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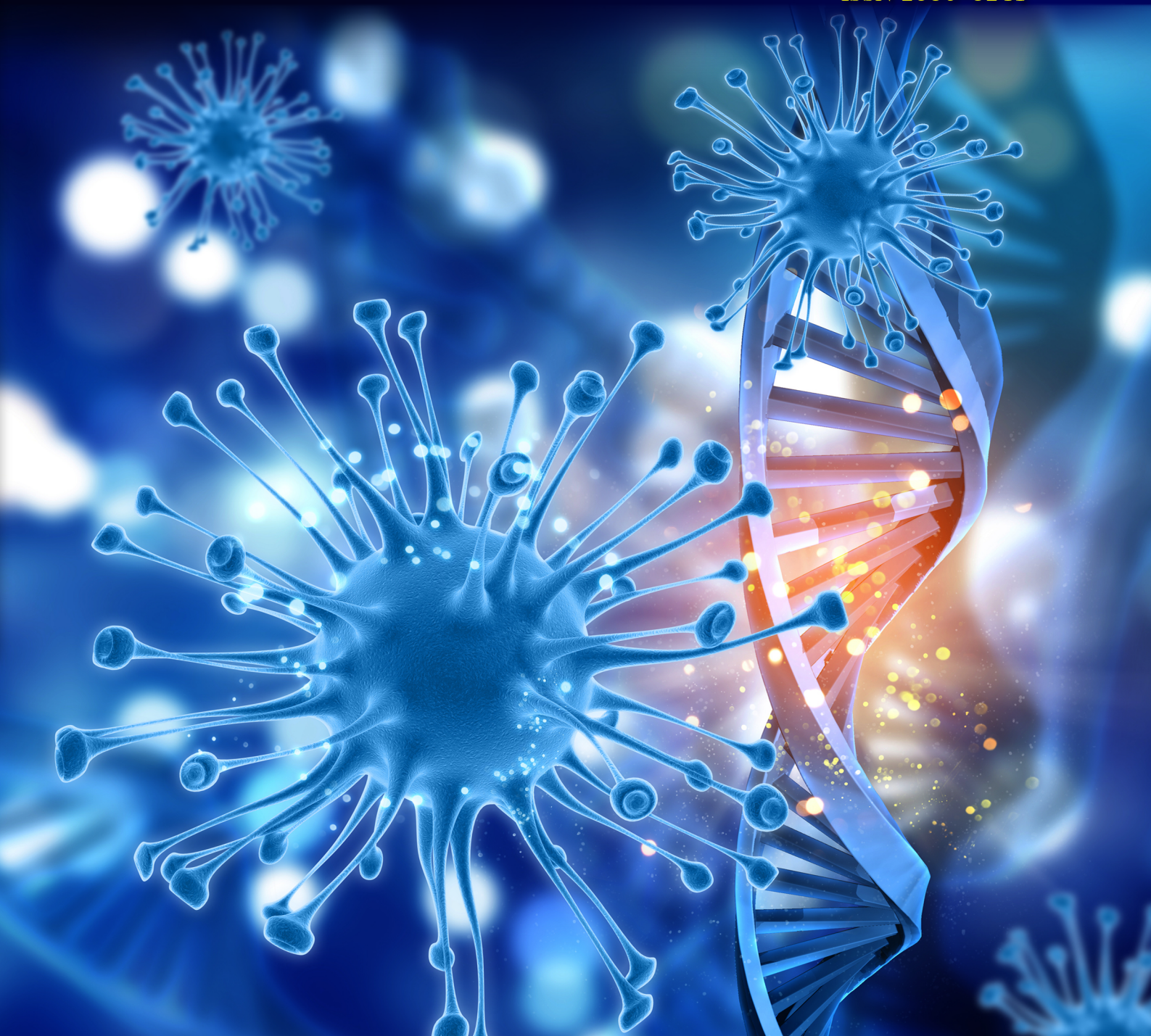

Introduction

The Journal of Southeast Asian Medical Research is a peer-reviewed journal with printing every 6 months. The main goal of this collaboration project is to distribute new knowledge in medical sciences to medical communities and scientists, as well as encouraging scientific collaborations within Southeast Asia and also other nations around the world. The journal publishes original research in the medical sciences: clinical and basic. We welcome original articles from across the world. The editorial board consists of international experts in various fields of medicine, ranging from internal medicine to a variety of surgeries. The full text of the journal is available online at http://www.jseamed.org

It is our aim to publish the most up-to-date and useful research information in medical sciences. In Southeast Asia, there are some unique problems in health care and diseases, such as tropical diseases, and it is crucial that health professionals can access, share and exchange knowledge promptly. In this region, there is still a gap of knowledge in health sciences that needs to be closed by scientific research, which we are hoping to close after this collaboration project. We hope that the journal will fulfill the objectives and will provide benefit to all, both medical practitioners and researchers alike.

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CONTENTS

A.Original Article

EFFECTS OF ULTRAVIOLET C (UVC) LIGHT AND DRY HEAT ON FILTRATION PERFORMANCE OF N95 RESPIRATOR MASK

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Abstract

Background: The emergence of the Coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) creates one of the most pressing issues with a severe shortage of personal protective equipment (PPE) particularly N95 respirators in healthcare settings worldwide. Recently, possible strategies to decontaminate disposable N95 respirators, including using ultraviolet C (UVC) irradiation and heat treatment, were reported to consider safely reusing the respirators. However, both methods create potential risks to reduce the ability of the respirator filter especially when exposed to these methods multiple times resulting in infectious agents passing through the filter.

Objective: The study aimed to ensure the effectiveness of UVC and dry heat to decontaminate N95 respirators.

Methods: N95 respirators were exposed continually to UVC and dry heat at 70°C. Then the ability of the aerosol penetration was assessed by introducing an aerosol containing a rotavirus used as a delegate for SARS-CoV2. The existence of the rotavirus at both external (front) and internal surfaces (back) of the N95 respirators was investigated using RT-PCR.

Results: UVC and dry heat administered at a 30-minute cycle up to 5 cycles did not change the filtration performance of the N95 respirators. Our results suggested that the reuse of disposable N95 respirators decontaminated by either UVC or dry heat could be possible under the test conditions used.

Conclusion: To reuse N95 respirators, UVC and dry heat were useful to apply amid the pandemic of respiratory diseases.

Keywords: COVID-19, N95 respirator mask, Ultraviolet C, Dry heat

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of an infectious respiratory disease named coronavirus disease 2019 (COVID-19).[1] Due to the increase in the number of cases and expansion of geographic areas, WHO has declared the global spread of COVID-19 as pandemic.[2] To date, no effective vaccination and specific antiviral treatment for COVID-19 is available.[3] Therefore, this infectious respiratory disease is of critical concern for health-care workers facing the high risk of exposure to infection with SARS-CoV-2. According to current evidence, the transmission of the virus from person to person mainly occurred through respiratory droplets and contact routes.[3-5] (However, airborne transmission might be possible.[6] To reduce the risk of respiratory infection in health-care settings, the US Centers for Disease Control and Prevention recommended healthcare workers to wear respiratory protection while treating patients.[7] The N95 respirator is a respiratory protection device that is the most commonly used in healthcare settings due to high filtering efficiency against airborne infectious agents and a tight-fitting face piece.[8, 9] The N95 respirator is originally designed for single use to avoid contamination. During the event of COVID-19 pandemic, supplies of N95 respirators have experienced a serious shortage worldwide. Therefore, decontaminating and reusing N95 respirators have been recommended as a crisis capacity strategy to preserve available supplies for healthcare settings.[10] Several methods have been explored for possible application in healthcare settings including ultraviolet C (UVC) and dry heat.[11-13] However, both methods are at risk to reduce the ability of the respirator to filter out infectious agents especially when exposed to these methods multiple times. This study aimed to evaluate the possible loss of filtration efficiency of N95 respirators due to multiple exposures to UVC and dry heat. This study aimed to ensure the effectiveness of UVC and dry heat to decontaminate N95 respirators during respiratory disease pandemics.

Methods

Virus and viral quantity

The RIX4414 strain of the human rotavirus G1P[8] Wa strain (Rotarix®, GlaxoSmithKline Biologicals SA, Belgium) was used in this study to be a representative of SARS-CoV-2. The full dose (1 mL) of Rotarix vaccine suspension contained the viral quantity at least 106 CCID50 as mentioned in the pharmaceutical product information sheet.

Decontamination by Ultraviolet C

The surgical N95 respirator model 1870+ (3M, St. Paul, MN, USA) was used in this study. The N95 respirator was exposed to ultraviolet C (UVC) light (wavelength 254 nm) in a chamber 295 (w) x 375 (D) x 425 (H) mm. The N95 respirator was exposed to UVC on both external and internal sides (15 minutes per side) with a total duration of 150 minutes (5 cycles). After UVC exposure, the N95 respirator was placed on the solid board with sealing at the back for filtration test.

Decontamination by dry heat

Hot air incubator (Pol-Eko aparatura, Poland) was switched on until the temperature of the device stabilized at 70°C. After this, the N95 respirator was placed in a paper bag and placed in the incubator for 30 min per cycle. After each cycle, the N95 respirator was cooled down to room temperature before re-incubating under the same condition for 5 cycles (150 minutes). The filtration test was performed after the N95 respirator cooled to room temperature.

Table 1. RT-PCR detection for G1 and P[8] of rotavirus

Decontamination method	G1	P[8]
N95: 5 cycles of dry heat exposure	Not detected	Not detected
N95: 5 cycles of UVC exposure	Not detected	Not detected
Control positive	Detected	Detected
Control negative	Not detected	Not detected

Filtration test

To determine the filtration efficiency of the N95 respirators after being exposed to UVC and dry heat, a nebulizer attached with a face mask (Ningbo Runmai Medical Technology Co., Ltd., Zhejiang, China) was used in this study. The nebulizer was filled with a 1 mL unit dose of Rotarix set at 60 psi oxygen at 10 L/min. to deliver the aerosol of the Rotarix into the N95 respirators. To avoid contamination of the N95 respirators with residual Rotarix, the N95 respirators were laid and sealed on a support surface before the trial. After administering one dose of Rotarix via the nebulizer, the swab samples were immediately collected from both outer and inner surface of the N95 respirators and placed in a tube containing viral transport media to submit to the National Institute of Health of Thailand to detect VP7 and VP4 genes (defining G and P types, respectively) of the rotavirus by RT-PCR, as previously described.(14) We investigated the existence of the rotavirus at both external (front) and internal surfaces (back) of the N95 respirators.

Results

After five cycles of N95 respirators treatment by UVC and dry heat, no burning smell of the rubber mask compound was found. Next, the ability of aerosol particles to penetrate through the N95 respirators was determined by testing the filtration efficacy of N95 respirators. The results of RT-PCR for rotavirus are shown in Table 1. At the front, the rotaviral RNA was detected of both decontamination methods, while the back of N95 respirators, the rotaviral RNA was undetected.

Discussion

The emerging SARS-CoVs-2 resulting in the COVID-19 pandemic is considered a serious public health concern worldwide and has created a critical shortage of N95 respirators required for a component of PPE. The filtration mechanism of N95 respirators are based on mechanical filtration and electrostatic attraction.[15, 16] Related studies have reported that sterilizing with UV light could potentially be used to disinfect disposable N95 respirators.[10-13] The UV light is part of the electromagnetic radiation covering wavelength spectrum from 100 to 400 nm and is classified as UVA (320–400 nm), UVB (280–320 nm) and UVC (200–280 nm). UVC was reported to possess a high germicidal efficiency for disinfection with a broad spectrum against microorganisms, including viruses, bacteria and fungi. UVC is particularly damaging to microorganisms because they are absorbed by their nucleic acid. The UVC absorption induces the formation of pyrimidine dimers resulting in their inability to replicate.[17] Moreover, UVC has been reported to have the ability to decontaminate N95 respirators exposed to the bacteriophage MS2 and influenza viruses.[18-21] In 2020, Chotiprasitsakul et al.'s preliminary report revealed no significant change to the structure of the N95 polymer fibers was observed after UVC exposure (DOI: https://doi.org/10.21203/rs.3.rs-67838/v1).

However, decontaminating N95 respirators using UVC exposure might reduce the potential of N95 filtration.[22] Moreover, the number of cycles for decontamination seemed to be limited by N95 respirator model and the UVC dose

required to inactivate the pathogens.[11] Recently, Chin et al. reported that SARS-CoV-2 could be inactivated at 70°C for 5 minutes.[23] Nevertheless, no scientific evidence for re-use of the N95 respirators after decontaminating using the dry heat strategy. To extend the supporting scientific evidence of both strategies, we re-exposed the surgical N95 respirator model 1870+ with UVC (254 nm, 8 W) in the cabinet and dry heat (70°C for 30 minutes) for 5 cycles and subsequently evaluated the effect of both methods. Herein, the rotavirus was used as a representative viral particle to determine the filtration performance of N95 respirators due to their safety, high stability and sizes closely fitting SARS-CoVs-2.[24-26] Interestingly, we found that the aerosol containing rotaviral particles generated by the nebulizer could not pass through the filter of the N95 respirators after exposure to either UVC or dry heat up to 5 times. The physical degradation of the respirator materials including the changes in the layer structure of the materials was not investigated in this study. However, our results suggested that UVC and dry heat did not change the filtration performance of the N95 respirators and both methods were appropriate to apply to decontaminate N95 respirators to re-use during the pandemic crisis with respiratory infectious diseases.

Conclusion

Treating the respirators for 30 minutes per cycle with both UVC (254 nm, 8 W) cabinet and dry heat (70°C) did not influence the filtration properties within a reasonable number of treatment cycles (up to 5 cycles). Therefore, both methods could mitigate the N95 respirators shortage during the pandemic of respiratory diseases.

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OUTCOME FOLLOWING ORBITAL FLOOR FRACTURE RECONSTRUCTION USING SILASTIC IMPLANTS

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Abstract

Background: Orbital floor fracture is typically present with peri-orbital ecchymosis, subconjunctival hemorrhage, enophthalmos and diplopia. The goals of reconstruction are to restore the volume and shape of the orbital cavity with autogenous or alloplastic materials. However, no gold standard exists for orbital implants to treat orbital floor fractures and remains controversial. Silicone was one of the most common biocompatible materials used for orbital floor reconstruction.

Objective: The study aimed to evaluate the outcomes of patients reconstructed using silastic sheets in the case of orbital wall fractures.

Methods: A multi-center, retrospective study of patients with orbital floor fractures was conducted from January 2010 to December 2019. Inclusion criteria included patients with orbital floor fractures and reconstruction using silastic sheets. Patients with orbital floor fractures and treated with other materials were excluded. The database included age, sex, cause of injury, size of floor defects, associated injury, underlying complication and period of follow-up.

Results: A total of 32 patients with orbital floor fractures divided in 20 patients from Phramongkutklao Hospital and 12 patients from Songkla Hospital were included. Twenty-five patients were male (78.13%). Mean age of patients was 35.62 years (range, 15 to 62 years). Causes of injury included traffic accident (78.13%) and body assault (18.75 %). Pure orbital floor fractures were found at 31.25%. Associated injuries included fractured zygoma 43.75%, nasal bone 21.87% and fractured maxilla 12.50%. Average size of defects was 2.01 cm^2. Average time to follow-up was 2.69 years. Complications were found in three cases (extrusion of silicone sheet, loss of sensation and dystopia). Extrusion was found 2 months postoperation and removal of silicone sheet was performed. Complete recovery of sensation of the infra-orbital nerve was shown at 6 months postoperation.

Conclusion: No gold standard exists for implants to treat orbital floor fractures. Orbital floor reconstruction using silastic sheets involves a low complication rate and satisfactory outcome. Herein, silastic sheets can be safely used for orbital wall augmentation and provides good long term outcomes.

Keywords: Orbital floor fracture, Reconstruction, Silastic sheets

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Introduction

Orbital floor fractures are common results of varying velocity and blunt facial trauma. They are typically caused by motor vehicle accident and assault with each being more common in differing demographic settings. They can occur as isolated orbital floor fractures or combined complex fractures involving other facial bones. Orbital trauma is a frequent cause of damage to both bony, soft tissue and neurovascular structures in the surrounding region. Injury patterns can be isolated to the bony orbit or part of a much larger zygomaticomaxillary complex (ZMC), or panfacial fracture patterns.[1] Patients typically present with peri-orbital ecchymosis, subconjunctival hemorrhage, enophthalmos and diplopia.

The goals of orbital reconstruction are to restore the orbital volume and shape of the orbital cavity with autogenous or alloplastic materials.[2, 3] Complications after orbital reconstruction may occur including infection, hematoma, nerve injury, diplopia, extra-ocular muscle limitation, enophthalmos and sensory change.[2-4]

Surgery is only the mainstay treatment, and several materials are suitable for orbital implants ranging from autogenous grafting to alloplastic implants. The most commonly used implants include bone, cartilage, porous polyethylene implants, titanium, poly L-lactide (PLLA) and polydioxanone (PDS).[1, 5, 6] However, no gold standard exists for orbital implants to treat orbital floor fractures and remains controversial. Silicone was one of the most common biocompatible materials used for orbital floor reconstruction.

Silastic or silicone sheet implants are often used to reconstruct orbital fractures because they are extremely cheap and seem to cause relatively few complications.[2] The advantages of silastic sheets include no resorption, short operative time and less tissue reaction. The disadvantages are infection, extrusion and implant displacement.

Silastic sheets are the main implant in Phramongkutklao Hospital and Songkhla Hospital in constructing the orbital floor but a study of long term outcome has never been conducted. This study aimed to evaluate the outcomes and complication rates of patients reconstructed using silastic sheets in the case of orbital wall fractures.

Methods

With the approval of the ethics committee and institutional review board of Phramongkutklao Hospital and following the Helsinki declaration, this multi-center, retrospective study of patients with orbital floor fractures was conducted in Phramongkutklao Hospital and Songkhla-nakarin Hospital from January 2010 to December 2019. Sample size was calculated using calculation PS Software (Power and Sample Size Calculation) Version 2.1. Inclusion criteria included patients with fractures of the orbital floor and treatment using silastic sheet. Patients with orbital floor fractures treated with other material or combined using silastic sheet were excluded. Data information included age, sex, cause of injury, size of floor defects, associated injury, underlying complication, period of follow-up, height, weight, blood pressure, demographics and level of injury. Analyses included descriptive statistics using SPSS for Windows, Version 21.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as number and percentage.

Results

A total of 32 patients with orbital floor fractures divided in 20 patients from Phramongkutklao Hospital and 12 patients from Songkla Hospital were included in this study (Table 1-3). Twenty-five patients were male (78.13%), and mean age of patients was 35.62 years (range, 15 to 62 years). Causes of injury included traffic accident (78.13%), body assault (18.75 %) and falls from height (3.12 %). All patients were followed-up at least 12 months. Pure orbital floor fractures were found at 31.25%. Associated injuries included fractured zygoma 43.75%, fractured nasal bone 21.87%, fractured maxilla 12.50%, fractured mandible 9.37% and fractured frontal sinus 3.12%.

Average size of defects was 2.01 cm^2 and average time to follow-up was 2.69 years. Complications were found in three cases (extrusion of silicone sheet, loss of sensation and dystopia). Extrusion was found two months postoperation and silicone sheet was removed. Completed recovery of sensation of the infra-orbital nerve showed six months postoperation. **Figures 1-5** illustrate some of these patients with orbital floor fractures.

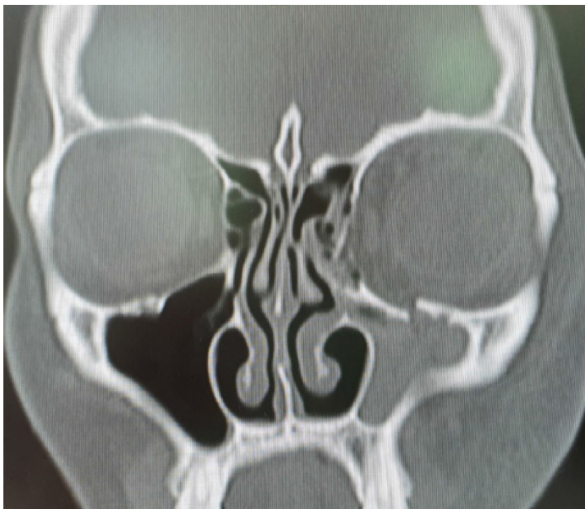

Figure 1. Computed tomography scan of facial bone showing isolated left orbital floor fracture

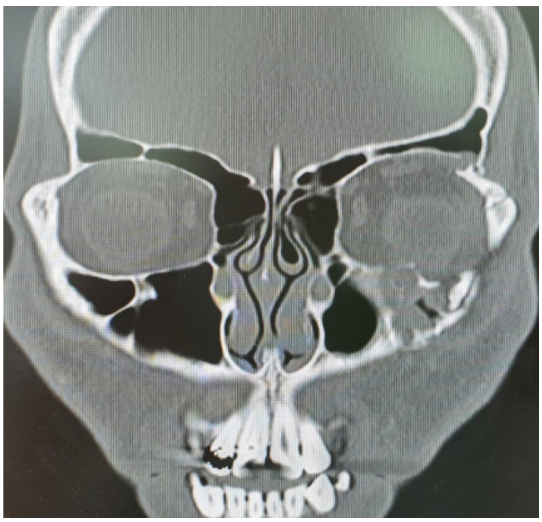

Figure 2. Computed tomography scan of facial bone showing combined fracture left orbital floor and zygoma

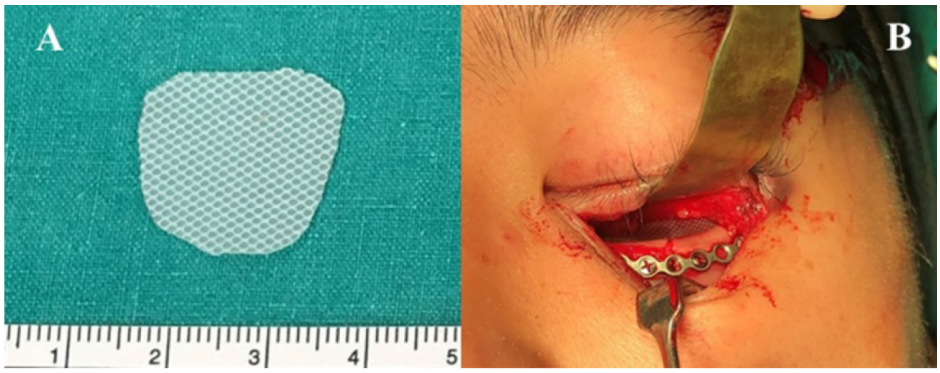

Figure 3. A) demonstrated silastic sheet B) Intra-operative view of corrected floor orbit with silastic sheet

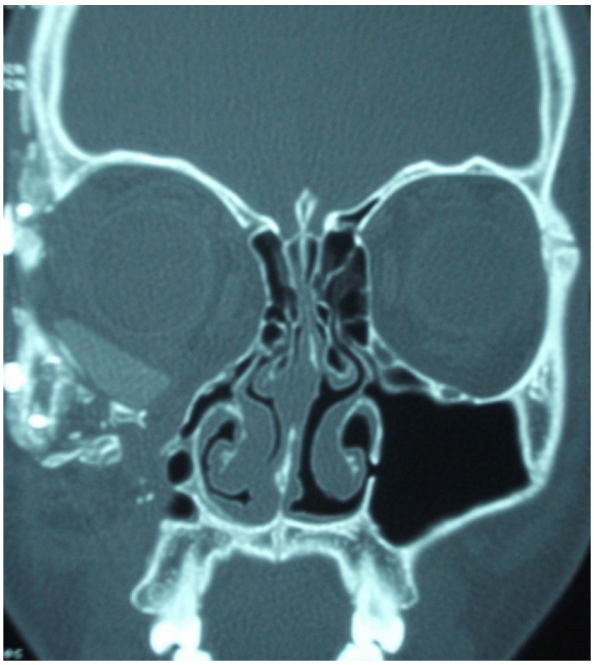

Figure 4. Computed tomography scan of facial bone demonstrated silastic sheet at right orbital floor

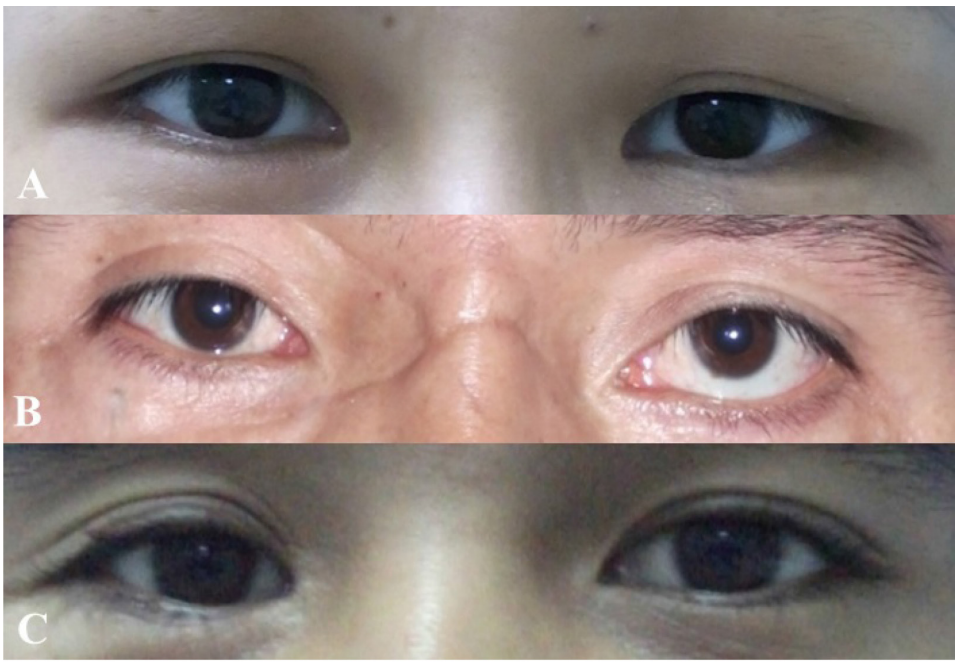

Figure 5. A) A 30-year-old female presented with fracture left orbital floor and corrected with silicone sheet. She was followed up 4 years without any complications. B) A 48-year-old male presented with combined fracture left orbital floor and Lefort II. He was followed up 4 years without any complications. C) A 22-year-old male presented with combined fracture right orbital floor, zygoma and Lefort II. One year follow-up showed mild dystopia on his right eye. Images were obtained with permission.

Discussion

Orbital floor fractures are a result of varying velocity and blunt facial trauma. They are often complex fractures involving other facial bones. They are most common in the male population between the ages of 20 and 40. Pure orbital floor fractures or blowout fractures occur through force transmission from the more rigid infra-orbital rim to the relatively weak orbital floor, known as the "buckling" theory.[7] Globe-directed trauma results in blowout fractures. Hydraulic theory states that hydraulic pressure from the globe is transmitted to the bony orbit, resulting in fracture of the thin orbital floor.[7, 8]

Despite extensive literature regarding orbital floor reconstruction, controversy still exists. Surgical indications, timing of surgery and preferred implant materials remain unclear. Most surgeons agree that strong surgical indications include enophthalmos greater than 2 mm during the first weeks, significant hypoglobus, mechanical entrapment, diplopia, and large orbital floor defect (>1 cm^2).[2, 9, 10] The aim of the surgery should be to restore the orbital volume to its premorbid condition, and to achieve this, an implant is often required.

Currently a wide array of implants are available to choose from including silastic, titanium, porous polyethylene, resorbable implants as well as autologous bone or cartilage. Teflon and silicone implants have been used since 1963.[11] They are considered to be valuable materials used in diverse surgical applications. However, some surgeons prefer using autogenous materials such as iliac or maxillary bone graft to avoid complications from alloplastic implants. Some concerns regard complications due to alloplastic implants. Infection, extrusion and implant displacement are the common complications of silastic implants.

As Morrison et al. reported the majority of silastic complications are observed during the early postoperative period and chances of complications decrease with longer asymptomatic periods.[12] In other words, chances of observing a patient with silastic infection after orbital reconstruction decreases over time. In addition, silastic sheets become difficult to detect by computed tomography scan and magnetic resonance imaging after silicone deterioration. Therefore, diagnosis of silastic complications long after the primary surgery becomes very

difficult for the new physician in charge when not knowing the details of past orbital reconstruction.

Mwanza T-C. K et al. showed satisfactory results regarding late repair of the orbital floor blowout fracture using silastic implant.[13] Simon J.B. et al. reported that the appropriate use of silastic implants for orbital floor reconstruction showed good results involving low complication rates including an acceptably low rate of infection and extrusion, as well as high patient satisfaction levels.[14] However, Muneo et al. reported a case of chronic infection seen after 28 years of silastic implant used in orbital floor repair.[15]

One advantage of orbital floor augmentation with autogenous bone graft is less infection. Disadvantages of orbital floor augmentation include autogenous bone graft were donor site paresthesia bone resorption, postsurgical pain, excessive blood loss and increased operative time. Advantages of orbital floor augmentation using alloplastic comprise no resorption and less operative time. Disadvantages of orbital floor augmentation with alloplastic include extrusion and infection.

A recent systematic review, evaluating materials for orbital floor reconstruction, found no conclusive evidence to suggest one material was better than another; rather, the surgeon must rely on his or her own experiences and the unique characteristics of each material to individualize treatment plans.[7, 16]

Retrospective study design may have been a limitation of this study; however, data from a multicenter study may increase the reliability of results. From our data, long term complication was at acceptable rate. The results confirmed silastic sheets can be carefully applied in good candidate patients.

Conclusion

No gold standard exists for orbital implants to treat orbital floor fractures and remains controversial. Orbital floor reconstruction using silastic sheets involves a low complication rate and satisfactory outcomes. Herein, silastic sheets can be safely used for orbital wall augmentation and good long term outcomes.

Potential conflicts of interest

The authors declare they have no potential conflicts of interest.

Disclosure

None of the authors have a financial interest in any of the products, devices or drugs mentioned in this article.

Data availability statement

Individual clinical data used to support the findings of this study are available from the corresponding author upon request.

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EFFICACY OF DOUBLE DOSE VERSUS STANDARD DOSE ERGOCALCIFEROL ON VITAMIN D STATUS AMONG PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Background: Patients with chronic kidney disease (CKD) have an exceptionally high rate of 25-hydroxyvitamin D (25-OHD) deficiency. Modest supplementation with ergocalciferol to raise serum 25-OH-D levels might improve bone and mineral disorders in CKD. Limited evidence is available regarding dosage of ergocalciferol supplement in CKD populations.

Objectives: The study aimed to examine the effectiveness of double-dose ergocalciferol on serum 25-OHD, serum intact parathyroid hormone (PTH) levels and mineral and safety profiles compared with standard-dose ergocalciferol among CKD subjects.

Methods: The study employed a 12-week open labeled, randomized, controlled design among patients with CKD at stages III-IV and serum 25-OHD <30 ng/mL. Patients were randomized in 2 groups: standard dose treated with ergocalciferol as recommended by K/DOQI guidelines or double dose of ergocalciferol from recommendations. Serum testing including 25-OHD, intact PTH, phosphate and calcium was performed at baseline and week 12.

Results: Sixty-three patients were included [standard-dose group (N=30) and double-dose group (N=34)]. At the end of the 12 weeks, 20 (58.8%) patients in the double dose ergocalciferol group achieved sufficiency compared with 6 (20%) patients in the standard dose ergocalciferol group ($p<0.05$). A significant increase in serum 25-OHD levels (13.6±9.9 vs. 8.5±6.8 ng/mL, $p=0.030$) and decrease in serum PTH level group (-16.8±26.4 vs. -0.3±26.8 pg/mL, $p=0.030$) was found in the double-dose group compared with the standard-dose group. No adverse effect was associated with the treatment.

Conclusion: The study demonstrated that high dose oral ergocalciferol had higher efficacy to increase serum 25-OHD and decrease serum PTH levels among patients with CKD than standard-dose ergocalciferol after 12 weeks of treatment.

Keywords: Hyperparathyroidism, Chronic kidney disease, 25-hydroxyvitamin D deficiency, Ergocalciferol

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Introduction

Vitamin D deficiency has a significantly higher prevalence in chronic kidney disease (CKD)[1] and is associated with increased mortality in CKD populations. [1-3] Current evidence has indicated that low serum 25-hydroxyvitamin D (25-OHD) concentrations are related to higher albuminuria, a rapid decline in renal function and progression to dialysis among predialysis patients with CKD.[4-6] Replete 25-OHD concentrations using vitamin D supplementation on clinical outcomes needs to be evaluated in this population.

Secondary hyperparathyroidism, attributed to vitamin D deficiency, has developed among patients with CKD progression.[7] Several studies have indicated that vitamin D supplementation to optimal vitamin D status provided parathyroid hormone (PTH) suppression in early stage CKD[8, 9], but the results were discordant concerning beneficial effects of vitamin D supplementation.[10] Current guidelines support native vitamin D supplementation in CKD based on extrapolation from cohorts conducted in the general population. An initial study demonstrated that high dose ergocalciferol supplement for eight weeks produced benefits on serum 25-OHD and PTH level among subjects with CKD.[11] More clinical studies need to test the optimal target of serum 25-OHD concentrations after vitamin D therapy in CKD populations. [12] The primary aim of the study was to determine whether double-dose ergocalciferol supplementation for 12 weeks was sufficient to maintain optimal vitamin D status and reduce serum PTH levels among patients with CKD compared with standard dose ergocalciferol supplementation.

Methods

This open labeled, randomized controlled trial compared two dosing regimens of ergocalciferol among patients with CKD stages III to V at Phramongkutklao Hospital and College of Medicine from October 2013 to September 2014. Patients were included in the study if they were aged ≥18 years, had estimated GFR <60 ml/min/1.73 mm^2 by CKD-EPI creatinine base formula and serum 25-OH-D <30 ng/dL. Patients were excluded if they had vitamin D analog supplement within 12 weeks, serum hypercalcemia, hyperphosphatemia, malabsorption syndrome, active malignancy or chronic illness with life expectancy <6 months. The study was approved by the Institutional Review Board of the Royal Thai Army Medical Department. Written informed consent was obtained from all subjects.

Study patients were randomized by a block of four randomizations assigned to two groups. The sample size calculated from the previous study was used to determine the mean difference of intact-PTH between standard dose ergocalciferol and double dose ergocalciferol. [11] To test the hypothesis, approximately 28 individuals per group plus dropout rate 20% were selected. Finally, 64 patients were included in this study. The standard dose ergocalciferol was prepared according to regimen based on KDOQI recommendations: (50,000 IU of ergocalciferol once weekly for 8 weeks for serum 25-OHD <5 ng/mL, 50,000 IU of ergocalciferol once weekly for 4 weeks for serum 25-OHD 5-15 ng/mL and 50,000 IU of ergocalciferol once monthly for 8 weeks for serum 25-OHD 16-30 ng/mL and then 50,000 IU of ergocalciferol once monthly). The double dose ergocalciferol was prepared from the KDOQI recommended dose. Follow-up visits were performed at 4, 8, and 12 weeks and at start and end of treatment with serum calcium, phosphorus, intact PTH and 25-OHD levels were measured. A 12-week follow-up visit was included to assess response durability. Serum total 25-OHD and intact-PTH levels were measured using electrochemiluminescence binding assay (Elecsys and Cobas e 601 immunoassay analyzers, Roche Diagnostics).

The primary endpoint was achieving vitamin D sufficiency (25-OHD >30 ng/mL) at the end of the 12-week treatment period. Secondary endpoints included measures of mineral metabolism (calcium, phosphate and parathyroid hormone [PTH] levels). Mild, moderate and severe vitamin D deficiency were defined as serum 25 OH-D 16-30, 5-15 and <5 ng/mL, respectively. Adverse events that were or were not considered to be related to treatment were monitored during the study.

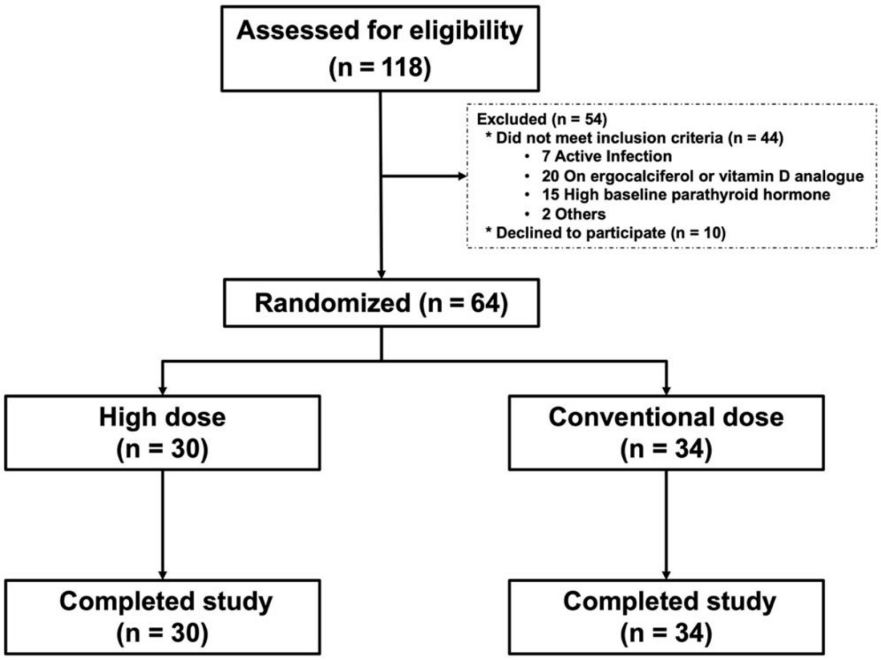

Figure 1. Flow chart study

Table 1. Baseline characteristics of enrolled participants

	Standard Dose Ergocalciferol (N= 30)	Double Dose Ergo-calciferol (N=34)	*p*-value
Male (%)	15 (50)	19 (57.6)	0.547
Age (years)	69.2±11.6	66.9±13.6	0.479
Body weight (kg)	66.6±15.0	63.6±13.1	0.404
Body mass index (kg/m^2)	25.0±5.9	23.7± 4.1	0.297
Systolic blood pressure (mmHg)	136.2±13.9	139.5±18.3	0.435
Diastolic blood pressure (mmHg)	74.9±9.0	76.8±13.2	0.506
Comorbid diseases (N, %)			
- Hypertension	27 (90)	30 (90.91)	1.000
- Type 2 diabetes	14 (46.7)	15 (45.5)	0.923
- Dyslipidemia	18 (60)	22 (66.7)	0.583
- Cardiovascular disease	3 (10)	3 (9.1)	1.000
- Gout	5 (16.7)	3 (9.1)	0.462
Chronic kidney disease staging (N, %)			
- Stage III	21 (70)	20 (60.61)	0.575
- Stage IV	8 (26.7)	10 (30.3)	
- Stage V	1 (3.3)	3 (9.09)	
Vitamin D status (N, %)			
- Mild vitamin D deficiency	17 (56.7)	16 (48.48)	0.516
- Moderate vitamin D deficiency	11 (36.7)	16 (48.48)	0.344
- Severe vitamin D deficiency	2 (6.7)	1 (3.03)	0.601

Data are mean ± SD and percentage. Mild, moderate and severe vitamin D deficiency are defined as serum 25 OH-D 16-30, 5-15 and <5 ng/mL, respectively. The standard dose ergocalciferol was prepared according to regimen based on KDOQI recommendations and the double dose ergocalciferol was prepared from KDOQI recommended dose

Study patients were followed for toxicity and compliance every four weeks during treatment. Any patients with serum calcium >10.5 mg/dL, serum phosphate >5.5 mg/dL and serum 25 OH-D > 80 ng/mL were immediately withdrawn from the study and the primary care physician was notified. Pill counts were used to track compliance.

Statistical Analysis

Clinical, and laboratory data were collected and entered in an electronic database. Categorical data were compared using the Chi-square test and Fisher's exact test. Comparison of continuous variables between two groups was tested using the Student t-test and Mann-Whitney U test. Paired t-tests and Wilcoxon signed ranks sum test were used to analyze the differences between various parameters at baseline and after treatment. All statistical analyses were performed using SSPS Software Program, Version 16.1 and $p<0.05$ was considered significant. Values were expressed as mean ± SD and percentage.

Results

A total of 118 patients in the outpatient department were screened for possible study enrollment (**Figure 1**). Sixty-three patients were eligible according to the entry criteria. Thirty patients were assigned to the standard dose ergocalciferol group and 34 patients were assigned to the double dose ergocalciferol group. Two groups were similar with respect to age, sex, clinical characteristics and baseline laboratory profiles including serum 25(OH)D, calcium, phosphate and PTH levels (**Tables 1 and 2**). Mean serum 25-OHD level was 18.7±7.2 ng/mL and mean plasma intact PTH level was 94.7±68.5 pg/mL. Thirty-three patients (51.5%) had mild vitamin D deficiency (25-OHD level, 16 to 30 ng/mL), 27 patients (42.8%) had moderate vitamin D deficiency (25-OHD level, 5 to 15 ng/mL) and 3 patients (4.7%) had severe vitamin D deficiency (25-OHD level, <5 ng/mL). In total, 41 patients (66.6%) had CKD stage III, 18 patients (28.5%) had CKD stage IV and 3 patients (4.7%) had CKD stage V.

Table 2. Baseline biochemical data of enrolled participants

	Standard Dose Ergocalciferol (N= 30)	Double Dose Ergocalciferol (N=34)	*p*-value
Serum 25-OHD (ng/mL)	18.9±7.3	18.2±7.4	0.660
Intact PTH (pg/mL)	94.8±70.7	94.6±65.4	0.990
BUN (mg/dL)	28.8±16.4	29.9±19.1	0.815
Cr (mg/dL)	4.2±12.1	2.1±0.9	0.321
Serum calcium (mg/dL)	9.1±0.4	9.3±0.4	0.097
Serum phosphate (mg/dL)	3.6±1.3	3.5±0.4	0.719
Hb (g/dL)	11.42 ± 1.55	11.84 ± 1.93	0.357
Plasma sodium (mmol/L)	138.79 ± 3.19	139.86 ± 2.45	0.138
Plasma potassium (mmol/L)	4.21 ± 0.47	4.34 ± 0.54	0.137
Plasma chloride (mmol/L)	103.42 ± 3.82	104.46 ± 3.24	0.247
Plasma bicarbonate (mmol/L)	23.92 ± 3.22	23.6 ± 3.3	0.699

Data are mean ± SD. No significant difference was detected in both groups. Standard dose ergocalciferol was prepared according to regimen based on KDOQI recommendations and the double dose ergocalciferol was prepared from the KDOQI recommended dose.

Table 3. Change of serum 25-OHD, parathyroid hormone, calcium, and phosphate levels after ergocalciferol treatment

	Standard Dose Ergocalciferol (N= 30)	Double Dose Ergocalciferol (N=34)	*p*- value
Serum 25-OHD (ng/mL)			
- Baseline	18.9±7.3	18.2±7.4	0.660
- At 12 weeks	27.9±10.1	32.1±9.0	0.111
- *p*- value	<0.001	<0.001	
- Mean change	8.5±6.8	13.6±9.9	0.030
Intact PTH (pg/mL)			
- Baseline	94.8±70.7	94.6±65.4	0.990
- At 12 weeks	96.6±82.9	77.4±52.4	0.326
- *p*- value	0.961	0.004	
- Mean change	-0.3±26.8	-16.8±26.4	0.030
Serum calcium (mg/dL)			
- Baseline	9.1±0.4	9.3±0.4	0.097
- At 12 weeks	9.3±0.4	9.0±1.2	0.833
- *p*- value	0.791	0.562	
- Mean change	-0.2±1.2	-0.3±1.1	0.743
Serum phosphate (mg/dL)			
- Baseline	3.6±1.3	3.5±0.4	0.719
- At 12 weeks	3.6±0.8	3.5±0.5	0.561
- *p*- value	0.338	0.584	
- Mean change	0.0±1.4	0.1±0.5	0.899

Data are mean ± SD. The standard dose ergocalciferol was prepared according to regimen based on KDOQI recommendations and the double dose ergocalciferol was prepared from KDOQI recommended dose.

After 12 weeks of supplement with ergocalciferol, 20 (58.8%) patients in the double dose ergocalciferol group achieved sufficiency compared with 6 (20%) patients in the standard dose ergocalciferol group ($p<0.05$) (**Figure 2**). A significant increase was observed in serum 25-OHD levels from 18.9±7.3 to 27.9±10.1 ng/mL in the standard dose ergocalciferol group ($p<0.001$) and 18.2±7.4 to 32.1±9.0 ng/mL in the double dose ergocalciferol group ($p<0.001$). Also, a significantly greater increase of serum 25-OHD levels was found in the double dose ergocalciferol group compared with the standard dose ergocalciferol group (mean change 13.6±9.9 vs. 8.5±6.8, p =0.030, respectively) (**Table 3**).

Regarding secondary outcomes, serum PTH levels significantly decreased from 94.6±65.4 to 77.4±52.4 at 12-weeks (p=0.004) in the double dose ergocalciferol group, while no change was found in the standard dose ergocalciferol group. A significantly greater decrease in serum intact PTH was observed in the double dose ergocalciferol group as compared with the standard dose ergocalciferol group (mean change -16.8±26.4 vs. -0.3±26.8, p=0.030, respectively) (**Table 3**). No differences in serum Ca and phosphate were detected between groups at any of the study visits, and no patients exhibited any serious adverse events during the study.

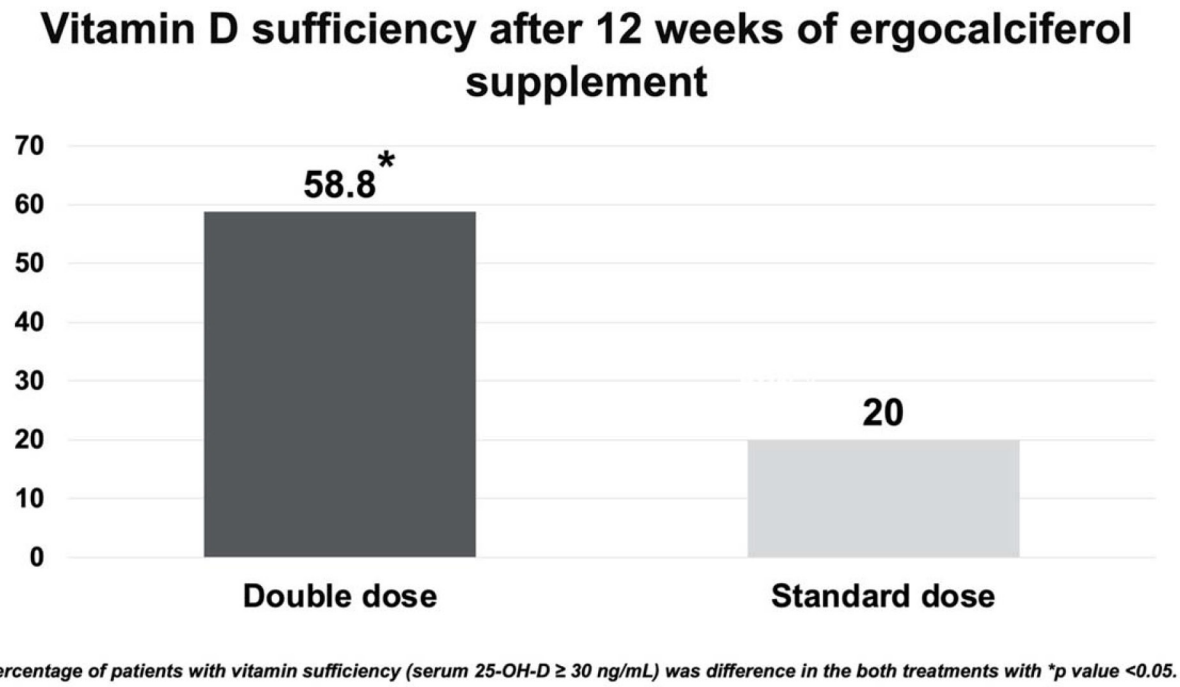

Figure 2. Vitamin D status after treatment with double dose ergocalciferol compared with standard dose ergocalciferol

Discussion

Progressive vitamin D deficiency worsens from CKD stages III-IV. Extrarenal conversion of 25(OH)D to 1,25(OH)2D by macrophages leads to autocrine and paracrine effects on immune function and inflammatory responses.[13] Thus, replacing 25-OHD by native vitamin D supplementation regimens would be beneficial even among patients with CKD while supplementation regimens remain debatable among patients with CKD. Many regimens using either ergocalciferol or cholecalciferol have been reported and data are limited regarding appropriate dosing, safety and efficacy. Our study indicated that double dose ergocalciferol was more efficient to increase serum vitamin D levels and decrease serum PTH levels. No notable persistent changes were observed regarding serum calcium and phosphate levels.

Vitamin D deficiency has been suggested to constitute a risk factor for hyperparathyroidism and low serum 25(OH)D levels cause a negative calcium balance, high bone turnover, secondary hyperparathyroidism and decreased bone mineral density among patients with CKD.[14,15] Conventional dose vitamin D supplement including ergocalciferol supplement showed benefit concerning level of PTH in only early CKD stage III[16], but other studies failed to show benefit to control of PTH among patients with CKD stages 3 to 4.[17, 18] Inadequate and short duration of vitamin D supplement might not be sufficient to correct abnormal bone metabolism. Serum 25OH-D level correlated positively with serum calcitriol level and negatively with serum PTH level among advanced patients with CKD.[2] Later studies have found that high dose ergocalciferol or cholecalciferol supplement produced positive effects in suppressing PTH level among subjects with CKD.[11, 19, 20] One meta-analysis and systematic review suggested that native vitamin D supplement improved serum 25-OHD and was associated with declined PTH levels with low incidence of hypercalcemia and hyperphosphatemia among nondialysis patients with CKD.[21] This was consistent with our finding that oral high dose ergocalciferol for 12 weeks had a beneficial effect in decreasing serum PTH and achieving vitamin D sufficiency among patients with CKD. Possibly patients with advanced CKD stages may require a higher

dose of native vitamin D supplement to increase biologically active vitamin D production, reversing resistance to paricalcitol induction and suppressing parathyroid gland enlargement.[22] The discrepancies of native vitamin dosage in the general population and among patients with CKD might be related to differences in gastro-intestinal absorption, liver metabolism and vitamin D receptor genetic polymorphisms. [24] We assessed any potential adverse effects of short term vitamin D treatment. We found no differences in adverse events between groups, including hypercalcemia, hyperphosphatemia, hospitalizations and cardiovascular events. The finding is consistent with previous data of patients with CKD. [22] One limitation was single center studies may limit generalizability to other populations. Our study was also limited by a short follow-up of 12 weeks without apparent treatment-related benefits on cardiovascular events and renal outcomes among patients with CKD. Further study is needed to confirm these outcomes.

In conclusion, replacing double dose ergo-calciferol over 12 weeks resulted in increased vitamin D sufficiency status and decreased PTH levels among patients with CKD stages 3 to 5 without any hypercalcemia or hyperphosphatemia compared with standard dose ergocalciferol.

Acknowledgments

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Potential conflicts of interest

The authors declare they have no potential conflicts of interest.

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COVID-19 SEROPREVALENCE AMONG ROYAL THAI ARMY PERSONNEL IN BANGKOK METROPOLITAN AREA FROM JULY-SEPTEMBER 2020

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Abstract

Background: COVID-19 is an ongoing pandemic that causes millions of deaths worldwide. Seroprevalence studies play a crucial role in identifying asymptomatic infection and providing the true prevalence of COVID-19 in the community. However, no COVID-19 seroprevalence in Thailand has been reported before.

Objective: The study aimed to measure the prevalence of the SARS-CoV-2 antibody among army personnel residing in the Bangkok Metropolitan Area.

Methods: All army personnel receiving health checkups from 1 July - 30 September 2020 were invited to participate in the study after providing informed consent. The seroprevalence was conducted using leftover serum without additional venipuncture. The screening conducted using the Rapid test by Wondfo®. When a screening test was positive, a confirmation test would be performed using ELISA by EuroImmun®. In case of a positive ELISA confirmation test result, the COVID-19 investigation team would be activated and deployed.

Results: In all, 6,651 army personnel participated in this study. The age of participants ranged from 20-60 years with mean age of 40.5±12.02. Most participants were male (85.5%). The rapid screening test using Wondfo® was positive in 41 cases (0.61%). The confirmation test using ELISA yielded a positive result in 1 subject (0.015%). That person was a known case of COVID-19 infection, who received a full course of treatment and was confirmed to have negative RT-PCR before being discharged from the hospital a few weeks earlier.

Conclusion: This was the first large scale seroprevalence surveillance of COVID-19 in Thailand. Our study revealed no new detectable case of asymptomatic COVID-19 infection in the Bangkok Metropolitan Area**.**

Keywords: COVID-19 infection, Military personnel, Bangkok Metropolitan Area

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Introduction

Coronavirus disease 2019 (COVID 19) is a pandemic caused by severe respiratory syndrome coronavirus (SARS-CoV)-2. The first case was reported in Wuhan, Hubei Province in PR China in December 2019.[1, 2] Shortly after, it spread to countries in Europe and the US. [3-5] The World Health Organization (WHO) declared COVID 19 a public health emergency of international concern (PHEIC) 30 January 2020. On 11 March 2020, WHO declared COVID 19 a global pandemic. At the time of this manuscript, more than 73 million persons had contracted this disease with more than 1.6 million deaths in 235 countries.

COVID-19 infection is acute without any carrier status. Symptoms usually begin with nonspecific syndromes, including fever, dry cough and fatigue, and multiple systems may be involved. After the onset of illness, the symptoms are somehow mild and the median time to first hospital admission is 7.0 days.[6] During this period, the patient could transmit SAR-CoV-2 to other people. Furthermore, many infected patients are asymptomatic. This group of patients is usually not tested for COVID 19 infection and may potentially be a source of infection. To achieve effective control of this COVID 19 pandemic, active surveillance of asymptomatic infection is also necessary.

The Armed Forces Research Institute of Medical Science (ARFIMS) has the duty of providing annual health checkup services for Military Personnel in Bangkok and the Metropolitan Area. More than 15,000 army personnel complete health questionnaires, receive a physical examination, blood test, and chest X-RAY every year. Health education is usually given to all army personnel during the annual checkup event. Therefore, this checkup service is an ideal platform for conducting an additional epidemiological study on the COVID-19 endemic. The study aimed to conduct a seroprevalence survey among army personnel residing in the Bangkok Metropolitan Area.

Methods

This constituted a cross-sectional study to identify the prevalence of seropositive COVID-19 cases in the Bangkok Metropolitan Area. All enlisted army units were contacted and the study was approved by the commander of each unit. The liaison officers of each army unit were explained the details of the study. All army personnel receiving health check-ups from 1 July to 30 September 2020 were invited to participate in the study after providing informed consent. Each personnel went through the usual process of health check-up programs, including physical examination and blood tests, except for answering a few additional questions regarding the risk of COVID-19 infection. The seroprevalence was conducted using leftover serum without additional venipuncture. The screening was conducted using the Rapid test by Wondfo®. When the screening test result was positive, a confirmation test would be performed using ELISA by EuroImmune®. In the case of a positive ELISA confirmation test result, the COVID-19 investigation team would be activated and deployed. Thorough disease investigation was undertaken and the standard surveillance protocol was followed. The flow diagram of the study is shown in **Figure 1.**

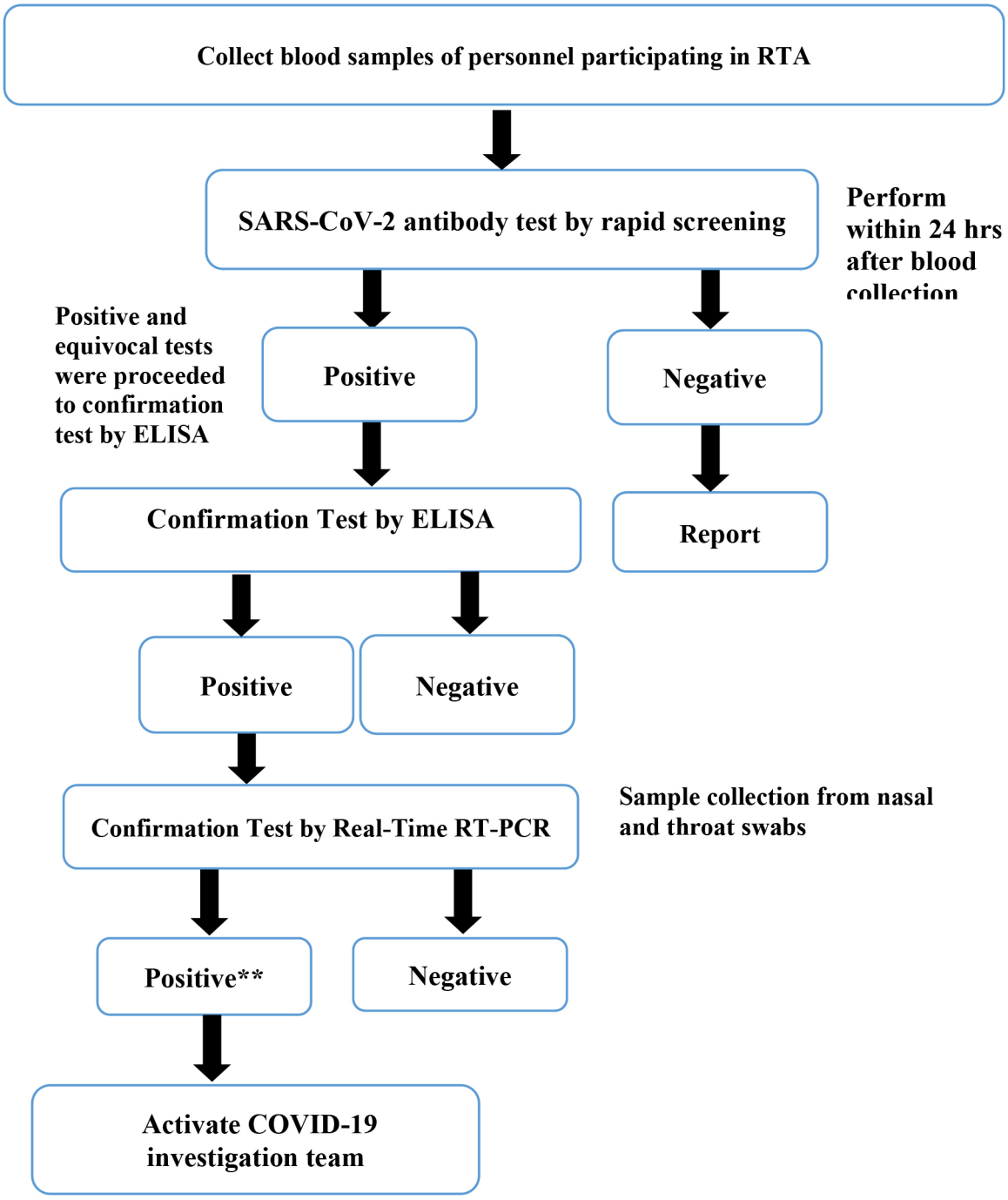

Figure 1. Flow diagram of the study

Table 1. Demographic data of enrolled participants

Characteristics		n	Mean (SD)	Percentage
Age			40.5 (12.02)	
Sex	Male	5,684		85.5
	Female	967		14.5
Rank	Non-commissioned officer	4,301		64.7
	Commissioned officer	1,583		23.8
	Civilian employees	747		11.2
	Others	20		0.3
BMI		6,651	25.04 (3.9)	

Results

In all, 6,651 army personnel were included in this study. The age of participants was from 20 to 60 years with mean age of 40.5±12.02. The baseline demographic data are shown in **Table 1**. (n=6,651)

The location of army units participating in this study is depicted in **Figure 2**. The rapid screening test using Wondfo® was positive in 41 cases (0.61%). The confirmation test by ELISA yield positive results in one subject (0.015%). **Table 2** reveals the result of a positive rapid screening and ELISA classified by unit.

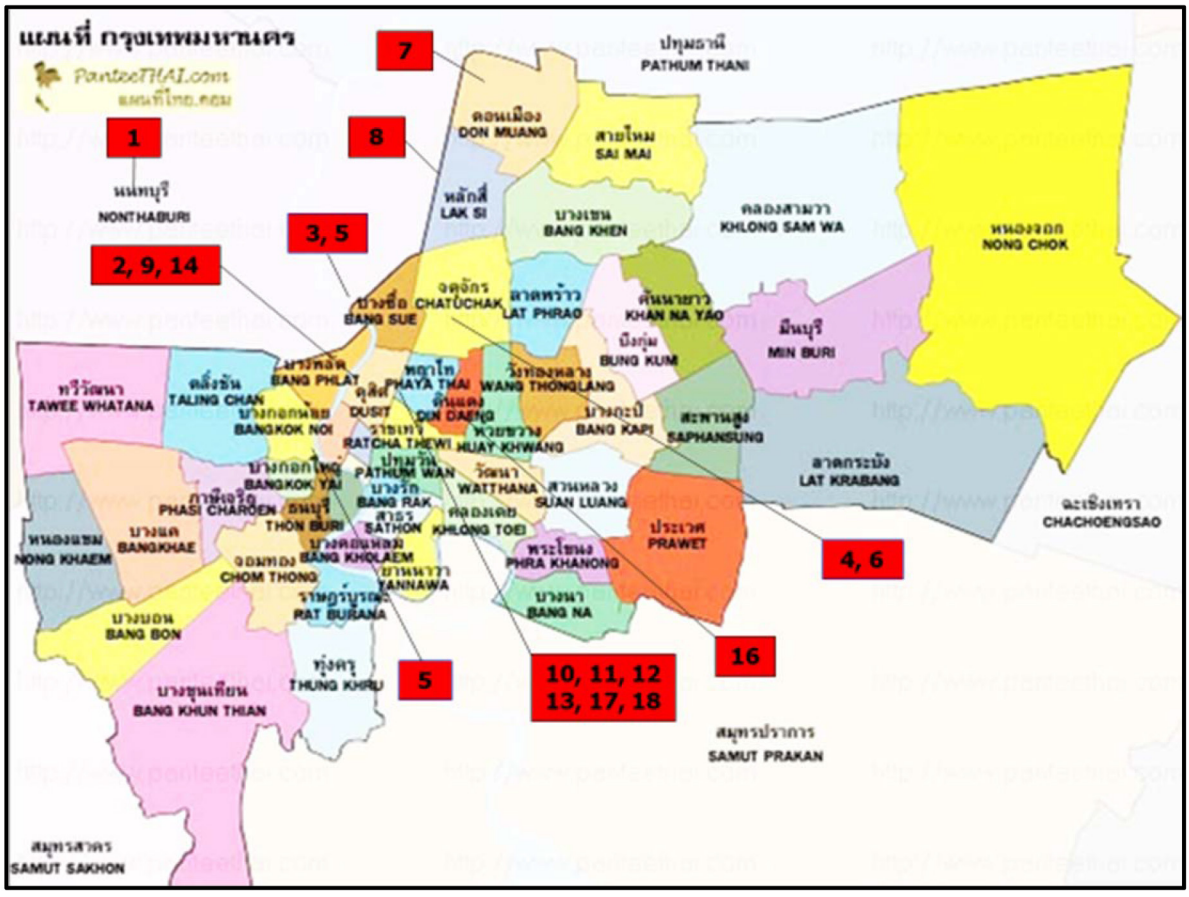

Figure 2. Map of Bangkok Metropolitan Area and location of army units participating in this study

Table 2. Results of the rapid screening test and ELISA in each army unit

Unit number	Number of personnel	Positive by rapid screening	Positive by ELISA
1	1,474	8	0
2	392	4	0
3	130	0	0
4	329	0	0
5	429	2	0
6	126	1	0
7	439	0	0
8	458	0	0
9	603	4	0
10	290	3	1 **(**Ig G**)**
11	93	0	0
12	249	3	0
13	125	1	0
14	163	4	0
15	328	4	0
16	581	5	0
17	198	2	0
18	244	0	0
	6,651	41	1

After confirming a positive blood sample using the ELISA test, an AFRIMS investigation team was deployed. The investigation revealed that the person with a positive SAR CoV-2 antibody was a 20-year-old man who was a known case of COVID-19 infection residing with his father and mother. Both he and his mother contracted the disease from his father who was part of the Thai-boxing cluster of epidemics. All three were treated at Pharmongkutklao Hospital for 7 days from 28 March 28 to 6 April 2020, and were discharged from the hospital after their clinical symptoms resolved and their RT-PCR results were negative. All their neighbors and possible contact persons had already received an RT-PCR test when this family was admitted to the hospital and all tests yielded negative results. Therefore, no additional action was taken.

Discussion

Severe acute respiratory syndrome coronavirus (SARS-CoV)-2 has infected more than 46 million people worldwide leading to nearly 1.2 million deaths and an unprecedented impact on economics, society, and life style of people globally. Thailand is among the first countries to report COVID 19 outside China when a traveler from Wuhan was confirmed to have SAR-CoV-2 infection 8 January 2020.[7] The number of cases in Thailand remained low from January to February followed by a big outbreak in March. A state of emergency was declared 26 March. A nationwide curfew was declared from 3 April to 15 June 2020. However, the state of emergency has not been waived until now. With the rapid response, prompt policy and effective intervention from the government together with great cooperation from Thai citizens, the situation of

COVID-19 infection in Thailand was maintained under control. The strong network of Village Health Volunteers played important role in screening, detecting and active surveilling of possible infected cases as well as educating local communities and implementing health campaigns. Thailand is one of the two countries that have been chosen by the WHO as successful models to be featured in a documentary about handling and stemming the spread of COVID 19. The current situation of Thailand revealed total cases of 3,784 with 59 mortality cases. Bangkok is the city with the highest number of COVID-19 cases.

Because COVID-19 could present with mild symptoms or could be asymptomatic, a concern existed that the incidence of the actual infection in Thailand might be underreported. No active surveillance using antibody detecting in Thailand has been reported before. Related studies in many countries have revealed that seroprevalence for COVID-19 varied from and 3.2 to 3.8% in Wuhan, 4.65% in LA County, 5% in Spain and 7.3% in Stockholm.[8-12]

This study was the first report of a large-scale seroprevalence survey in Thailand. In this study, we chose Bangkok and the Metropolitan Area because it constituted the area with the greatest incidence of COVID-19 infection in the country and potentially the highest chance of asymptomatic infection. We conducted a seroprevalence survey as an annex to an established program of annual health checkup services. The integration of the study in a solid and well-established platform was the key success of this study. We received great cooperation from both commanders of the units and army personnel. Only a few questions were added to the regular health questionnaire and no additional venipuncture was required.

The screening was conducted using Wondfo® rapid test. Wondfo® was the first officially approved antibody test for SAR-CoV-2 in China. The total antibody test indicated a sensitivity and specificity of Wondfo® reported by the company product description to be 86.43% (95% CI = 82.51-89.58%) and 99.57% (95% CI = 97.63-99.52%), respectively(13). The sensitivity of Wondfo® varied according to the time between the onset of symptoms and the antibody test. One related publication revealed a sensitivity of 52.2% (95%CI = 37.0 - 67.1%) when Wondfo® was used within two weeks of the onset. The sensitivity increased to 91.3% (95% CI = 72.0 – 91.9%) when the test was performed from days 15 to 21. The sensitivity further increased to 100% (95% CI = 88-100%) when tested among patients after three weeks of symptom onset, while the specificity in this study was reported to be 100% (95% CI = 69.2-100%) (14). Similar findings were reported by Serrano et al. (15). The sensitivity of Wondfo® in this study was 66.7% (95% CI = 46−83.5%), 97.4% (95% CI = 86.5 to 99.9%), and 98% (95% CI = 89.4 to 99.9%) when the test was performed days 1 to 7, days 8 to 14 and days 15 to 28, respectively. The specificity was 95.2% to 100%. The related publication also revealed low sensitivity when Wondfo® was performed using capillary blood (55%) but high sensitivity when a serum sample was used (96%)(16). In our study, we used the leftover serum and all equivocal test results from Wondfo® were initially classified as positive and were proceeded to be confirmed using ELISA test to ensure the highest possible sensitivity.

Among 6,651 blood samples obtained, 41 samples (0.61%) yielded a positive screening test result (including equivocal test results). ELISA by EuroImmun® was used as a confirmation test. Euroimmun® is a standard antibody test that received both FDA EAU approval and CE mark. It has been used as a confirmation test for many rapid tests in many related publications. Euroimmun® had the sensitivity and specificity of 90% (95% CI = 74.4 to 96.5%) and 100% (95% CI = 95.4 to 100%) according to FDA EUA website. [13] Charlton et al. reported the sensitivity of Euroimmun® to be 83% (95% CI = 67-93%). The sensitivity increased with a longer time from the onset of symptoms. The sensitivity of Euroimmun® was 76% (95% CI = 53-92%) when the test was conducted at days 0 to 14 after the onset of the symptoms and increased to 82% (95% CI = 48-98%) when conducted from day 15 to 21. The sensitivity was 100% (95% CI = 68-100%) after day 21 of symptoms onset, while specificity in this study was 100% (95% CI = 93-100%).[17]

Among 41 positive (and equivocal) screening tests, one case (0.015%) was confirmed to have antibodies to COVID 19. That person was a

known case of COVID-19 infection who had already received full treatment and was fully recovered from the infection. There has been no confirmation of asymptomatic infection from this active seroprevalence surveillance. There might be a question of whether the number of blood samples tested in our study was sufficient to reflect the true prevalence of infection in the Bangkok Metropolitan Area. According to Hilborne et al., when the size of the population is large, the number of required samples for a seroprevalence study is nearly identical and not dependent on the increase in the number of the total population. Hilbourne et al. proposed the maximum number of screening tests required for seroprevalence to be 2,377 tests which was far less than the number of blood tests in our survey. [18]

Conclusion

This constituted the first large scale seroprevalence surveillance of COVID-19 in Thailand. Our study revealed no new detectable cases of asymptomatic COVID-19 infection in the Bangkok Metropolitan Area. Most people in Bangkok have no immunity against SAR-CoV-2 and are vulnerable to the infection. The proposed approach to achieve herd immunity in Thailand is very unlikely to be successful and is unethical in this circumstance.

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EFFICACY OF ANESTHETIC COCKTAIL WOUND INSTILLATION FOR POSTOPERATIVE ANALGESIA FOLLOWING POSTERIOR SPINAL SURGERY

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Abstract

Background: Posterior spinal surgery is a common procedure in orthopedic practices that causes severe pain after surgery. Proper postoperative pain controls not only benefit early mobilization and initiation of physiotherapy but they also play important roles in reducing morbidity and mortality.

Objective: This prospective, double-blinded, randomized controlled study investigated the efficacy of anesthetic cocktail wound instillation for postoperative analgesia following posterior spinal surgery.

Methods: After posterior spinal surgery, 54 patients were randomized to instill 20 mL of normal saline (Group N) or anesthetic cocktail consisting bupivacaine, ketorolac and morphine (Group A) in the wound after securing hemostasis and leaving a contact time of 60 seconds. After a dwell time of 60 seconds, the wound layers were closed without mopping or suctioning. All patients in both groups received patient-controlled analgesia using morphine for 24 hours post surgery, followed by standard analgesia. The analgesia consumption (morphine), visual analog scale (VAS) at specific hours after the operation, and time for first demand of analgesia were recorded. Morphine-related side effects were also monitored.

Results: The patients in group A consumed significantly less morphine at 4, 8, 12 and 16 hours after the surgery (p=0.048, 0.007, 0.005 and 0.026, respectively). In addition, they had lower VAS over the first 24 hours (p<0.05) and longer median duration of first demand of analgesia (p=0.013). Morphine-related side effects were also lower in group A (p=0.024).

Conclusion: The simple technique of wound instillation with anesthetic cocktail significantly reduced postoperative requirements of morphine and improved pain control with lower rates of nausea and vomiting over the first postoperative day after posterior spinal surgery.

Keywords: Posterior spinal surgery, Anesthetic cocktail, Postoperative pain, Wound instillation

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Introduction

Posterior spinal surgery is a common procedure in orthopedic and neurosurgical practices and considered one of the top six procedures causing the highest degree of postoperative pain especially for the initial few days. [1-3] Pain is the fifth vital sign, [4] that not only proper postoperative pain controls can benefit early mobilization and initiation of physiotherapy, but also plays important roles in reducing morbidity and mortality. Interest in understanding of the pathophysiology of acute pain and development in newer modalities of analgesic treatment have been increasing. Currently, several analgesic techniques are available. Intrathecal administration of opioids or local anesthetics and epidural administration of drugs using a catheter for continuous infusion provide the highest level of pain control; however, such therapies may be limited by highly invasive procedures, high cost, technical challenges, adverse or toxic effects of drugs and procedure-related complications such as reversible loss of sensory function and motor weakness. [2, 5, 6] Although intravenous opioids or NSAIDs administration via Patient-Controlled Analgesia (PCA) provides less technical demand and decreased incidence of drug effects, analgesic efficacy remains inconclusive when compared with other options. [9-11]

Regional techniques, such as intra-articular injection and wound infiltration are commonly used alone or with other analgesic regimens for postoperative pain control. These offer many advantages, i.e., pain is relieved close to the damaged tissue, analgesia is provided when local anesthetic cocktails are used and opioid-related side effects are substantially reduced by minimizing opioid consumption.[5, 6, 7] Instilling local anesthetic drugs in the wound was found to provide postoperative analgesia in certain surgical and gynecological procedures.[1] However, the role of a single time wound instillation with anesthetic cocktails in postoperative spinal surgery has not been explored earlier.

This prospective, double-blinded, randomized controlled study aimed to investigate the efficacy of anesthetic cocktail wound instillation for postoperative analgesia following posterior spinal surgery and evaluate opioid-related side effects.

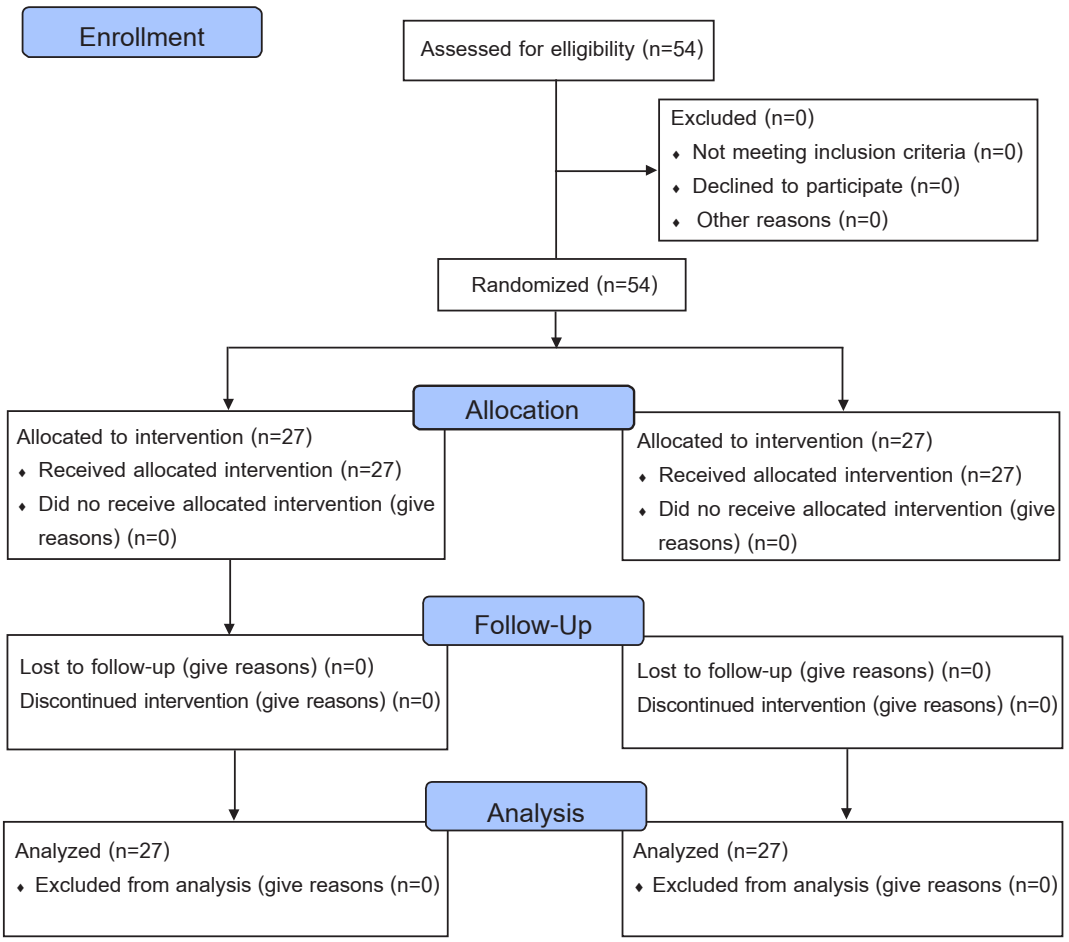
Methods

This study was approved by the Institutional Review Board, Medical Department, Royal Thai Army. Written informed consent was obtained from all enrolled patients. Sample size calculation was used to determine the number of enrolled patients (N=27). This study enrolled 54 patients, 27 patients in each group, using the American Society of Anesthesiologists (ASA) physical status I, II and III undergoing posterior spinal surgery at Phramongkutklao Hospital from May 2017 to July 2018.

The inclusion criteria were patient's conditions, age, willingness and mentality. This study covered patients scheduled for posterior decompression with instrumentation not more than five levels with diagnosis of degenerative change of spine and failed conservative treatment, spinal fracture indicating surgery or patients who had complications due to undergoing prior spinal surgery. The patients' ages ranges from 18 to 80 years. Moreover, patients agreed to participate, had good mentality and were able to receive PCA in the postoperative period.

Patients who had ASA IV status, and were allergic to bupivacaine, ketorolac (NSAIDs) or morphine were excluded from the study. In addition, patients with massive bleeding (more than 2,000 mL), or cerebrospinal fluid leak were excluded after initial recruitment.

The block size of four was used to randomly separate patients in two groups. Group N represented the control group while Group A represented the intervention group that received anesthetic cocktails **(Figure 1).** We observed no difference in demographic data except age. Two patients in the intervention group were younger than other patients and underwent posterior spinal surgery due to fracture from trauma **(Table 1).**



Flow Diagram

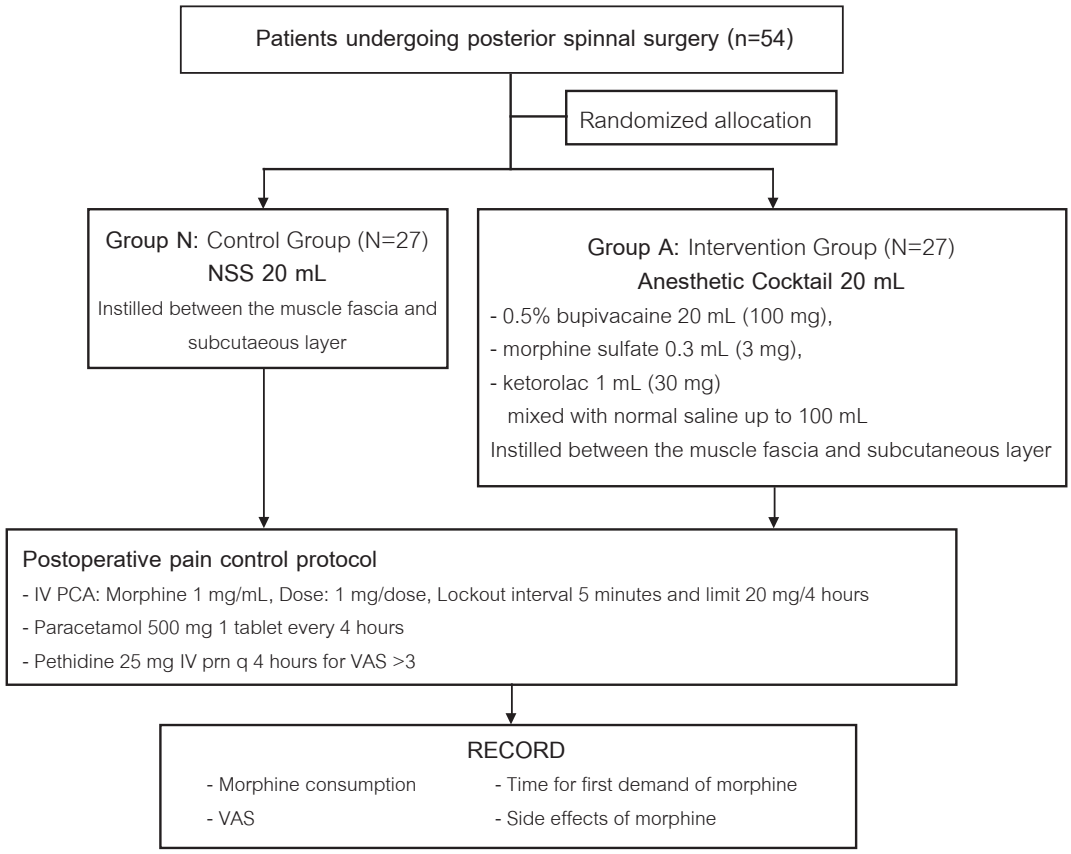


Figure 1. Flow chart shows the protocol of this study
IV PCA = Intravenous patient-controlled analgesia

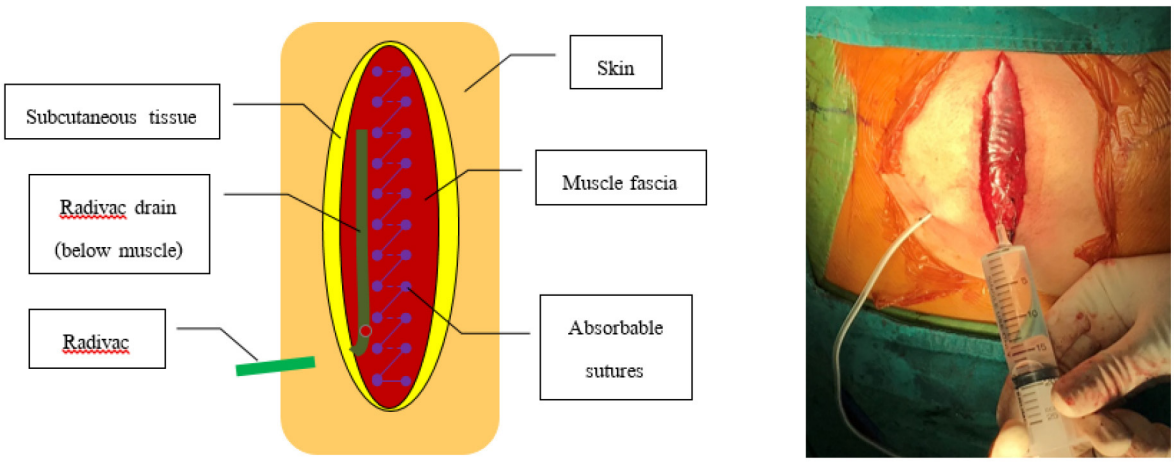


Figure 2. Instilled anesthetic cocktails or NSS 20 mL between the muscle fascia and subcutaneous layer

Operative procedure

All patients received standard general anesthesia with an appropriate sized endotracheal tube. Fentanyl 1-2 µg/kg was administered intravenously after induced anesthesia for intraoperative analgesia. Once the surgical procedure was completed, hemostasis was secured and a radivac drain (without suction) was placed under the muscle layer. Patients in group N received 20 mL of normal saline instillation remaining in the wound between the muscle and subcutaneous layers for a dwell time of 60 seconds. Patients in group A received 20 mL of anesthetic cocktails for the same contact period **(Figure 2)**. The anesthetic cocktails comprised 100 mg bupivacaine (0.5%, 20 mL), 3 mg morphine sulfate (0.3 mL), and 30 mg ketorolac (1 mL). These were mixed with sterile normal saline solution to make up a combined volume of 20 mL. Then the wound was closed in layers without mopping or suctioning and radivac drain was opened after the patient was placed in the supine position.

Before surgery, all patients were informed about how to use the PCA device to control pain adjusted to their comfort level. Post-operation, both groups of patients received intravenous PCA for 24 hours using morphine. The PCA device was set to inject 1 mg in 1 mL (100 mg of morphine in 90 mL normal saline) when patients pressed a button with a five-minute lockout period. No continuous infusion was available and the maximal dose was limited to 20 mg every 4 hours. In addition to PCA, paracetamol 500 mg was administered every 4 hours. Moreover, pethidine 25 mg was intravenously administered for rescue analgesia every four hours when the patient requested or visual analog scale (VAS) >3 after using maximal dose of PCA. The time for first demand of analgesia and total 24 hours analgesia consumption (morphine) were recorded. Morphine-related side effects were also monitored. In case of vomiting, metoclopramide 10 mg was intravenously given at every eight hours until nausea and vomiting improved. Chlorpheniramine 10 mg maleate was also used intravenously every six hours for pruritus. Omeprazole 40 mg was given intravenously twice daily in all patients since the day of surgery to prevent gastrointestinal bleeding from stress ulcer.

Patients were assessed for postoperative pain by VAS, a 10-point scale ranging from "0" minimum or no pain to "10" maximum pain score perceived by the patient. Postoperative pain was assessed by an independent observer blinded to the study first at 0 hour (at recovery room, after extubation) and then at 2, 4, 8, 12, 18 and 24 hours after the surgery.

Statistical Analysis

Data were analyzed using IBM SPSS Software, Version 24. The Mann-Whitney U test was used to determine differences in estimating blood loss, amount of morphine consumption through PCA, time for first demand of analgesia and VAS between Groups N (normal saline) and A (anesthetic cocktails). Wilcoxon Signed

Ranks test was also used to assess the amount of morphine consumed through PCA and VAS in both groups. Fisher's exact test was used to compare the ASA physical status, diagnostic group, number of demand pethidine for rescue analgesia and morphine-related side effects. Operative time was also analyzed for differences by independent t-test and number of spinal surgery levels was compared using the Chi-square test. A two-sided $p<0.05$ was considered statistically significant.

Results

Demographic data were compared between the two groups. No significant differences of operative conditions were observed including diagnosis, number of spinal surgery levels, operative time and estimated blood loss between the control and anesthetic cocktail groups **(Table 1).** We observed no intra-operative complications among any patients in either group. For the first 24 hours after surgery, the patient in the anesthetic cocktail group consumed significantly less morphine at 4, 8, 12 and 18 hours after the surgery (p = 0.048, 0.007, 0.005, and 0.026, respectively) but no difference was found for consumption at 2 and 24 hours (p=0.032 and 0.166, respectively) **(Figure 3).** In addition, postoperative VAS was significantly lower in the anesthetic cocktail group at all time intervals of the first 24 hours compared with those of the control group **(Figure 4)** and longer median duration of first demand of analgesia (p = 0.013). The patients in the control group had eight times higher incidence (p = 0.024) of morphine-related side effects such as nausea, vomiting and pruritus compared with patients in the anesthetic cocktail group (29.63 versus 3.7%). No incidence of urinary retention or respiratory depression was reported in either group **(Table 2).**

Discussion

The result of this prospective, double-blinded, randomized controlled study showed that the group of patients having postoperative posterior spinal surgery receiving wound instillation with 20 mL of anesthetic cocktails (Group A) experienced better postoperative analgesia as compared with the group of patients receiving normal saline solution (Group N). Postoperative morphine consumption via PCA during the 4- to 18-hour interval, which was recorded at specific hours, showed that those in the normal saline group consumed substantially more analgesics than those in the anesthetic cocktail group. The postoperative pain scores (VAS) of the patients in anesthetic cocktail group were lower at all time points in first 24 hours. Furthermore, the time to first demand of analgesia was significantly prolonged in the anesthetic cocktail group.

Proper postoperative pain control after spinal surgery plays important roles in reducing morbidity and mortality. Currently several analgesic techniques are available. Wound infiltration with local anesthetics with or without adjuvant drugs has long been known to produce efficient postoperative analgesia. Bianconi et al. evaluated the efficacy of ropivacaine continuous wound instillation after joint replacement surgery and spine fusion surgery and found that significant analgesia, less pain scores and rescue medication requirements were observed compared with those of the placebo group. [13, 16] Pediatric patients following orthopedic extremity surgery received wound instillation of 0.5% bupivacaine 0.2 mL/kg via a catheter. [14] Yuenyongviwat et al. studied the effectiveness of local peri-articular injection with bupivacaine in total knee replacement surgery and found effective and prolonged postoperative analgesia with few morphine-related complications. [15] In addition, Jonnavithula's study also reported that bupivacaine wound instillation technique was simple, safe and effective in managing acute pain after lumbar laminectomy. [1] Moreover, no complications were observed related to the infiltration of the local anesthetics. The efficacy and safety of local anesthetic drugs could reduce postoperative pain; however, using high volumes of local anesthetics should be restrained because they can affect the central nervous and cardiovascular systems. [27, 28] Anesthetic cocktails were used to reduce the dose of local anesthetics and could inhibit pain pathway by several mechanisms. Several studies have reported the efficacy and safety of peri- and

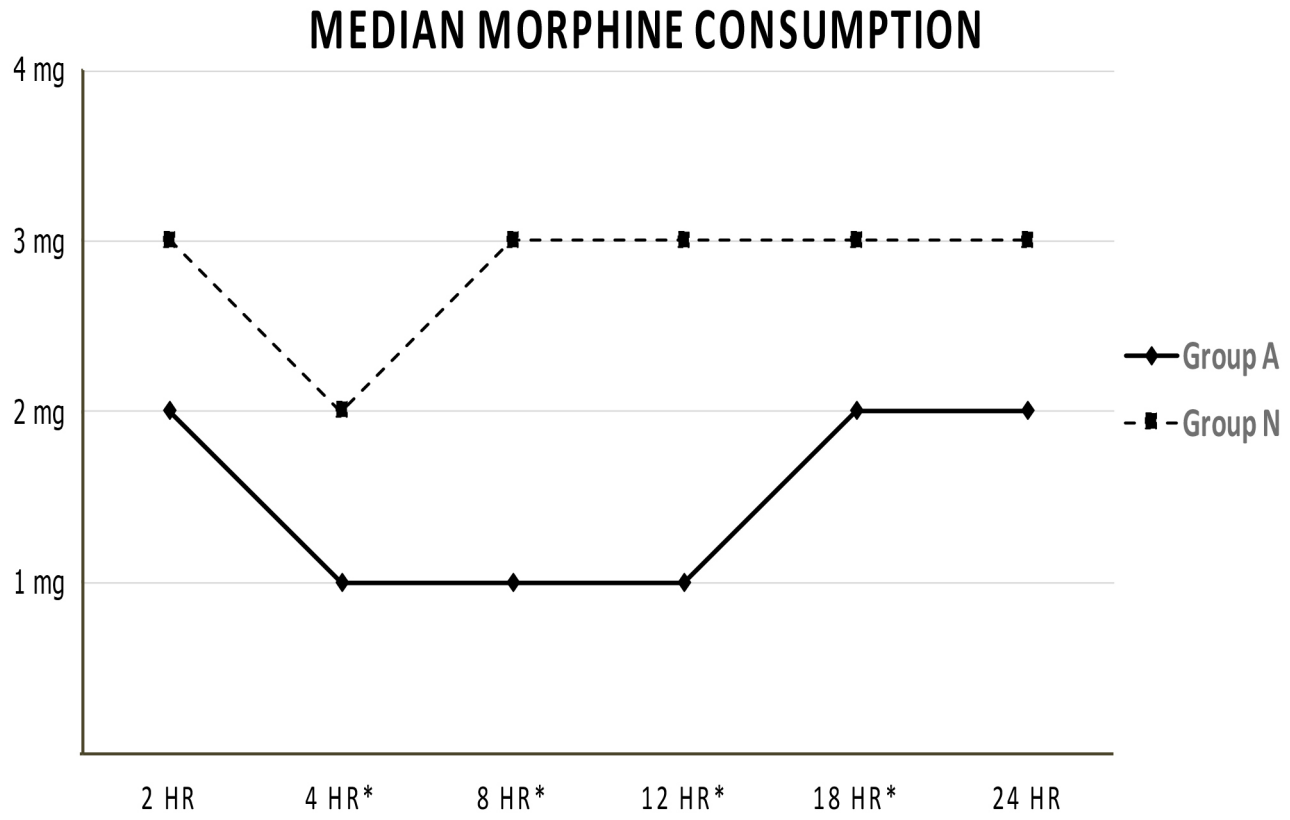


Figure 3. Comparison of median morphine consumption between group A (anesthetic cocktail group) and group N (control group) at specific postoperative time points (*p-value <0.05 using the Mann-Whitney U test)

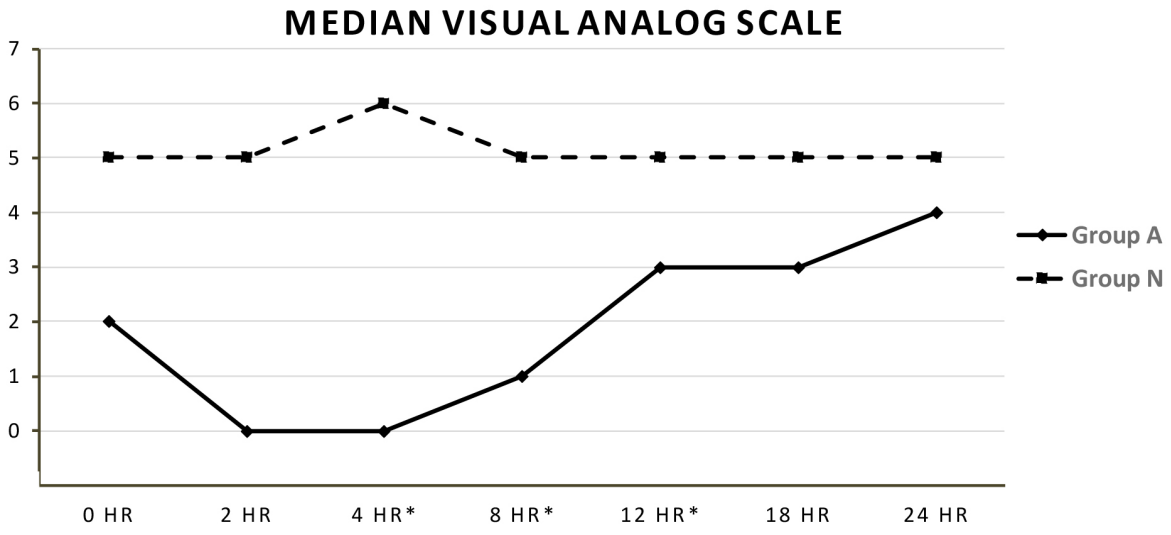


Figure 4. Comparison of median morphine consumption between group A (anesthetic cocktail group) and group N (control group) at specific postoperative time points (*p-value <0.05 using the Mann-Whitney U test)

Table 1. Demographic data of enrolled participants and operative conditions[#]

Data	Group N (N=27)	Group A (N=27)	*p*-value
Demographic data			
Gender (Female/Male)	18/9	17/10	0.776
Age (years)	58.22 ± 16.42	66.33 ± 9.51	0.031*
Height (cm)	159.04 ± 10.45	160.30 ± 8.80	0.634
Weight (kg)	62.26 ± 12.33	64.30 ± 12.04	0.542
BMI (kg/m^2)	24.59 ± 4.13	24.96 ± 3.62	0.730
ASA status (I/II/III)	6/18/3	11/13/3	0.380
Operative conditions			
Diagnosis (D/F/FB)[##]	17/3/7	20/2/5	0.688
Number of surgery levels (1/2/3/4/5)	8/7/7/3/2	4/6/9/7/1	0.464
Operative time (min)	312.04 ± 96.43	335.37 ± 82.3	0.343
Estimate blood loss (mL)	400 (50-1500)	500 (10-1900)	0.430
Intra-operative complication	No	No	-

[#] Data presented as mean ± SD, except for gender, ASA physical status, diagnosis, and number of surgery levels, which are presented as numbers. While estimate blood loss presented with median with min-max in parentheses and intra-operative complication presented as incidence.
(Group N = control group; Group A = anesthetic cocktail group)
[##] Diagnosis: D = Degenerative, F = Fracture, FB = Failed back surgery
* Statistically significant; *p*-value < 0.05

Table 2: Comparison of the outcomes between two groups[#]

Data	Group N (N=27)	Group A (N=27)	*p*-value
Postoperative morphine consumption (mg)			
2 hours	3 (0-11)	2 (0-11)	0.320
4 hours	2 (0-13)	1 (0-5)	0.048*
8 hours	3 (0-7)	1 (0-6)	0.007*
12 hours	3 (0-7)	1 (0-4)	0.005*
18 hours	3 (1-13)	2 (0-5)	0.026*
24 hours	3 (0-8)	2 (0-8)	0.166
Postoperative VAS for pain			
At recovery room (0 hour)	5 (0-10)	2 (0-10)	0.048*
2 hours	5 (0-10)	0 (0-10)	0.001*
4 hours	6 (0-10)	0 (0-7)	<0.001*
8 hours	5 (0-8)	1 (0-6)	<0.001*
12 hours	5 (0-8)	3 (0-6)	<0.001*
18 hours	5 (0-8)	3 (0-10)	0.001*
24 hours	5 (0-8)	4 (0-8)	0.018*
Duration of first demand of analgesia (min)	5 (1-500)	30 (3-576)	0.013*
Number of morphine-related side effects (nausea, vomiting and pruritus)	8 (29.63)	1 (3.70)	0.024*

[#] Data presented as mean ± SD, except for gender, ASA physical status, diagnosis, and number of surgery levels, which are presented as numbers. While estimate blood loss presented with median with min-max in parentheses and intra-operative complication presented as incidence.
(Group N = control group; Group A = anesthetic cocktail group)
[##] Diagnosis: D = Degenerative, F = Fracture, FB = Failed back surgery
* Statistically significant; *p*-value < 0.05

intra-articular multimodal drug injections after knee surgery such as ACL reconstruction, high tibial osteotomy and total knee arthroplasty. [17-25] Regarding spinal surgery, Kadir Ozyilmaz et al. reported that wound infiltration with levobupivacaine and tramadol resulted in eliminating postoperative analgesic demand and reducing the incidence of side effects.[26] Moreover, combining levobupivacaine and tramadol provided significantly better analgesia compared with levobupivacaine or tramadol alone.

In our study, we used anesthetic cocktails that combine100 mg bupivacaine (0.5%, 20 mL), 3 mg morphine sulfate (0.3 mL) and 30 mg ketorolac (1 mL). The local anesthetic bupivacaine blocks C-fiber input to the dorsal horn; and may thereby, inhibit central sensitization. This could also provide potential benefits such as inhibiting both the early inflammatory response and the late effects of this process (proliferation of capillaries and fibroblasts, collagen formation and scarring). The analgesic effect of locally administered morphine could be mediated by μ-opioid receptors located in the bone. However, ketorolac alleviates pain by inhibiting cyclooxygenases 1 and 2 and lowering levels of prostaglandins at the peripheral pain receptors.

We recognize limitations in our study. First, this present study covered small numbers of subjects that might have led to statistically insignificant parameters when comparing between the two groups. Second, evaluation was performed only during the first 24 hours postoperative. Therefore, pain and opioid consumption could not be assessed after the first 24 hours until patients were discharged from the hospital. In addition, the patients in this study had various pathologies and underwent different procedures which might have interfered with interpreting outcome measurement.

In conclusion, the simple technique of wound instillation using anesthetic cocktails significantly reduced the postoperative requirements of morphine and improved pain control with lower rates of nausea and vomiting over the first postoperative day after posterior spinal surgery.

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SURGICAL TREATMENT FOR A PATIENT WITH MARFAN SYNDROME BY POSTERIOR STABILIZATION: A CASE REPORT

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Abstract

Scoliosis in Marfan syndrome is a common occurrence, constituting up to 63% prevalence. Correction is not always easy as the structural anatomy differs from the general population. We present a female 23 years old with chief complain of curved back since 10 years before admission. The patient had high stature and positive Marfan syndrome's criteria. The patient also complained of shortness of breath. The curvature was progressive becoming more severe over time. In radiographs we found that the main thoracic curve Cobb's angle of 92^0 and main lumbar curve Cobb's angle 76^0. We performed scoliosis correction with pedicle screws and rod by posterior approach. Intra-operative blood loss was 1900 cc. Postoperatively, the patient had weakness at the lower limbs but resolved after several days and gained full motoric function after one week. Severe scoliosis is an indication for surgery to correct the spinal deformity that causes several complications such as pulmonary and cardiac complications. The result was satisfying proving that the procedure is safe and with proper peri-operative preparation, we may achieve a good functional outcome.

Keywords: Marfan syndrome, Scoliosis, Surgery

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Introduction

Marfan syndrome is a common connective tissue disorder compromising around 0.01% of the general population. The disorder is due to dominant mutation of the fibrilin-1 gene located on chromosome 15. Traditionally, diagnosis is made using the Ghent criteria although newer revised criteria has been proposed.[1]

Spinal deformity is one of the most dreaded clinical features in Marfan syndrome that often needs correction. Although more patients will not require correction, the clinical consequences of patients with spinal deformities are often severe and troublesome. Spinal deformities in Marfan syndrome include progressive scoliosis and thoracic lordosis with concomitant loss of lumbar lordosis, and more rarely, thoracolumbar kyphosis, severe spondylolisthesis and cervical problems. Marfan syndrome is often associated with scoliosis, with two thirds of cases having the aforementioned deformity. Approximately one quarter to one half of those patients have curves severe enough to consider surgical correction after nonoperative approach. Scoliosis in Marfan syndrome has a higher prevalence of double thoracic curves and triple major curve.[2-3] Almost one half of patients have kyphosis up to 50^0.[4]

Newer methods and instrumentation have improved the outcome of scoliosis treatment, including for patients with Marfan syndrome. The aim for treatment for scoliosis among patients with Marfan syndrome is to achieve spinal correction and good general functional outcome. As bracing is often ineffective in treating the scoliosis associated with Marfan syndrome, surgery has been considered as the current definitive treatment among patients with scoliosis more than 40^0.[5] We present a case of Marfan syndrome with a severe scoliosis corrected using the surgical posterior approach.

Case Report

Clinical condition

We present a woman 23 years old with curved back since ten years previously. At first the curvature was not severe, and the patient did not seek medical attention. Five years later, the curve worsened, and the patient sought medical attention. The patient went to an orthopaedic clinic and was suggested to undergo the operation. The family refused the operation due to financial problems. The patient then decided to take out health insurance first. The patient returned three years later with complaint of shortness of breath, back pain and fatigue. The patient could not stand for long periods. No history of neurological deficit, defecation and urinal problem was present. The patient had high stature, positive Steinberg sign and Walker-Murdoch sign. Forward flexion was $0\text{-}90^0$, extension was $0\text{-}25^0$, right lateral bending was $0\text{-}40^0$ and left lateral bending was $0\text{-}40^0$. Body height of the patient was 164 cm with sitting height of 74 cm, plumb line was to the right side around 3 cm and rib hump was 5 cm (**Figure 1**). No shoulder tilt or pelvic tilt was evident, and the body-arm distance was 3 cm. From the neurological examination, no neurological deficit was present. The X-ray of the patient is shown in **Figure 2**, and radiologic parameter is shown in **Table 1**. From the physical examination, we concluded the patient to have a diagnosis of neurogenic scoliosis due to Marfan syndrome. Before the operation, we consulted a cardiologist and pulmonologist for echocardiography and spirometry and evaluated the tolerance for operation. This was the step for peri-operative preparation.

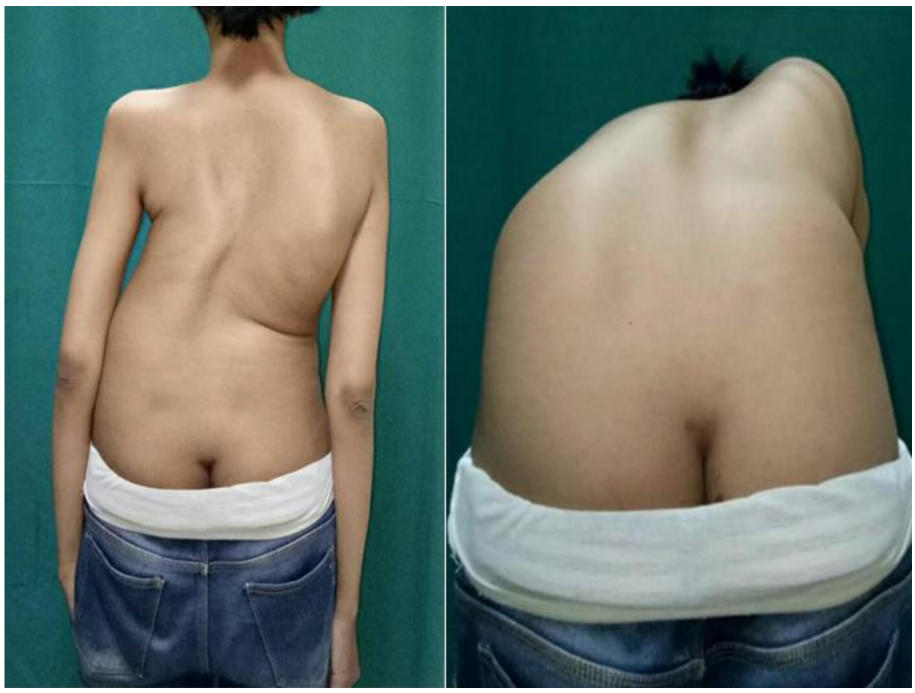


Figure 1. From the clinical picture, a curved back was present with right thoracic curve and left lumbar curve, with rib hump, no step off and no tenderness.

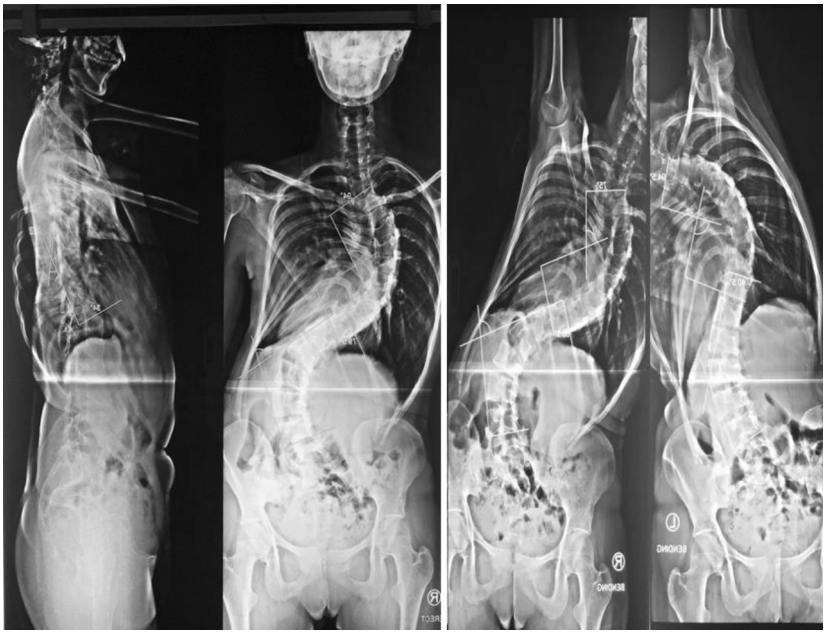
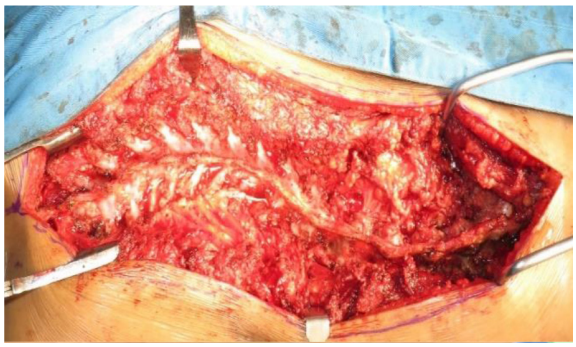


Figure 2. X-ray of the patient, from the left, lateral erect, AP erect, right lateral bending, left lateral bending

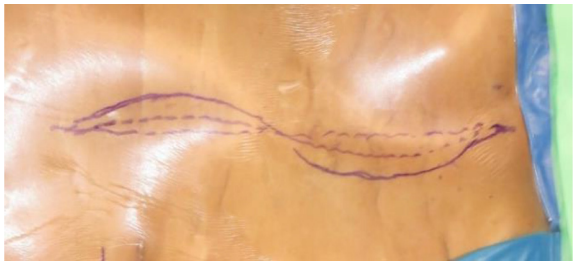
Table 1. Radiological scoliosis profile measurement of the patient

		Cobb angle	UEV	LEV	Apex
Proximal thoracic		15^0	Thoracal 2	Thoracal 4	Thoracal 3
Main thoracic		92^0	Thoracal 5	Thoracal 11	Thoracal 7
Lumbal		76^0	Thoracal 12	Lumbar 4	Lumbar 2
Riisse	R5				

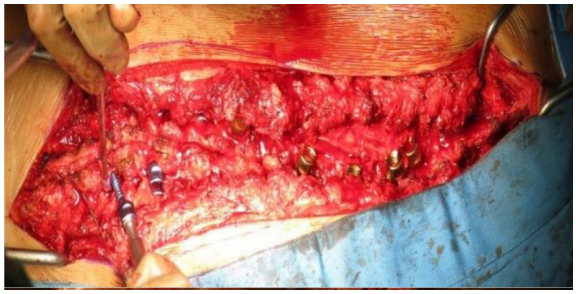
*UEV: upper end vortex, LEV: lower end vortex



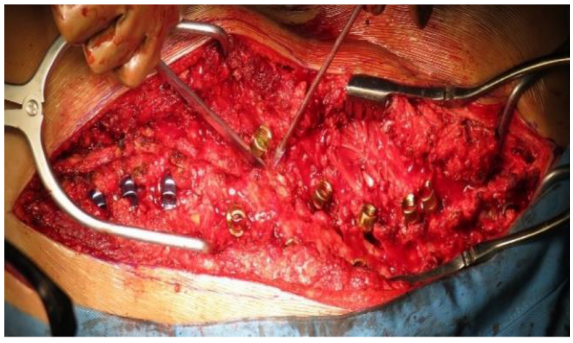
Step 1. Incision design was made. From the picture, we can see the scoliosis curve (a dash-dotted line), midline (inside dots), and incision landmark (middle dots).



Step 2. After incision layer by layer, the whole spine was exposed. The rotational deformity is clearly observed.

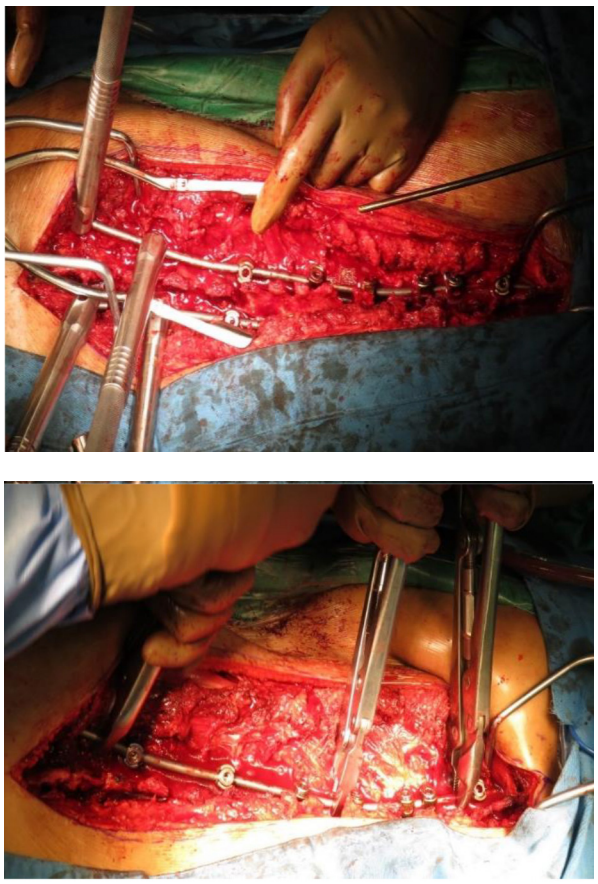


Step 3. Pedicle screws are inserted into Thoracal 3, 5, 8, 10, and 12 (monoaxial), and Lumbar 2, 3 and 4 (polyaxial). The pedicles are around 4.5 to 5.5 mm in diameter.



Step 4. Facetectomy and release of interspinosus ligament are done to further free the vertebral body. Knubble was used to harvest bone graft.

Figure 3. Surgical procedure step by step



Step 5. A rod is placed afterwards. Translational (the upper figure) and rotational (the lower figure) correction are done.

Figure 3. Surgical procedure step by step (Next)

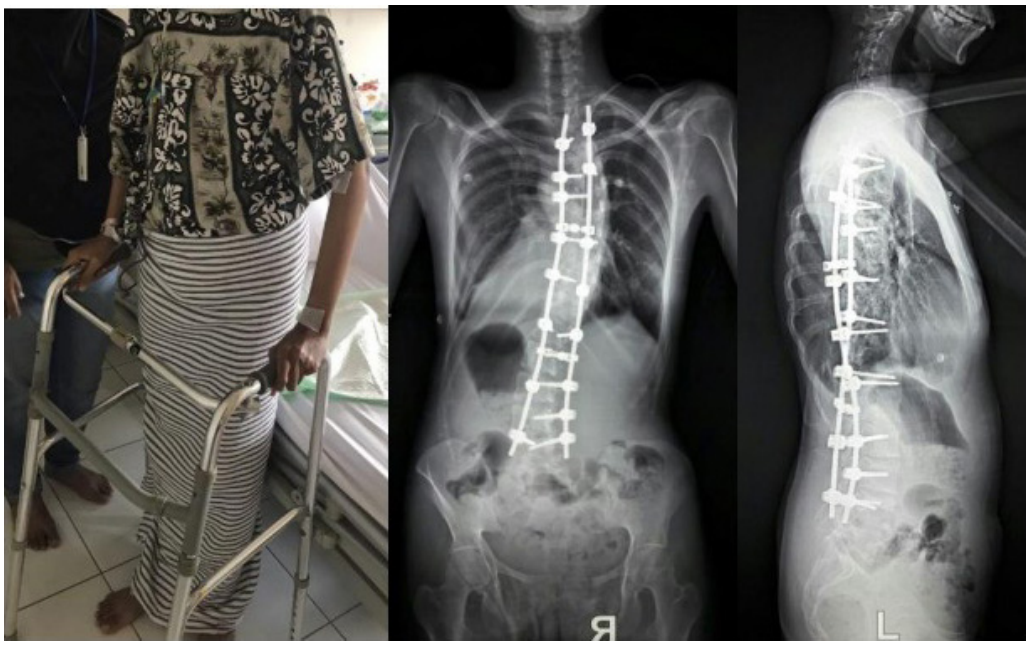


Figure 4. From left to right, clinical picture showing the patient had a good functional outcome, and the AP and lateral x-ray postoperatively.

Table 2. Pre-operative and postoperative comparison of Cobb's angle

	Pre-operative	Post-operative	Angle Difference
Proximal thoracic	15^0	3.9^0	11.1^0
Main thoracic	92^0	46.2^0	45.8^0
Lumbal	76^0	32^0	44^0

Surgical technique

We performed scoliosis correction using pedicle screws and rod by posterior approach. The surgical steps for treating the scoliosis are shown in **Figure 3**. Intra-operatively the blood loss was 1900cc, with additional transfusion of 750cc of packed red cell and 500 cc of fresh frozen plasma. After the operation on the third day, more transfusion was given due to a drop in the hemoglobin. Immediately after the operation, patient complained of weakness on both of her legs; however, the weakness improved. On the seventh day, she was able to stand on both of her legs and walk with the help of assisted walking device. The postoperative X-ray is shown in **Figure 4**. The comparison of Cobbs' angle pre- and postoperative is shown in **Table 2**. Three months after the operation the patient was able to walk without assisted device, without complaint of shortness of breath or back pain.

Discussion

Spinal deformity characteristic in Marfan syndrome

The spectrum of spinal deformity is wide ranging from lumbar lordosis, or thoracal kyphosis to severe scoliosis. The classic Marfan syndrome features include vertebral scalloping, higher prevalence of lumbosacral transitional vertebrae, lengthened process distance and a reduction in pedicle width; therefore, causing the mean pedicle width to be smaller than the smallest pedicle screw. Laminar thickness is also smaller than normal controls. In our patient, we tended to use a smaller pedicle screw with 4.5 to 5.5 mm in diameter due to smaller size in the pedicle. [2, 4, 6]

Scoliosis is prevalent in Marfan syndrome, reaching a fascinatingly 63% of patients. [7] Although similar to cases of idiopathic scoliosis, Marfan syndrome with scoliosis usually presents with deformities that are more severe and progressive. A higher prevalence of double thoracic curves and triple major curves has been noted among patients with Marfan syndrome. A severe scoliosis case may also cause problem in cardiac and pulmonary systems. The threshold of curve progression is below 40^0 at the age of maturity, but the Ghent criteria includes Marfan syndrome with a scoliosis curve more than $20^{0.2}$ In our patient, the main thoracic curve was 92^0. The curvature was progressing at a great rate that after ten years, the patient had more than 90^0 of angle. The patient also complained of shortness of breath, which probably manifested due to her scoliosis. After the correction, the patient gradually diminished the complaint, a few months after follow-up no further shortness of breath was observed, and the motoric function returned to normal with grade 5 in each of the limbs. Unfortunately the lung function was not performed postoperation.

Indication of surgery

Spine surgery is indicated for approximately 10 to 15% of cases. Braces may be indicated for less severe cases, but due to its progressiveness usually surgery is more appropriate. Scoliosis progresses faster among patients with Marfan syndrome than the general population, with mean progressivity at the age of 3 years old and mean progression of 19 ± 17^0 per year.[7] Curves greater than 40^0 traditionally are noted to be more progressive and will give significant clinical impact for the patient. At this rate, brace treatment was not indicated for the patients. Brace treatment is usually indicated for patients with curvature less than 20^0 but with the understanding that in the future, a scoliosis correction by surgery may be needed. [1] Including our patients, we proposed the need for scoliosis correction per surgery so

that we may achieve a more acute correction; thus, correcting the associated deformities and cancel the notorious complications. Although an anterior release and discectomy before the posterior instrumentation may improve correction in severe scoliosis in Marfan syndrome, we performed posterior stabilisation only. This is in line with the study by Silvestre et al. which stated satisfactory stabilisation of scoliosis could be achieved by posterior instrumentation alone among patients with Marfan syndrome. [3]

In the past, due to the respiratory insufficiency and cardiology problems caused by the syndrome, surgery was not an exciting option, especially scoliosis correction. However, due to improved surgery techniques and supporting systems, this is no longer justifiable; instead, this makes surgery become one of the mainstay treatments of those living with Marfan syndrome to definitively correct the deformity and control the rate of associated complications. [3] Based on this optimism, we proceeded to surgery, especially choosing the posterior approach; we further reduced the risk associated with pulmonary deficiency or cardiology; thus, marking the safety of this procedure.

In our study the blood loss was 1900 cc with additional transfusion of 750 cc of packed red cell and 500 cc of fresh frozen plasma. This was higher than the mean reported blood loss in idiopathic scoliosis, with a range of 800-1400 cc. [8-9] This was probably due to the higher severity of the scoliosis curvature and length of operation to correct the deformity. However, this was lower than the mean blood loss in a serial study of scoliosis among patients with Marfan syndrome by Jones, which reached 2400 cc. [5] After the surgery, the thoracic curve achieved 45.8^0 (~50%) and lumbar curve achieved 44^0 (~56%) correction. The correction was acute at first causing the patient to have neuropraxia; thus, causing sudden weakness in both the lower extremities. The weakness; however, was temporary and after a few days the patient had fully gained the motoric function. The rate of this surgical complication is unclear in recent literature reports. [10] The correction was also in accordance with the recommendation given by Jones that the correction achieved should be around 50-60% to avoid curve decompensation.[5] However, the patient did not complain of numbness or neuropathic pain afterwards.

The need for treatment guidelines for spinal deformity

Overall, spinal deformity correction has shown good results, providing good functional and physiological outcomes for patients. Patients were satisfied and we can hope for a longer life for the patient. Nevertheless, the treatment can be considered late as the patient was 23 years old and already had a curved back for 10 years. Therefore, a guideline consensus for surgery may be needed to improve the overall outcome. However, as the literature for this kind of deformity is still lacking, more research on comparing the clinical outcome of patients treated early or late may be needed first. Guidelines will be needed to help clinicians make decisions on a daily basis

Conclusion

Severe scoliosis with Marfan syndrome could be corrected acutely and safely by surgery using the posterior approach. The procedure is important to improve functional and physiological outcomes for the patient.

CONFLICT OF INTEREST

The authors declare they have no conflict of interest.

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