Original Article

Assessing the knowledge of medical undergraduates on oral anticoagulation therapy

Chayna Sarkar[1], Julie B. Wahlang[1], Reuben P. Syiem[1], Arky J. Langstieh[1], Biswadeep Das[2], Melam Surong[1]

[1]Department of Pharmacology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong, Meghalaya, India, [2]Department of Pharmacology, AIIMS, Rishikesh, Uttarakhand, India

Abstract

Objective: Oral anticoagulant drugs, such as warfarin, are widely used for preventing and treating vascular and thromboembolic disease in patients with chronic atrial fibrillation, venous thrombosis, and coronary heart disease. As oral anticoagulant therapy has such a narrow therapeutic range, complications in administering these drugs can prove to have a detrimental effect on patients such as life-threatening bleeding might occur. It is therefore necessary to have an adequate knowledge about its actions and its interactions with other dietary factors or any other medication involved. This study was therefore formulated in order to evaluate the knowledge as well as to impart proper awareness to the medical undergraduate students about oral anticoagulation therapy such as to prevent any untoward situation that may arise from the process. **Methods:** A cross-sectional descriptive study was used to assess the knowledge on oral anticoagulant therapy among the medical undergraduates of a tertiary care hospital. A pre-validated structured questionnaire consisting of 28 questions was adopted, and a separate questionnaire was used for each student. Timing of answering the questionnaire was set at 30 minutes. Scores were evaluated such as a correct answer was given a score of one and wrong answer awarded as zero. Adequate knowledge sore was set above 70% and inadequate knowledge at less than 40%. **Results:** The response rate was found out to be 67.33% with gender distribution observed to be 71% females and 29% males. From the answers evaluated, overall average score of 67.3 ± 15.9 was obtained indicating that most of the respondents have adequate knowledge about the different mechanism, drug–drug interactions, drug–food interactions, and side effects of anticoagulant therapy, and 100% of the students are well aware about the complications and procedures involved to dissipate information about warfarin therapy. **Conclusions:** Adequate exposure of students to clinical cases will further help them to focus on the importance of anticoagulation and strengthening their knowledge regarding anticoagulant drug therapy. This will influence the process of physician–patient communication for improving anticoagulation outcome.

Keywords: Knowledge, medical undergraduates, oral anticoagulants, warfarin therapy

Introduction

Oral anticoagulants are widely used for preventing and treating vascular and thromboembolic disease in patients with chronic atrial fibrillation, venous thrombosis, and coronary heart disease.[1,2] The most common oral anticoagulant drugs are the Vitamin K antagonists such as warfarin. However, its unpredictable pharmacological nature makes warfarin administration a challenge. Several drugs when administered concomitantly can alter its pharmacokinetics by either reducing its absorption from the GI tract or by interrupting its metabolic clearance.[3] Its narrow therapeutic range and pharmacodynamics are largely affected by genetic and environmental factors. Warfarin is mainly metabolized by the hepatic enzyme, cytochrome P450 complex; hence, several

Address for correspondence: Dr. Julie B. Wahlang. Assistant Professor, Department of Pharmacology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong - 793018, Meghalaya, India. E-mail: juliewahlang@gmail.com

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genetic mutations in this enzyme complex can show a variation in the anticoagulant efficacy in different individuals.[4] Warfarin therapy is also sensitive to type of diet intake and metabolic state of an individual. In brief, the effect of warfarin is influenced by many factors including known and unknown genetic factors, drugs, diet, and also various disease states.

The wide range of interactions exhibited by warfarin in relation to drugs, food, and herbs; its narrow therapeutic range and unpredictable pharmacology may lead to patients being over anticoagulated or under anticoagulated,[5] and this may result in nontherapeutic anticoagulation or life-threatening hemorrhagic complications.[6-9]

Inadequate knowledge among healthcare professionals providing anticoagulation services can lead to poor patient compliance and increased of these life-threatening risks and complications[10] Most common mistakes encountered during anticoagulation therapy include improper continuation or discontinuation of anticoagulatory agents, unintended administration of interacting drugs like aspirin or NSAIDS, and other anticoagulant drugs being co-administered.[11] Another common factor contributing to poor anticoagulation therapy is under dosing of warfarin or other anticoagulants by physicians. It is reported that patients already on oral anticoagulants with INR in therapeutic range were 35% in Indian population and 36% among Chinese patients as compared to 67% in Western Europe. Fewer facilities and poor access to INR testing as well as lack of proper anticoagulation management and awareness accounts for the low-quality care.[12]

Studies show that awareness about warfarin therapy greatly improved with effective communication imparted by healthcare professionals.[13] A study in England reported that patients are well aware of the importance to inform the pharmacist or physician regarding taking over the counter (OTC) medicines or herbal products while on anticoagulant therapy.[11] Therefore, in order to improve the quality care in anticoagulation therapy, it is important that interventions be made from the physicians for proper awareness and education on anticoagulant management.[12] As such, medical undergraduates who are the future clinicians in health care need to be alert in monitoring warfarin therapy and its potential interactions with drugs, foods, and medicinal herbs, thereby counseling their patients accordingly.

The aim of this study is to evaluate the knowledge of medical undergraduates and to impart proper awareness such that effective and reliable communication can be conveyed to patients receiving oral anticoagulants.

Materials and Methods

Study setting

A cross-sectional descriptive research design was used to assess the knowledge on oral anticoagulant therapy among the undergraduate medical of a tertiary care hospital. The purpose of the study was explained to all the participants before commencing, and a separate questionnaire was used for each student. Confidentiality of all study participants was maintained by making their information anonymous, and they were requested to provide authentic answers. Confidentiality of all data was strictly maintained by the investigators. There was no recording of interviews as it only included structured type of questionnaire.

Study design

A pre-validated structured questionnaire with little modification was adopted which consisted of 28 multiple-choice questions which included only one component on the knowledge about the oral anticoagulant therapy [Annexure I]. The core information on the knowledge was the main aspect of the questionnaire.[14] The scoring method of Kumari MJ *et al.*[1] was followed where each correct answer was given a score of one and the wrong answer awarded as zero score.

Scoring of the response to the questionnaire was done as follows:

- Inadequate knowledge: A total score between <40%
- Adequate knowledge: A total score above >70%

Study duration

Each student was given a timing of 30 minutes and was instructed to complete the questionnaire independently and without assistance.

Sampling method and size

A total of 75 students who fulfilled the inclusion criteria of having completed their pharmacology curriculum were recruited as respondents for the study.

Data collection

All the data were collected strictly from the answers provided on the pre-validated questionnaire.

Data analysis

Data analysis was conducted using SPSS version 27. Data were presented as percentages and Mean ± SD. Variables included were age, sex, and grade point average.

Ethical approval

The ethical approval was obtained from the Institutional Ethics Committee [NEIGR/RCELL/2016/0060].

Results

A total of 52 students out of 75 participated in the study taking the response rate at 69.33%. Gender-wise distribution of study population is given in Figure 1.

The analyzed results of the questionnaire showed an overall average score of 67.3 ± 15.9 of adequate response implying

that the students have an adequate knowledge regarding the warfarin therapy.

Drug–drug and drug–food interaction

Knowledge score on DDIs of warfarin with other drugs when evaluated was seen to be highest related to use of alternative medicine along with warfarin with majority of the respondents corresponding to the adequate response. This was followed by an adequate response related to use of warfarin with other generic drugs and other medications, respectively. Least number of respondents was seen to be with the case of concomitant medication of warfarin with multivitamins. Adequate number of respondents educated with interaction of warfarin therapy with alcohol and food was reported to be 90% and 84%, respectively. Very few respondents were aware of interaction of warfarin with multivitamins [Table 1].

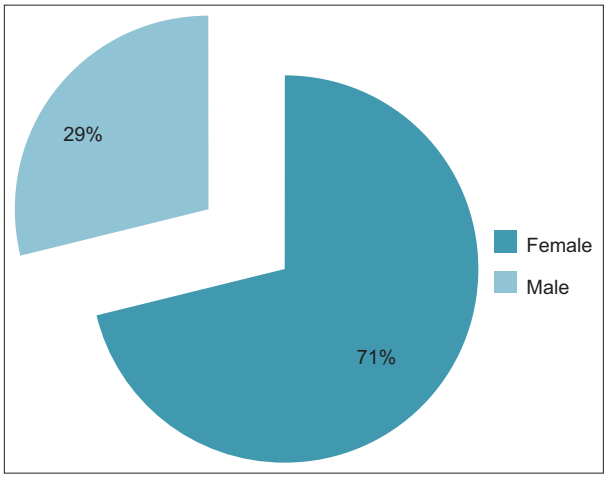

Figure 1: Gender-wise distribution of the study population

Pharmacokinetic/pharmacodynamic factors

Assessment of the knowledge of the respondents on the basis of effect of different pharmacokinetic/pharmacodynamics factors on warfarin therapy was seen to be mostly adequate in nature with scores ranging from 72–92% accordingly except on two cases where response of 12% and 4% was seen [Table 1].

Adverse effects of warfarin

Maximum respondents were observed in the case in which emergency admission is warranted while on warfarin treatment. Adequate numbers of students were also aware of the side effects of warfarin therapy, while only few respondents were affirmative about the effects of warfarin if INR value being high, and 14% of the response was positive when dealing with adverse effects of warfarin and its management [Table 1].

Information to health providers about warfarin

All the participants (100%) taking part in the study were well-aware of the procedure in providing vital information to physicians and dentists about the adverse effects of warfarin treatment [Table 1].

Drugs and food items to be avoided

Table 2 represents the response of the participant's regarding their knowledge about different medications and foods to be

Table 1: Assessment of knowledge on anticoagulant usage among medical undergraduates

Variables	Adequate response (%)	Inadequate response (%)
Drug-Drug interaction		
Knowledge regarding multivitamin intake	6	94
Effect of other medications on warfarin	80	20
Usage of alternative medicine	96	4
Drug-Food interaction		
Warfarin and fruit juice interaction	4	96
Effect of alcohol on warfarin	90	10
While on warfarin intake of spinach	46	54
Effect of food on warfarin	84	16
Pharmacokinetic/pharmacodynamic		
Meaning of INR	84	16
Value of INR testing while on warfarin treatment	88	12
Mechanism of action of warfarin	86	14
Elimination time of warfarin	84	16
Situation need attention of emergency room	84	16
Manifestation leading to emergency room	84	16
Proper physical activity	88	12
Adverse effects of warfarin		
Adverse effects of warfarin and need of going to outpatient clinic	14	86
Effect of warfarin medications if INR is high	12	88
Symptoms where there is need of going to emergency room while on warfarin	92	8
Information to health providers about warfarin		
Informing clinic about which medication to take for headache when on warfarin treatment	100	0
Informing dentist about warfarin therapy	100	0

Data represented as % of the study population (n=52); INR=International Normalized Ratio

Table 2: Knowledge on self-medicated drugs and food items which should be avoided when taking anticoagulants

Variables	Types of medications and food items	Adequate response (%)
Drugs to be avoided	Aspirin	80
	Multivitamins	6
	Alternative Medicine	96
	Antibiotics	84
Food items to be avoided	Spinach	46
	Alcohol	90

Data represented as % of the study population (n=52)

avoided while on warfarin therapy. It is to be noted that >80% response was seen in case of interaction of warfarin with drugs like aspirin, antibiotics, and alternative medicine, while only 6% responders were knowledgeable about its interaction with vitamins. Also, majority of the responders were well aware of the fact that alcohol interferes with the activity of warfarin.

Discussion

Our study report is based on the knowledge and awareness of medical undergraduates regarding the different factors involved in the usage of anticoagulant therapy. This includes its interactions with other drugs, food, pharmacokinetic/pharmacodynamics factors, and their proper knowledge in imparting proper education or counseling to patients.

Drug–drug and drug–food interaction

Our findings showed that majority of the respondents have adequate knowledge regarding the effect or interaction of other drugs or herbal treatment or any form diet intake with anticoagulant efficacy of warfarin. For instance, some drugs, e.g., cholestyramine and sucralfate, reduce the gastrointestinal absorption of warfarin thereby affecting its bioavailability and other drugs, e.g., ibuprofen, quinidine potentiates its activity by displacing it from the protein binding sites.[3,15] Aspirin and NSAIDS, however, can increase bleeding by inhibiting platelet function thereby altering homeostasis and inhibiting formation of thrombus.[3] Similarly, a few herbal products also show the possibility of interacting with warfarin.[16] Dietary supplements or concurrent use of vitamin K also has the potential to reduce the anticoagulant effect of warfarin.[3] Fruit juices like grapefruit juice have an inhibitory effect on the CYP3A4 activity,[15] and cranberry juice inhibits warfarin metabolism (CYP2C9).[17-19] Reports linking the risk of bleeding between alcohol intake lead to poor indicators on quality of life while on therapy with anticoagulants have also been established.[20,21] Our study also report that majority of the responders have adequate information regarding the interaction of alcohol intake on the anticoagulation effect of warfarin. Therefore, proper education given to patient regarding warfarin therapy and food interactions, as well as to reduce smoking and drinking while they are on anticoagulant (warfarin) therapy as such to prevent treatment failure or complications arising during therapy is therefore essential.

Pharmacokinetic/pharmacodynamics factors associated with anticoagulation

Assessment of the knowledge domain on duration of action and side effects of warfarin showed adequate response about INR or International Normalized Ratio (INR) and its various pharmacokinetic/pharmacodynamics-related factors. INR is a measurement of the duration or time that it takes for a blood to clot and a range of 2.0–3.0 is the normal range for patients under anticoagulant therapy. The higher the INR value, the longer the blood will clot. This INR value will determine the amount of warfarin dose of needed to take.[22] The blood report of INR shows stability of INR after two–three months of warfarin therapy with marked individual variation making standardization of warfarin dose a difficult task with reports of 30% of drug-related errors occurring in patient.[23,24] Regular physical activity is encouraged as it is associated with lower risk of hemorrhage in patients on chronic anticoagulation therapy, which is also reflected in the adequate knowledge about it among our responders.[25-29] An adequate score among the participants was also seen in the cases where emergency admission while on warfarin therapy is entailed. Abdullah *et al.* reported that moderate bleeding do occur in patients during dental extractions that are on warfarin therapy. Failure to provide prior information to the dental clinic regarding their drug therapy on warfarin would arise to unwanted bleeding complications during dental procedure.[30-32]

Adverse effects associated with anticoagulation

Oral anticoagulants especially warfarin can cause serious adverse drug reactions, and they have been kept as high-alert medications. It is to be emphasized that warfarin is included among the top 10 drugs with the most number of serious adverse effects reported by the FDA's Adverse Event Reporting System with over-anticoagulation and fatal bleeding complications among few of them. However, our study report shows that few responders have proper adequate knowledge pertaining to reporting and management of adverse reactions of warfarin whereas majority of them lack this information.[33,34] It is therefore advisable that physicians are well informed and timely reporting of the signs and symptoms of bleeding be carefully and appropriately done. Further, it is seen that the responders have inadequate knowledge on the aspect of warfarin effect if INR is high. This issue needs to be thoroughly addressed only through proper counseling and education by well-trained and well-versed healthcare providers.

Information relating to warfarin treatment

It is seen that all of the respondents (100%) were aware of the importance to inform clinicians or dentists while on warfarin treatment. This particular response is important in that it might help in reducing any unwanted adverse reactions that might occur in case another interacting medication[3] was prescribed or any interacting food or herbal supplements taken concomitantly.[16] For instance, a study in England reported the clinical importance of informing the pharmacist or physician regarding taking over-the-counter (OTC) medicines or herbal products while on anticoagulant therapy.[11]

Conclusion

Adequate education of medical students in their levels of knowledge about anticoagulation include drug therapy, patient lifestyle modification due to potential drug–food interaction with safe physical outdoor activities would bring about an improved adherence to therapy and good health outcomes. Proper exposure of students to clinical cases will help to focus on the importance of anticoagulation medical education in addition to conventional lecture-based should include workshops with clinical exposures. This will influence the process of physician–patient communication for improving anticoagulation outcome.

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Conflicts of interest

There are no conflicts of interest.

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ANNEXURE I

1. Age:
2. Sex: Male/ Female
3. Course: MBBS/
4. Year of admission:
5. Current Semester: 6^{th}/ 7^{th}/ 8^{th}/ 9^{th}/ Interns

Section 2: *Anticoagulation Knowledge Assessment (AKA) Questionnaire* **(MCQ with *a single Correct answer*)**

***(*Students may kindly imagine that they are patients and under warfarin therapy. They are requested to kindly answer the following MCQs by encircling the correct option)**
INR = international normalized ratio; PT=prothrombin.

1. Which one of these medications is recommended if you are taking Warfarin and want relief from a headache?
a) Aspirin
b) Diclofenec
c) Ibuprofen
d) Paracetamol

Ans: a/ b/ c/ d

2. Which of the following food items would interfere with your Warfarin medication?
a) Bacon
b) Broccoli
c) Bananas
d) Peeled cucumbers

Ans: a/ b/ c/ d

3. While on Warfarin medication, in which of the following situation would you go directly to the emergency room?
a) Small bruises

b) Your appetite dramatically increases
c) Nosebleed which will not stop bleeding
d) Gums which bleed for a few seconds after brushing teeth

Ans: a/ b/ c/ d

4. You just remembered that you forgot to take your evening Warfarin medication dose last night. You would—
a) Skip the dose of Warfarin you missed
b) Take the missed Warfarin dose right now
c) Wait and take 2 doses of Warfarin this evening
d) Take one-half of the missed dose of Warfarin right now

Ans: a/ b/ c/ d

5. While on Warfarin you—
a) Should not eat spinach
b) Can eat spinach one time a month
c) Can eat as much spinach as you would like whenever you would like
d) Can eat spinach but need to eat the same amount regularly every week

Ans: a/ b/ c/ d

6. While out with friends for dinner, you have just finished your third glass of wine. This amount of alcohol consumed in a single evening will—
a) Cause a decrease in your INR
b) Cause an increase in your INR
c) Not affect you or your Warfarin in any way
d) Make you sick when taking Warfarin medication

Ans: a/ b/ c/ d

7. While in pharmacy, you notice multivitamins are on sale. After some thought, you decide that you may need a multivitamin. You would—
a) Purchase the multivitamin and begin taking it regularly
b) Not take a multivitamin because it will cause a blood clot while taking Warfarin
c) Start taking it and bring the multivitamin to your next Warfarin Clinic visit to show the pharmacist/ physician
d) Purchase the multivitamin but not start taking it until you talked with the Pharmacist/ Physician at your Warfarin Clinic

Ans: a/ b/ c/ d

8. If you ran out of your prescription for your Warfarin you would—
a) Borrow Warfarin from a friend, as long as it is the same dose as yours
b) Call and ask for refills for that day so you do not miss a dose of Warfarin
c) Wait until your next appointment that is just a few days away to get a new prescription
d) Do Nothing Because you have taken Warfarin long enough, otherwise there would be more refills on your prescription

Ans: a/ b/ c/ d

9. Which of the following is an effect of Warfarin medication that will most likely be experienced?
a) Stroke
b) Leg Clot
c) Bruising
d) Blood in the urine

Ans: a/ b/ c/ d

10. You have a cold, which includes a runny nose and cough. You—
a) Could safely take Polypill to help get rid of the runny nose and cough
b) Take your friend's medication that he/she uses for a bad cold because he/she is also on Warfarin medication
c) Would call the Warfarin Clinic and tell him/her you are on Warfarin medication and ask what you can take for your cold
d) Decide it is safer to suffer through the cold because most cold medications will interact with your Warfarin medication

Ans: a/ b/ c/ d

11. When making a dental appointment while taking Warfarin medication, you need to remember you—
a) Cannot have procedures done on your teeth while taking Warfarin
b) Must tell your dentist you are taking Warfarin well in advance of having any procedure done
c) Can have procedures done and there is not a need to tell the dentist about the Warfarin
d) Can have the dental procedure done if when you arrive at your dental appointment you tell the dentist you are taking Warfarin

Ans: a/ b/ c/ d

12. When the need arises to take an antibiotic (to get rid of an infection) while taking Warfarin, you need to—

a) Take half of the prescribed length of therapy, and then call the Warfarin clinic
b) Refuse to take any new medication because you are taking Warfarin
c) Wait until your next Warfarin clinic visit and then tell the pharmacist about the antibiotic
d) Call the Warfarin Clinic right away and let them know you are starting a new medication

Ans: a/ b/ c/ d

13. Warfarin works—

a) in my liver to make my blood thicker
b) in my liver to make my blood thinner
c) in my kidneys to make my blood thicker
d) in my kidneys to make my blood thinner

Ans: a/ b/ c/ d

14. The best time of day for me to take my Warfarin is—

a) at lunchtime
b) in the evening
c) in the morning before breakfast
d) any time of day when I remember

Ans: a/ b/ c/ d

15. Which of the following is an effect of my Warfarin medication that I will most likely experience if my INR is too high?

a) A clot in the leg
b) Minor bleeding
c) Clot in the lung
d) Bleeding in the brain

Ans: a/ b/ c/ d

16. Which of the following drinks can decrease the effectiveness of your Warfarin?

a) Amul's low-fat milk
b) Hershey's chocolate shake
c) Tropicana orange juice
d) Ensure nutritional supplement

Ans: a/ b/ c/ d

17. While taking Warfarin, which of the following represents a situation when you should go to the emergency room?
a) You cough up blood
b) Your nose bleeds slightly while blowing it
c) Your gums bleed after brushing your teeth then it stops quickly
d) You have cut yourself while shaving and you control the bleeding

Ans: a/ b/ c/ d

18. Your neighbor brings over this great "all natural" herbal supplement she just bought from her chiropractor. She swears that this helps all her aches and pains and recommends that you take it when you ache. Your decision is to—
a) take her advice, realizing that you could use this herbal supplement
b) start taking the herbal supplement and tell your pharmacist at the next office visit
c) ask your Pharmacist/Physician if the herbal supplement will interact with your medications before you take it
d) avoid taking herbal supplements altogether because all medications interact with Warfarin

Ans: a/ b/ c/ d

19. Once you have reached a stable Warfarin dose, a PT/INR blood test—
a) should be checked once a year
b) should be checked once every 3 months
c) should be checked at least once every 4 weeks
d) does not need to be checked once you are on a stable Warfarin dose

Ans: a/ b/ c/ d

20. The results of your PT/INR test tells the pharmacist—
a) how thick or thin your blood is while taking Warfarin
b) how well your kidneys are working since taking Warfarin
c) what your average blood sugar level was since taking Warfarin
d) how much alcohol you have been drinking since taking Warfarin

Ans: a/ b/ c/ d

21. While taking Warfarin, you should call your Warfarin Clinic when you get:
a) a backache
b) an upset stomach
c) a tension headache

d) diarrhea for more than 1 day

Ans: a/ b/ c/ d

22. While on Warfarin you need to be routinely monitored for which of the following:
a) PT/INR tests
b) Potassium levels
c) Blood glucose levels
d) Kidney function tests

Ans: a/ b/ c/ d

23. Which of the following may have a significant effect on how well your Warfarin works?
a) Changes in your mood
b) Changes in sleep habits
c) How much water your drink
d) Using over the counter medications

Ans: a/ b/ c/ d

24. While taking Warfarin, which of the following should lead you to the emergency room?
a) Loss of appetite
b) Brown loose stools
c) Urine becomes red in color
d) A quarter size bruise on your arm

Ans: a/ b/ c/ d

25. You have generic and brand Warfarin tablets at home that are both the same dose. You should—
a) take both because they work differently
b) take only brand or generic, but not both
c) not take either until you call the Warfarin Clinic
d) alternate days by taking brand on one day and generic on the next day

Ans: a/ b/ c/ d

26. Once your Warfarin is stopped, how long does it take to get the medication to get out of your system?
a) 5 hours
b) 5 days

c) 5 weeks
d) 5 months

Ans: a/ b/ c/ d

27. After starting Warfarin, how long (in months/years) would you expect to be taking Warfarin?
a) 1 year
b) 1 month
c) It depends on each person's needs
d) If you start Warfarin, you will have to be on the medication for the rest of your life

Ans: a/ b/ c/ d

28. Which of the following activities are more risky while taking Warfarin?
a) Playing football, because you can hit your head
b) Taking a bath, because soap interacts with Warfarin
c) Playing cards because using your hands a lot will cause a blood clot
d) Walking a lot, because exercise is not good for you while taking Warfarin

Ans: a/ b/ c/ d

Thank You !