and metabolic syndrome are also associated with VTE [17,18]. Furthermore, a recent cohort study in Swedish women disclosed that moderate alcohol intake and heavy smoking decreased and increased venous thrombosis incidence, respectively. Nevertheless, similar investigations in Asians are still lacking. The diet and lifestyle of different ethnic population are certainly disparate. Therefore,

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International Diabetes Federation

Brief report

Clinical characteristics of diabetic ketoacidosis in newly diagnosed adult patients

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Yotsapon Thewjitcharoen *, *Sarat Sunthornyothin*

Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine, Chulalongkorn University Rama IV Rd, Bangkok 10330, Thailand

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ABSTRACT

A retrospective review was conducted of medical records of newly diagnosed diabetes in adults who presented with DKA between 2003 and 2007. The majority of DKA in Thailand could not be classified as classical type 1 diabetes. Some newly diagnosed people presenting with DKA could be safely withdrawn from insulin treatment.

1. Introduction

Diabetic ketoacidosis (DKA) is a serious hyperglycemic emergency in patients with type 1 and type 2 diabetes. In contrast to common belief, several studies have shown that DKA is more common in adults than in children. In one community-based study [1], more than 40% of patients with DKA were older than 40 years and more than 20% older than 55 years.

Since the mid 1990s, an increasing number of ketoacidosis episodes without precipitating factors have been reported in obese African American patients [2–5]. Following episodes of ketosis these patients could be safely treated with oral agents or diet only. This atypical form of diabetes is now recognized as a subtype of ''syndromes of ketosis-prone diabetes'' [6] and this form of diabetes appears to be increasingly recognized worldwide in the past decade [7–9].

Little is known about the type of Thai diabetic patients who present with DKA as an initial presentation. This study aimed to elucidate the clinical characteristics of newly diagnosed diabetic patients admitted with DKA in a tertiary care hospital.

2. Materials and method

The authors performed a retrospective analysis of hospital admissions for DKA in people with newly diagnosed diabetes age ≥16 years admitted to the department of internal medicine in King Chulalongkorn Memorial Hospital (KCMH) between January 2003 and December 2007. Patients with secondary diabetes from pancreatic disease or drug-induced diabetes were excluded.

Laboratory data on arrival were reviewed and patients were included if each of the following criteria was fulfilled: plasma

* *Corresponding author*. Tel.: +66 02 256 4246.
E-mail address: kamijoa@hotmail.com (Y. Thewjitcharoen).

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Lipiodol as a marker for hepatocellular carcinoma migrating into the bile duct

Transarterial chemoembolization (TACE) is an effective palliative treatment for unresectable hepatocellular carcinoma (HCC). However, several complications of TACE have been reported, including transient fever and pain after the procedure, hepatic infarction, liver abscess, hepatic failure, biliary stricture, and biloma [1 – 3], although acute obstructive cholangitis due to migration of the necrotic tumor after TACE is very rare. We report two cases of acute cholangitis secondary to biliary migration of necrotic hepatocellular carcinoma, both of which were diagnosed pre-endoscopically by computed tomography (CT) scan of the abdomen. Lipiodol stain was used as a marker for necrotic tumor migration.

Our first patient was a 63-year-old man who had undergone three sessions of TACE without any complications. Subsequently, a new lesion was identified adjacent to the previous lesion and a percutaneous ultrasonography-guided liver biopsy was done just before the fourth session of TACE. However, 1 day later the patient developed fever with progressive jaundice. A CT scan of abdomen showed a tiny, hyperdense spot obstructing the common bile duct (CBD). The spot was of the same density as the Lipiodol stain in the liver (**Fig. 1**). Another hyperdense spot was also detected in the intestinal lumen (**Fig. 2a, b**). Endoscopic sphincterotomy and balloon removal were carried out, and 1 month after endoscopic retrograde cholangiopancreatography (ERCP), another abdominal CT scan demonstrated disappearance of Lipiodol stain (**Fig. 3**).

Our second patient, a 63-year-old man with known HCC, presented with acute cholangitis within 3 weeks of TACE. A CT scan of the abdomen showed intraluminal Lipiodol stain in the distal CBD and a small Lipiodol stain in the stomach (**Fig. 4a, b**). On day 1 after the procedure, his symptoms, including fever and abdominal pain, resolved spontaneously and subsequently serum total bilirubin also decreased. A repeat CT scan of the abdomen did not reveal any Lipiodol stain in the gastrointestinal tract.

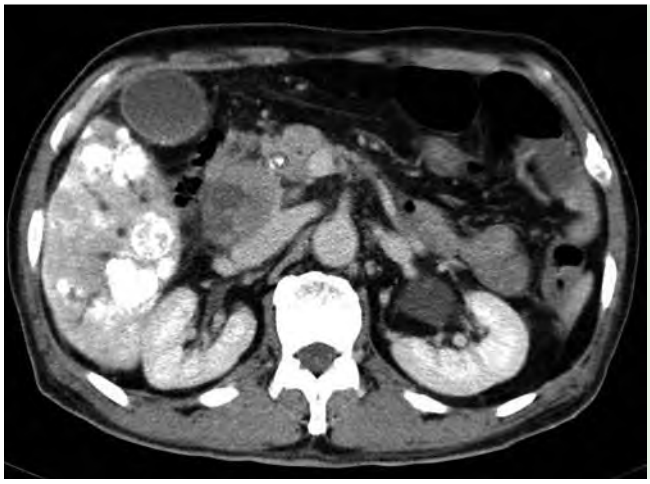


Fig. 1 Computed tomography (CT) scan of the abdomen showing a tiny, hyperdense spot in the distal common bile duct.

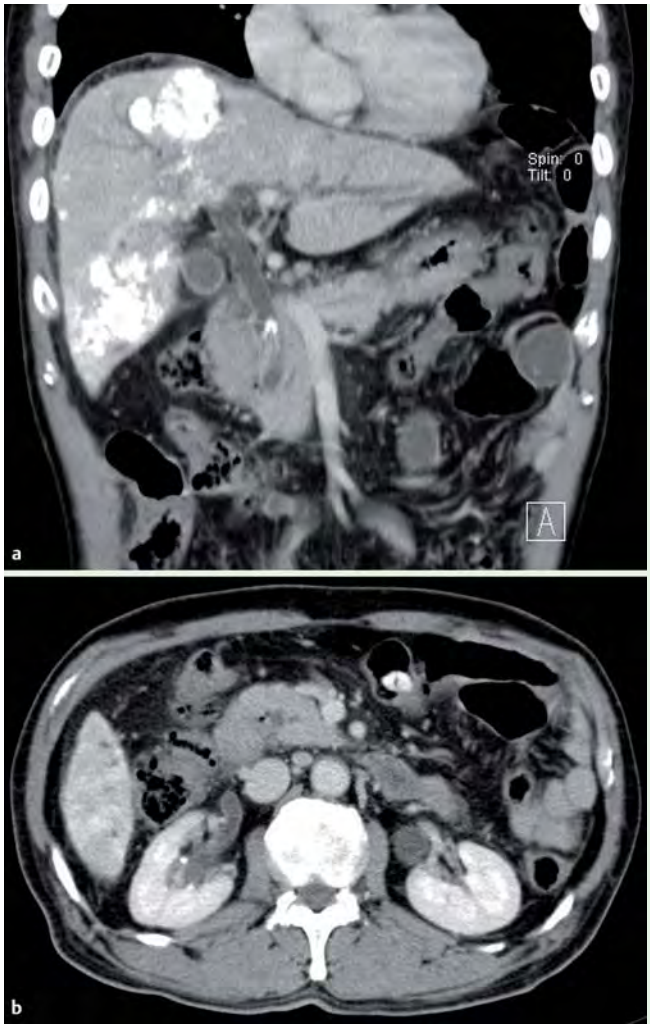
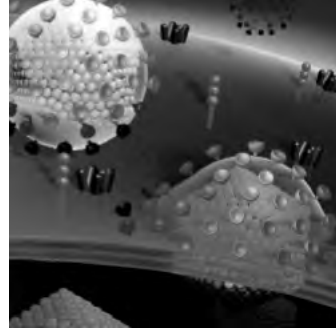


Fig. 2 **a** Coronal section computed tomography (CT) scan taken 1 day after chemoembolizaion and liver biopsy showing a hyperdense spot in the common bile duct. **b** Another hyperdense spot is seen in the intestine.

Competing interests: None

no IF



The 13th Bangkok International Symposium on HIV Medicine

The 13th Bangkok International Symposium on HIV Medicine, Queen Sirikit National Convention Centre, Bangkok, Thailand, 20–22 January 2010

Each January, the HIV Netherlands-Australia-Thailand Research Collaboration (HIV–NAT) organizes this symposium on HIV medicine. The symposium aims to present a comprehensive review of the management of HIV infection to physicians from Thailand and the Asia-Pacific region. This review includes updates on antiretroviral therapy, new research and efforts to improve access to care. The major sponsors were the Foundations for AIDS Research through its TREAT Asia Initiative, Australia's National Centre in HIV Epidemiology and Clinical Research and Thailand's National Health Security Office, IDS Marketing, Bristol Myersquibb and Merck & Co, Inc. The Symposium attracts more than 500 participants from Thailand, Laos, Myanmar, Vietnam, Cambodia, Indonesia, India, Singapore, Hong Kong, Taiwan, China, Bangladesh, Papua New Guinea, Australia, The Netherlands and South Korea.

Reshmie Ramautarsing†, Pirapon June Ohata, Anchalee Avihingsanon, Stephen J Kerr, Jintanat Ananworanich, Somporn Chatbuddhiwet, Nadia Kancheva Landolt, Chris Duncombe, Wasana Prasitsuebsai, Thanyawee Puthanakit & Kiat Ruxrungtham

†Author for correspondence:
The HIV Netherlands, Australia, Thailand Research Collaboration (HIV-NAT), 104 Ratchadamri Rd, Bangkok, 10330 Thailand
Tel.: +66 2652 3040
Fax: +66 2252 5779
reshmie.r@hivnat.org

Morning plenary sessions covered antiretroviral therapy (ART) for adults and children in resource-limited settings, HIV prevention and eradication, and challenges in HIV care. Afternoon interactive workshops explored adult and pediatric management, drug resistance and the laboratory in HIV care. During The Great Debate, viral load testing as part of first-line ART monitoring was addressed. Slides from the plenary sessions can be downloaded at [1].

HIV prevention

David Celentano (Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, MA, USA) presented an overview of biomedical prevention studies. Studies exploring HIV vaccines, microbicides and HSV-2 suppressive therapy showed disappointing results, but other interventions have been more successful. Circumcision and prevention of mother-to-child transmission (PMTCT) have been shown to be effective, but both have shortcomings, such as the lack of benefit of circumcision for the female partners of HIV-infected men and drug resistance in infants after exposure to HAART for PMTCT. It is important to promote combination preventative methods. The basic HIV prevention package should include education, outreach, voluntary counseling and testing, condom promotion and STI treatment and care.

ART in adults

Andrew Hill (University of Liverpool, UK) discussed d4T. At present, 3 million people are treated with a Stavudine (d4T)-containing regimen, mostly in developing countries. The first dose ranging trials showed similar efficacy at 20 mg twice daily (b.i.d) and 40 mg b.i.d doses, with much higher rates of peripheral neuropathy at 40 mg b.i.d. In 1995, the US FDA approved the 40(30) mg b.i.d dose: 40 mg b.i.d when the body weight is more than 60 kg and 30 mg b.i.d when the body weight is less. Subsequently, several low dose studies were conducted; 30 mg b.i.d was better tolerated and had equivalent rates of HIV RNA suppression. In 2007, the WHO recommended 30 mg b.i.d for all patients. Hill raised the question of whether a lower dose of d4T should be investigated: 30 mg b.i.d for those weighing more than 60 kg and 20 mg b.i.d for those weighing less. d4T is a potent and inexpensive drug. The ability to reduce cost and side effects of d4T may serve as a treatment option for resource-limited settings.

Pediatric & adolescent care

Pediatric HIV treatment was discussed by Thanyawee Puthanakit (Chulalongkorn University, Thailand). An important achievement is the progress made in providing access to care among children in resource-limited settings. Worldwide, the PMTCT coverage increased from 10% in 2004 to 45% in 2008, and pediatric ART coverage increased from 10% in 2005 to 38% in 2008. The current goal is to achieve universal access. Puthanakit gave an overview of ongoing key studies on pediatric HIV treatment. The results of two studies

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RESEARCH PAPER

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An HIV-1 clade A/E DNA prime, recombinant fowlpox virus boost vaccine is safe, but non-immunogenic in a randomized phase 1/11a trial in Thai volunteers at low risk of HIV infection

Atchriya Hemachandra,[1,†] Rebekah L. Puls,[2,*,†] Sunee Sirivichayakul,[3] Stephen Kerr,[1,2] Pattarawat Thantiworasit,[3] Sasiwimol Ubolyam,[1] David A. Cooper,[2,4,5] Sean Emery,[2] Praphan Phanuphak,[1] Anthony Kelleher[2,4,5] and Kiat Ruxrungtham[1,3,6]

[1]HIV-NAT; Thai Red Cross AIDS Research Centre; Bangkok, Thailand; [2]National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, Australia; [3]Vaccine and Cellular Immunology Laboratory; Chulalongkorn Medical Research Centre (CHULA-MRC) and Division of Allergy and Clinical Immunology, Bangkok, Thailand; [4]Immunology and Infectious Diseases Clinical Services Unit; St. Vincent's Hospital; Sydney, Australia; [5]National Centre in HIV Epidemiology and Clinical Research; University of New South Wales; St. Vincent's Centre for Applied Medical Research; Darlinghurst, Australia; [6]Department of Medicine; Faculty of Medicine; Chulalongkorn University; Bangkok, Thailand

[†]These authors contributed equally to this work.

Key words: HIV, AIDS vaccine, DNA/fowlpox, clinical trial, Thailand

Abbreviations: BSA, body surface area; CMV, cytomegalovirus; CTL, cytotoxic T lymphocytes; DSMB, data safety monitoring board; ICS, intracellular cytokine staining assay; mAbs, monoclonal antibodies; pHIS-HIV-AE, AE clade DNA vaccine; pHIS-HIV-B, B clade HIV vaccine; rFPV-HIV-AE, AE clade recombinant fowlpox HIV vaccine; rFPV-HIV-AE, B clade recombinant fowlpox HIV vaccine; SEB, staphylococcal enterotoxin B

Background: Previously demonstrated safe and highly immunogenic in non-human primates, this study assessed DNA (pHIS-HIV-AE) prime, recombinant fowlpox (rFPV-HIV-AE) boost vaccines in humans.

Results: Eight participants (6 active vaccine, 2 placebo) received all vaccinations; local and systemic reactions were mild to moderate. The percentage $CD4^+$ and $CD8^+$ T cells responding to HIV-1 Gag antigens by ICS (mean ± SD) was 0.16 ± 0.12 and 0.10 ± 0.12 for active and 0.01 ± 0.01 and 0.00 ± 0.00 for placebo vaccine respectively. The percentage of T cells responding did not reach pre-defined thresholds to be considered positive responses. Consequently, the Data Safety Monitoring Board recommended cessation of further recruitment. Existing volunteers were followed to 52 weeks.

Methods: Vectors expressing homologous HIV-1 clade A/E gag, pol, env and regulatory genes or matched placebo were administered intramuscularly at weeks 0, 4, 8 (6 mg pHIS-HIV-AE) and week 12 (3.0×10^8 pfu rFPV-HIV-AE) in this randomized, double-blind, placebo-controlled phase I/IIa study in healthy Thai adults at low risk of HIV infection. Immunogenicity was determined by interferon-gamma and IL-2 expression using intracellular cytokine staining assay (ICS), 13 weeks after randomization. Interim analysis was performed when eight volunteers reached 16 weeks follow-up.

Conclusions: Vaccine candidates were generally well tolerated, but showed limited immunogenicity. Better vaccines and delivery systems are required.

Introduction

Since 1992, extensive national education and prevention programs in Thailand have lead to a substantial decline in HIV prevalence, including in women attending antenatal clinics, military recruits and in certain groups of commercial sex workers.[1,2] The number of infections in Thailand has fallen, from a peak of approximately 143,000 new infections per year in 1991 to around 14,000 new infections estimated for 2006.[2,3] Current data suggest that these new infections are in injecting drug users and women infected by their husbands or sexual partners.[2] In addition, 17.3% and 28.3% of men who had sex with men were HIV-positive in Thai Ministry of Public Health surveys conducted in Bangkok in 2003 and 2005, respectively and in 2006, only 19.2% reported always using a condom with sexual partners in the previous three months.[4]

Although effective treatments for HIV infection exist with reasonable availability in Thailand, prevention remains the most sustainable strategy to curb the HIV-1 pandemic. A safe and effective vaccine for HIV-1 infection is urgently needed. Intensive

*Correspondence to: Rebekah L. Puls; Email: rpuls@nchecr.unsw.edu.au
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A census of movement disorders at a Thai university hospital

Roongroj Bhidayasiri [a,b,*], Karn Saksornchai [a], Lalita Kaewwilai [a], Kammant Phanthumchinda [a]

[a] Chulalongkorn Comprehensive Movement Disorders Center, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, 10330, Thailand
[b] Department of Neurology, Geffen School of Medicine at UCLA, Los Angeles 90095, USA

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Thailand

ABSTRACT

There is little information available on the number of patients with movement disorders seen by physicians in Thailand. The authors reviewed the medical records of all movement disorders patients seen at the Chulalongkorn Comprehensive Movement Disorders Center (CUMDS) in Bangkok, Thailand over a 4.5-year period to determine the number of patients with movement disorders and disease characteristics. A total of 1993 patients were assessed at CUMDS. Most of these patients had a diagnosis of parkinsonism (72%), including Parkinson's disease (PD) (60.9%), followed by tremor (9.6%), and dystonia (8.4%). The diagnostic accuracy of PD according to United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria was 90.3%. The average referral period waiting for the consultation was more than 2 years. In spite of the limited availability of medical resources in Thailand, patients with movement disorders tend to seek specialist care and most often it is indicated. This finding documents the need for awareness of PD and other movement disorders by health professionals in Thailand, including the need for specialized training in movement disorders for physicians, including neurologists.

1. Introduction

Although the subspecialty of movement disorders has been established in neurology for more than 20 years, it is relatively new in Thailand and there are only a few clinics dedicated to movement disorders in the country. The Chulalongkorn Comprehensive Movement Disorders center (CUMDS) was recently established by the Thai Red Cross Society as the main tertiary care center in Thailand specializing in the treatment and study of Parkinson's disease (PD) and various other movement disorders. Currently, the center is staffed with two full-time board-certified neurologists with fellowship training in movement disorders, two clinical fellows, three clinical and research nurses, and two support personnel. A multidisciplinary approach is taken in the care of patients with movement disorders and there is strong collaboration between the Center and Neurosurgery, which has an active deep brain stimulation program, Psychiatry, Rehabilitation and the laboratories.

In a recent survey of 2326 PD patients who attended the Parkinson's Disease Awareness Day, organized by the CUMDS and the Thai Red Cross Society on 10 July 2010, more than 90% of the patients indicated that they would like to be seen by a specialist in movement disorders. However, fewer than 30% of PD patients who attended the event had ever consulted a neurologist. This is consistent with other surveys which show that most PD patients in Thailand are treated by general internists without specialty training in neurology. 63% of patients who completed the survey live outside of Bangkok and have to commute to PD clinics for their follow-up visits, which usually require a trip to the city every three months.

Since the establishment of the Center in 2005, there has been a large increase in the number of referred patients from all over the country. With a staff of seven (two fellowship trained in movement disorders, two fellows in movement disorders, two nurses, and one study coordinator) operating three movement disorders outpatient clinics at CUMDS, we provided 2855 movement disorders consultations in 2007, 2957 consultations in 2008, and 2753 consultations in 2009. Despite this increasing number of movement disorders consultations provided since the opening of the Center in 2005, there has been a concurrent increase in demand so that we have adopted a referral-back policy in which uncomplicated movement disorders patients are transferred back to their primary physicians for follow-up. With this approach, we have been successful in reducing the number of new patients on the waiting list by more than 20% per year. Nevertheless, this situation indicates that there are still a large number of patients suffering from movement disorders who may not be able to get the specialist care they need, even after such a long waiting period, because of the following realities:

- Limited access — very few PD clinics are available and they are located only in major cities,
- Availability — there are only 278 board-certified neurologists in Thailand serving a population of 65 million populations, and

* Corresponding author. Chulalongkorn Comprehensive Movement Disorders Center Division of Neurology, Chulalongkorn University Hospital 1873 Rama 4 Road Bangkok 10330, Thailand. Tel.: +662 256 4627; fax: +662 256 4630.
E-mail address: rbh1@ucla.edu (R. Bhidayasiri).

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REVIEW

Major lupus organ involvement: severe lupus nephritis

Y Avihingsanon[1,2] and N Hirankarn[1,3]
[1]Lupus Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; [2]Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; and [3]Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Lupus nephritis is a common and severe complication of systemic lupus erythematosus. A number of patients have nephritis as a presenting feature that, in its severe form, can shortly lead to end-stage renal disease and/or death. Renal flare usually occurs a few years after the first episode and is remarkably predominant in the Asian population. Frequent monitoring for renal flare enhances early recognition and timely treatment. The mainstay therapy continues to be the prolonged use of cytotoxic/immunosuppressive drugs that have a number of undesirable effects, particularly ovarian failure and development of opportunistic infections. This review will focus on the pathogenesis and the unique genetic factors found in Asian patients with lupus nephritis. Here, we propose an appropriate management scheme for the treatment of lupus nephritis in Asian patients. *Lupus* (2010) **19,** 1391–1398.

Key words: Asia; genetic; immunosuppressive therapy; lupus nephritis

Introduction

Renal disease is a common and serious manifestation of systemic lupus erythematosus (SLE). The presentation can range from asymptomatic urinary abnormalities to rapidly progressive renal failure leading to end-stage renal disease (ESRD). Renal failure remains an independent risk factor for death in patients with lupus nephritis (LN). Currently available immunosuppressive regimens are toxic due to their broad immunosuppressive effects. Cyclophosphamide (CY) plus prednisolone is the standard regimen for the severe form of LN. However, this regimen has several side effects and, as SLE usually affects women of child-bearing age, one of its serious adverse effects, gonadal toxicity, is of concern. Nevertheless, evidence from randomized controlled trials supports the use of CY as a remission induction therapy as it appears to have advantages in early therapeutic response and dramatically improves long-term outcomes.[1]

Unfortunately, most of the therapeutic data on LN and SLE are not applicable to the Asian population because they were conducted in African-Americans and Caucasians. There is a need to assess the appropriate dosage and genetic variations in Asian patients to avoid unnecessary toxicities and financial expenditure. Even though the mortality rate of LN in Asia has improved since the 1980s[2] with a 5-year survival rate of 76.5%, which is similar to that of Western countries,[3–5] there can be room for improvement.

In order to improve the supportive care and kidney specific therapy for LN and SLE, it is important to first understand the pathogenesis of the disease. Hopefully this information will help us direct treatment to specific and appropriate areas of the body. Recent progress in LN treatment includes the use of monoclonal antibodies, anti-cytokine therapies and other components of the complement-system blockade.[6] An example of this treatment is mycophenolate mofetil (MMF) and its potential use as an alternative agent. Unlike CY, MMF has a more specific immunosuppressive action and, therefore, causes fewer adverse events than CY. However, MMF is expensive and, in the long run, may not be feasible in resource-limited settings. Therefore this paper will review the immunopathogenesis of LN and the appropriate treatment from an Asian perspective.

Epidemiological and clinical outcomes in Asia

In Asia, the prevalence rate of SLE (per 100,000) varies from 19.3 to 60.[7] A study conducted in the

Correspondence to: Yingyos Avihingsanon, Lupus Research Unit, Renal Division, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
Email: yingyos.a@gmail.com

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Prevalence and Risk Factors of Parkinson's Disease in Retired Thai Traditional Boxers

Praween Lolekha, MD, MSc,[1,2] Kammant Phanthumchinda, MD,[1] and Roongroj Bhidayasiri, MD, FRCP, FRCPI[1]*

[1]*Chulalongkorn Comprehensive Movement Disorders Center, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[2]*Neurology division, Faculty of Medicine, Thammasat University, Pathumthani, Thailand*

Abstract: Boxing is often believed to be a frequent cause for parkinsonism caused by chronic repetitive head injury, with Muhammad Ali frequently cited as an example. The purpose of this study is to determine the prevalence of Parkinson's disease (PD) in retired Thai traditional boxers. Two standardized screening questionnaires were sent to all registered Thai traditional boxers. Subjects who screened positive for parkinsonism were invited for clinical examinations by two independent neurologists. Among 704 boxers (70%) who completed the questionnaires, 8 boxers (1.14%) had parkinsonism: 5 with PD, 1 with progressive supranuclear palsy and 2 with vascular parkinsonism. Boxers with PD were found to have an older mean age than those without PD ($P = 0.003$). The analysis of probable risk factors disclosed an association between the number of professional bouts (>100 times) and PD ($P = 0.01$). The crude prevalence of PD in Thai boxers was 0.71% (95% CI: 0.09–1.33), with a significant increase with age. The prevalence rate of PD in those aged 50 and above was 0.17% (95% CI: 0.15–0.20), age-adjusted to the USA 1970 census, which is comparable to that of the general populations. The analysis determined that the number of professional bouts is a risk factor among these boxers, supporting the notion that repetitive head trauma may pose an additional risk to certain individuals who are already susceptible to PD. © 2010 Movement Disorder Society

Key words: parkinsonism; Parkinson's disease; boxer; punch-drunk syndrome; dementia pugilistica

The exact etiology of parkinsonism, including PD, remains obscure but continues to attract much interest and investigation. A small number of PD patients have been found to be susceptible to the disorder because of an inherited vulnerability but the vast majority of cases occur sporadically with no obvious causes. Several hypotheses have been proposed to account for the etiology of parkinsonism, including sporadic PD. The most frequently cited risk factors are exposure to environmental hazards such as specific toxins in chemicals used in agriculture, certain occupational risks, and prior infections.[1]

*Correspondence to: Dr. Roongroj Bhidayasiri, Chulalongkorn Comprehensive Movement Disorders Center, Faculty of Medicine, Chulalongkorn University Hospital, Bangkok 10330, Thailand.
E-mail: rbh1@ucla.edu

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Chronic traumatic brain injury associated with boxing has long been linked etiologically to PD with the well-known trait of "Punch-drunk syndrome" or "Dementia pugilistica" that sometimes develops in boxers as a result of long-term subclinical concussions.[2–4] Despite this suggestion, there is a paucity of evidence to support this hypothesis. Thai traditional boxing has been a popular sport in Thailand for more than a century, encompassing different styles, practices, and regulations. Retired Thai traditional boxers, therefore, are an appropriate population in which to determine the role of chronic traumatic brain injury in parkinsonism, particularly PD, and to measure its prevalence.

SUBJECTS AND METHODS

Sample Selection

All registered retired boxers from the Sports Authority of Thailand, the Boxer's Club of Thailand and the

Priya Jagota, MD
Roongroj Bhidayasiri, MD, FRCP, FRCPI*
Department of Medicine
Chulalongkorn Comprehensive Movement Disorders Center
Faculty of Medicine
Chulalongkorn University and King Chulalongkorn Memorial Hospital
Thai Red Cross Society
Bangkok, Thailand
E-mail: rbh1@ucla.edu

Lingual Myoclonus Secondary to Bilateral Cortical Strokes in a Probable Case of Antiphospholipid Syndrome

Video 

Lingual myoclonus is a rare disorder, often of unknown etiology. A few cases of rhythmic myoclonic movements of the tongue[1–5] have been reported with other movement disorders such as a palatal myoclonus[6] because of brainstem lesions,[3–5] whereas others have no detected structural abnormalities.[1,2] This report describes a case of nonrhythmic lingual myoclonus after bilateral cortical strokes for which the patient was vulnerable as a corollary of probable antiphospholipid syndrome.

CASE REPORT

A 26-year old Thai woman was referred to our clinic to investigate the cause of repeated strokes. The precipitating event was drooling upon awakening 2 months earlier, accompanied by slurred speech. She had a history of nephrotic syndrome and had been treated with prednisolone and cyclophosphamide for 9 years, until she was lost to follow-up 2 years before the drooling episode. A CT scan of the brain after the onset of drooling showed a hypodense lesion at the right frontoparietal area. Ten days later her symptoms subsided, but after 3 weeks she was again unable to speak normally. Subsequent CT scans of the brain showed an additional hypodense lesion at the frontal and insular areas, but on the left side. There were no lesions in the brainstem or cerebellum.

On examination, the patient was found to be alert with bilateral lower facial weakness consistent with an upper motor neuron lesion and was severely dysarthric. Examination of the tongue revealed bilateral, nonrhythmic, asymmetric, and jerky movements involving the entire tongue. There were no voluntary and reflexive movements of the tongue. In addition, she had bursts of eyelid myoclonia. There was no dysphagia, no weakness of the limbs, and no abnormal movement of the palate. Sensory, deep tendon reflexes and cerebellar examinations were entirely normal.

A MRI of the brain showed hypersignal intensity of bilateral frontotemporal and insular areas on T1, T2, and fluid-attenuated inversion recovery (FLAIR) images without fluid restriction on diffusion-weighted images (Fig. 1a–d). A MRA of the cerebral vessels revealed irregularities of left internal carotid artery and left middle cerebral artery. Electromyography (EMG) of the genioglossi showed nonrhythmic bursts of activities consistent with myoclonus, the duration of which was <50 ms (Fig. 1e). Median nerve somatosensory evoked potential (SEP) showed low N20 amplitude on both sides, correlating with bilateral cortical lesions, but there was no giant SEP. Electroencephalography and visual evoked potentials were normal. Blink reflexes and auditory brainstem evoked responses (ABERs) were normal, suggesting intact brainstem pathways.

Protein C, protein S, antithrombin III and fibrinogen levels, and anticardiolipin IgG and IgM were all normal except for a positive lupus anticoagulant test. Carotid duplex ultrasonography did not reveal atherosclerotic plaque or significant stenosis. Echocardiography showed anterior and anteroseptal wall hypokinesia, but coronary angiography did not show significant coronary artery disease. From the laboratory results and two recent strokes, antiphospholipid syndrome was suspected and the patient was treated with hydroxychloroquine and warfarin.[7]

One year after initiating treatment, the patient was able to speak more clearly, protrude and move her tongue sideways, and the severity of lingual myoclonus was decreased. No further medication was given to treat the lingual myoclonus. Eyelid myoclonia was not ameliorated by the treatment regimen and it persisted.

DISCUSSION

The patient had lingual myoclonus because of arterial thromboses that resulted in infarction of bilateral cortical areas involving the homuncular representation of the tongue (Fig. 1). The propensity for strokes was due to probable antiphospholipid syndrome.

The cortical origin of lingual myoclonus in our case was supported by EMG of the tongue revealing bursts of myoclonic discharges of <50 ms in duration. Furthermore, the

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lower than the authors ascertained, these results are in line with the message emerging from epidemiological studies over the last decade: hyperuricemia, the metabolic condition that underlies gout, is an independent risk factor for cardiovascular disorders. Indeed, a recent meta-analysis showed that hyperuricemia increases the risk of coronary heart disease incidence by 9% and mortality by 16%.[4]

What pathophysiological mechanisms can explain these epidemiological observations? There are currently two main hypotheses: the first is based on the effects of hyperuricemia on blood pressure, and the second is based on the vascular changes that occur secondary to chronic systemic inflammation, a state that occurs in inflammatory joint diseases including gout. In gout, used in the study by De Vera *et al.* as a clinical surrogate for hyperuricemia, which mechanism is more responsible for the apparent increase in cardiovascular risk? In other words, is the reported increase in cardiovascular risk attributable to hyperuricemia or to having clinical gout? Hyperuricemia is known to be more common in men than women; however, serum urate levels rise in women after menopause, although in the general population these levels are still lower than they are in men. Hyperuricemia might predispose individuals to cardiovascular disease because it has pro-oxidant effects on vascular smooth muscle cells,[5] and it can decrease the availability of endothelial nitric oxide.[6] If the mechanism underlying the effects of hyperuricemia on the cardiovascular system are mediated by hypertension, then adjustment for this risk factor should abolish the association; however, this was not the case in the study by De Vera *et al.*,[2] since hypertension was among the cardiovascular risk factors accounted for in the multivariate analyses.

If gout itself contributes an additional cardiovascular risk, is this effect explained by the inflammatory state caused by the deposition of monosodium urate crystals? During an acute attack of gout, inflammatory mediators are released and vascular adhesion and chemotaxis of leukocytes to the inflamed joint is enhanced.[7] However, for this to have an impact on cardiovascular health would require a sustained period of inflammation, probably over years. Are occasional attacks of gout sufficient to drive inflammation that modifies cardiovascular and endothelial function? One would expect that there would be incremental gains in cardiovascular risk with a longer history of gout, an increased frequency of gouty attacks and with the presence of tophi. In the De Vera *et al.* study, information about these disease features was lacking, and the poor case definition of the gouty population leaves much to be desired.

> **"What pathophysiological mechanisms can explain these epidemiological observations?"**

Finally, the effect of gout on the incidence of AMI was more striking in women than men[2]—is there a biological explanation? Studies of hyperuricemia have found that genetic influences are not equal between the sexes, and that the effect of genetic variation within *SLC2A9*, which encodes a glucose and urate transporter in the kidney, on serum urate levels was more pronounced in women than men.[8,9] De Vera and colleagues did not provide data on hyperuricemia, so it is impossible to state, on the basis of their results, that a clinical diagnosis of gout represents an additional risk beyond that attributable to hyperuricemia.

As is generally the case with epidemiological studies, this study gives provocative suggestions for new avenues of clinical investigation but does not present clear disease mechanisms. Researchers in cardiovascular medicine, rheumatology, inflammation and other disciplines must now take up the challenge and identify what it is about hyperuricemia and gout that impacts on cardiovascular health.

Rheumatology Service, Department of Musculoskeletal Medicine, Avenue Pierre Decker, CHUV, 1011 Lausanne, Switzerland.
alexanderkai-lik.so@chuv.ch

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Competing interests
The author declares an association with the following company: Novartis. See the article online for full details of the relationship.

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PHARMACOTHERAPY

Is there a place for leflunomide in the treatment of RA?

Manathip Osiri

The nonbiologic DMARD leflunomide was approved for use in the treatment of rheumatoid arthritis in 1998. After being in use for more than a decade, which has also seen the introduction of highly effective biologic agents, a review of the benefits and risks of leflunomide therapy sheds light on the role of this drug in the treatment arsenal.

Advances in knowledge about the pathogenesis of rheumatoid arthritis (RA) have led to the development of targeted therapies that act directly on inflammatory cytokines or cell-surface molecules. Biologic agents are the mainstay of treatment for RA as they can induce disease remission. The use of nonbiologic DMARDs, especially leflunomide, declined rapidly after the introduction of tumor necrosis factor (TNF)-blocking agents. Nonetheless, leflunomide has now been licensed for use in RA for more than a

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Tetrahydrocurcuminoid Cream Plus Targeted Narrowband UVB Phototherapy for Vitiligo: A Preliminary Randomized Controlled Study

Pravit Asawanonda, M.D., D.Sc., and Siri-On Klahan, M.D.

Abstract

Objective: The aim of this study was to compare the efficacy of targeted narrowband UVB phototherapy plus topical tetrahydrocurcuminoid with that of targeted narrowband UVB monotherapy for induction of repigmentation in vitiligo. ***Background Data:*** The 308-nm excimer laser and targeted narrowband UVB phototherapy have recently been shown to be effective in repigmenting vitiligo. Studies have suggested that the combination of the 308-nm excimer laser and various topical treatments is more effective than UV monotherapy in the treatment of vitiligo. ***Materials and Methods:*** Ten subjects with focal or generalized vitiligo were enrolled in this study. Two similar lesions were treated with either targeted narrowband UVB plus topical tetrahydrocurcuminoid cream or targeted UVB alone. The UV treatments were carried out twice a week for 12 weeks. The degree of repigmentation, documented by monthly digital photography, was assessed by a blinded dermatologist. ***Results:*** On completion of the study, statistically significant repigmentation, compared with baseline, occurred in both treatment groups. The overall degree of repigmentation was slightly better in the combination group at 8 and 12 weeks ($p = 0.078$ and 0.158 respectively). Adverse effects were minor and well tolerated. ***Conclusion:*** Targeted narrowband UVB phototherapy plus topical tetrahydrocurcuminoid cream was slightly more effective than targeted narrowband UVB monotherapy for vitiligo located in UV-sensitive areas. However, the differences in degrees of repigmentation did not reach statistically significant levels.

Introduction

Curcumin (diferuloylmethane), a component of the roots of turmeric (*Curcuma longa*), is widely used as a food ingredient in various parts of Asia and Central America. Since ancient times, it has also been used for the treatment of a range of conditions, from rheumatism to intestinal worms, from diarrhea to constipation, from amenorrhea to skin diseases, including leukoderma.[1] This is not at all surprising given the various in vitro effects this natural orange-yellow compound possesses, e.g., increasing chymotrypsin-like activity in keratinocytes cell lines,[2] immunomodulatory,[3] anti-inflammatory,[4,5] antioxidant,[4,5] as well as radioprotective effects.[6] It is also known to enhance wound healing.[7]

More recently, curcumin has again received much interest in a wide variety of inflammatory and non-inflammatory diseases including diabetes, cardiovascular diseases,[8] arthritis, and psoriasis, among others. And most recently, because curcumin exerts immunomodulatory, pro-apoptotic, and antiangiogenic properties,[9,10] it has also received tremendous interest as cancer chemopreventative[11–13] and neuroprotective agents.[14]

Vitiligo is a common depigmenting skin condition of which pathogenesis involves a greatly varied array of mechanisms. One of the currently held theories is the overloading of oxidative stress within melanocytes, resulting in the disappearance of these important cells from the epidermis. The anti-inflammatory effect of curcumin mediated through its ability to inhibit cyclooxygenase-2 (COX-2), lipoxygenase, and inducible nitric oxide synthase (iNOS),[5] plus the fact that it also protects the skin by quenching free radicals and reducing inflammation through nuclear factor-KB inhibition, makes this compound attractive as a treatment for this depigmenting condition.

Curcumin is safe even when consumed in large quantities.[15,16] However, due to poor absorption, rapid metabolism, and rapid systemic elimination, very small amounts may reach the skin.[16] Moreover, when applied topically, curcumin's yellow-orange color makes it cosmetically unappealing. Recently, a colorless derivative of curcuminoid, tetrahydrocurcuminoid (THC), could be produced. The

Division of Dermatology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

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Spectrum of tardive syndromes: clinical recognition and management

Roongroj Bhidayasiri,[1,2] Suthida Boonyawairoj[1]

[1]Chulalongkorn Comprehensive Movement Disorders Center, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
[2]Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

Correspondence to
Roongroj Bhidayasiri, Chulalongkorn Comprehensive Movement Disorders Center, Division of Neurology, Chulalongkorn University Hospital, Bangkok 10330, Thailand; rbh1@ucla.edu

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ABSTRACT

Tardive syndrome (TS) refers to a group of delayed onset disorders characterised by abnormal movements and caused by dopamine receptor blocking agents (DRBAs). Classical tardive dyskinesia is a specific type of oro-buccal-lingual dyskinesia. However, TS may exist in other forms—for example, stereotypy, dystonia, and akathisia—and frequently occur in combination. The onset typically is insidious and after reaching its maximum severity it often stabilises. Frequently reported risk factors are age, dose and duration of neuroleptic exposure, the use of conventional DRBAs, and co-existing mood disorders. This review highlights the broad spectrum of TS, not limited to classical tardive dyskinesia, as well as the clues for its recognition. Despite challenges in the treatment of TS, dictated by the different phenomenology, severity of TS and the need for ongoing neuroleptic treatment, the authors provide evidence based recommendations for patient management, which is not restricted to only withdrawal of the offending neuroleptics or the selection of an alternative medication, such as clozapine. In a minority of cases with significant functional disability, symptomatic or suppressive treatments should be considered. Recently, there has been a resurgence of stereotactic pallidal surgery for the treatment of TS. Although the efficacy of both pallidotomy and pallidal deep brain stimulation in dystonia has been encouraging, the evidence is still limited.

The 'discovery' of tardive dyskinesia (TD) occurred more than five decades ago, about 5 years after the introduction of neuroleptic drugs into psychiatry. The original description of persistent abnormal involuntary movements induced by neuroleptic agents was published in a paper by Schonecker in 1957.[1] Since then, the phenomenon of TD alerted physicians and the public to its iatrogenicity and to its medicolegal impact, further enhancing clinical awareness of a potential negative and delayed impact of these useful drugs on the nervous system. While tardive syndromes (TS) encompass all aspects of abnormal movements, tardive dyskinesia (TD) specifically refers to classical oro-buccal-lingual dyskinesia associated with 'piano playing' finger movements. The involuntary movements of various phenomenology associated with neuroleptic agents are classified as TS, including classic oro-buccal-lingual dyskinesia, stereotypy, dystonia, akathisia, tics, myoclonus, tremor, and parkinsonism. TS is now accepted as a separate and unique entity as a result of the principal adverse effect of long term treatment with conventional antipsychotic agents. In this review, we discuss the clinical issues related to TS, including clinical recognition of various phenomenologies of TS, not limited to TD, and the practical management of this condition. Basic common principles of management of TS are also provided. When possible, preventive measures should be considered such as avoiding the use of neuroleptics when alternative treatments are available, limiting the course of neuroleptic treatment, and carefully watching for the earliest signs of TS. Once TS has developed, therapeutic choices often include the discontinuation of neuroleptics in patients with TS (if possible), and a determination of which medications may be considered for suppressing TS. In medically intractable cases, severe disability may force the need for chemodenervation or surgical intervention.

CLASSIFICATION OF TS

TD refers to a group of disorders characterised by predominantly late onset and sometimes persistent involuntary movements (or a sensation of restlessness), which are caused by exposure to dopamine receptor blocking agents (DRBAs). The first international congress of movement disorders defined TD as a hyperkinetic movement that develops during treatment with neuroleptics or within 6 months of stopping the offending agent, and it must persist for at least 1 month after discontinuing all neuroleptics. A somewhat different definition by the American Psychiatric Task Force requires 3 months of exposure to a DRBA for diagnosis of TD.[2 3] The *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) criteria specifies the shortest duration of exposure to DRBAs of at least 1 month in individuals ≥60 years. The French term 'tardive' is used to denote its late onset during the course of neuroleptic therapy, and 'dyskinesia' refers to unnatural movements which may or may not be involuntary. Generally, TD does not appear until after 1 or 2 years of continued neuroleptic treatment, and almost never before 3 months. Because virtually all types of movement disorders have been associated with neuroleptic therapy, and this identical clinical syndrome can be induced by other agents in addition to neuroleptics (box 1), the term 'tardive dyskinesia' is confusing and problematic. Traditionally and historically, the term 'tardive dyskinesia' was used to describe a specific type of movement, characterised by oro-buccal-lingual dyskinesias.[4] There are several phenomenological distinct types of abnormal movements and they are classified into classical tardive dyskinesia, tardive stereotypy, tardive dystonia, tardive akathisia, tardive tremor, tardive myoclonus, and tardive tourettism (box 2).[5] It remains unclear if tardive

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Original Article

Does CPAP treatment in mild obstructive sleep apnea affect blood pressure? ☆

Nattapong Jaimchariyatam [a,b,*], Carlos L. Rodriguez [b], Kumar Budur [b]

[a] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
[b] Sleep Disorders Center, Neurological Institute, Cleveland Clinic, Cleveland, OH, USA

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ABSTRACT

Objectives: Obstructive sleep apnea (OSA) is associated with significant cardiovascular (CV) morbidity. Continuous positive airway pressure (CPAP) is the standard treatment for moderate to severe OSA, resulting in a reduction in CV morbidity. No studies have compared CV outcomes between CPAP and no CPAP in mild OSA ($5 \geqslant AHI < 15$).
Methods: Retrospective cohort study of subjects (age $\geqslant 18$) with mild OSA diagnosed between 2004 and 2006. Subjects with a history of hypertension, angina, stroke and smoking were excluded. Subjects were stratified into two groups: CPAP ($n = 93$) or no CPAP ($n = 162$). The mean blood pressures (MBP) were compared 2 years after the diagnosis of OSA was established.
Results: Unmatched for covariates (age, sex, BMI, neck circumference, AHI, arousal index and family h/o CV disorders), subjects with mild OSA on CPAP had a 1.97 point reduction, and no CPAP resulted in a 9.61 point elevation ($p < 0.0001$) in MBP. With propensity score matching for covariates, the mean difference in MBP was −1.97 (95% CI: −14.03, −9.92; $p < 0.0001$) with a sensitivity analysis of 2.646.
Conclusion: This study shows an elevation of the MBP in mild OSA patients who were not treated with CPAP. CPAP treatment in mild OSA patients decreased the MBP over a 2-year period.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a common disorder and the prevalence has been estimated to be 4% in middle-aged men and 2% in middle-aged women [1]. It is characterized by repetitive partial or complete obstruction of airflow during sleep resulting from pharyngeal collapse with resultant increases in intrathoracic pressure, hypoxemia and sleep disruption. Temporally related elevations in blood pressure have been seen in association with oxygen desaturations, arousals, sympathetic activation [2,3], and alterations in the renin–angiotensin–aldosterone system [4]. Heightened sympathetic tone is also present during normal waking hours in many OSA patients [5,6]. These autonomic and hormonal alterations have been known to cause sustained daytime hypertension and ultimately other cardiovascular and cerebrovascular morbidities [7–9]. Observational and longitudinal studies have shown that hypertension and OSA often coexist, and OSA is possibly an independent etiologic factor for hypertension [7,10–13]. Although many studies have found an association between moderate to severe obstructive sleep apnea syndrome and cardiovascular morbidity or neurocognitive deficits, more recent evidence suggests that even mild obstructive sleep apnea syndrome may be correlated with hypertension and neurocognitive deficits [14–18].

Although there is clear evidence supporting the use of continuous positive airway pressure (CPAP) in patients with moderate to severe OSA, recent studies have also revealed a role for CPAP in the treatment of mild OSA with improvement in daytime sleepiness, fatigue and neurocognitive function [14–16,18]. In regard to hypertension, CPAP acutely reduces sympathetic activation and nocturnal blood pressure (BP) in OSA patients [5,19,20]. A number of studies have demonstrated that short-term (2–24 weeks) use of CPAP reduces BP levels in patients with moderate to severe OSA [14,21–35]. There have been no studies to date that have compared

Abbreviations: OSAS, obstructive sleep apnea syndrome; EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; TST, total sleep time; PSG, polysomnogram; AHI, apnea–hypopnea index; RDI, respiratory disturbance index; AI, arousal index; PLMI, periodic limb movement index; PLMAI, periodic limb movement arousal index; BMI, body mass index; CPAP, continuous positive airway pressure; REM, rapid eye movement; SPSS, statistical package for the social sciences; EOG, electrooculogram; EMG, electromyogram; ECG, electrocardiogram; SpO2, pulse oxygen saturation; WASO, wake after sleep onset; CVS, cardiovascular system.

☆ The institution: This research was conducted at the Cleveland Clinic Sleep Disorders Center, Neurological Institute, Cleveland Clinic, Cleveland, OH, USA.

* Corresponding author at: Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, 1873 Rama IV Road, Phathumwan, Bangkok 10330, Thailand. Tel.: +66 2256 4252/4246; fax: +66 2250 8890/2256 4563.
E-mail addresses: drboy48@yahoo.com (N. Jaimchariyatam), RODRIGC2@ccf.org (C.L. Rodriguez), ksbudur@yahoo.com (K. Budur).

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