Survey Report

Perception Mapping of Physicians on the Clinical Outcomes of Tranexamic Acid in AUB Treatment

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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1 INTRODUCTION

Abnormal uterine bleeding (AUB) may be acute or chronic and is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency, or duration and occurs in the absence of pregnancy [1, 2].AUB is a common clinical problem, affecting up to 14% of women during their reproductive years and impairing their quality of life by creating significant physical, emotional, sexual, social, and financial burdens [3-5]. Acute AUB refers to an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to prevent further blood loss [1]. AUB is the preferred term to describe a spectrum of symptoms, such as heavy menstrual bleeding (HMB), intermenstrual bleeding, and a combination of both heavy and prolonged menstrual bleeding [6].

Antifibrinolytic drugs, such as tranexamic acid, work by preventing fibrin degradation and are effective treatments for patients with chronic AUB. They have been shown to reduce bleeding in these patients by 30–55% [7,8]. Tranexamic acid effectively reduces intraoperative bleeding and the need for transfusion in surgical patients and is likely effective for patients with acute AUB, although it has not been studied for this indication [9,10]. Experts recommend using either oral or IV tranexamic acid for the treatment of acute AUB [10].Oral tranexamic acid is FDA approved for the treatment of ovulatory AUB; an IV formulation is approved for use in hemophilia. This medication works by competitively blocking plasminogen binding sites, preventing plasma formation, fibrin degradation, and clot degradation [11,12].

This study is important because it provides insights into physician’s perceptions of tranexamic acid's effectiveness in treating AUB. Understanding these perspectives can influence clinical practice, guide treatment decisions, and improve patient outcomes by identifying potential benefits, risks, and gaps in knowledge regarding tranexamic acid's role in AUB management.

2 RATIONALE OF THE STUDY

The rationale for this survey is to gather clinical insights and real-world practices regarding the management of AUB among healthcare providers. AUB is a prevalent gynecological condition that significantly impacts women's quality of life. By assessing the frequency with which AUB is encountered, the survey aims to quantify its burden on clinical practice, which is crucial for resource allocation and patient

care optimization. The survey evaluates diagnostic approaches used by clinicians, including patient history, structural and non-structural evaluations, and lab investigations. This information highlights the diagnostic strategies employed in practice and underscores the need for a comprehensive approach to accurately identifying the cause of AUB. Further, the survey investigates the therapeutic strategies used to manage AUB, with a focus on tranexamic acid, a commonly prescribed antifibrinolytic agent. Understanding the dosing patterns, use of oral versus intravenous formulations, and the combination with other drugs like mefenamic acid is essential for evaluating the effectiveness and safety of these treatments. Clinicians' perceptions of the reduction in menstrual bleeding and the frequency of adverse drug reactions provide valuable data on the efficacy and tolerability of tranexamic acid in routine clinical settings.

Additionally, the survey explores the circumstances in which tranexamic acid is used prophylactically and when it is contraindicated, reflecting the importance of individualized patient care. The follow-up protocols after AUB treatment are also examined to assess patient monitoring and outcomes.Collectively, the survey results will offer a comprehensive overview of current AUB management practices, providing insights into treatment patterns, efficacy, and safety considerations. This information can help guide future research and support the development of clinical guidelines for managing AUB more effectively.

3 STUDY OBJECTIVE

The objective of this survey is to assess current clinical practices in diagnosing and managing AUB, with a specific focus on the use, dosing, efficacy, and safety of tranexamic acid and related treatment modalities.

4 METHODS

The study is a cross-sectional survey designed to explore healthcare providers' practices regarding the management of abnormal uterine bleeding (AUB). It consists of 16 structured questions addressing the prevalence of AUB, diagnostic methods, treatment goals, and medication use, with a focus on tranexamic acid. Participants will be asked to select responses from multiple-choice options, allowing for quantitative analysis. Key areas of inquiry include the use of tranexamic acid, its

dosing regimen, effectiveness, safety concerns, and follow-up practices. The goal is to gather data from diverse healthcare providers to understand treatment preferences and trends in AUB management, which can help improve clinical practices and patient outcomes.Physicians practicing in India, particularly gynecologists and general practitioners, will be invited to participate via professional networks. Before beginning the survey, participants will receive detailed information about the study. The survey will be administered electronically, with responses securely stored for analysis. Statistical methods will be used to summarize the findings and identify trends, which will be compiled into a report for possible publication or presentation.The study's design is ideal for capturing a snapshot of current physician practices and perceptions, using questionnaires to collect diverse data efficiently. It will examine factors such as treatment preferences, clinical outcomes, safety concerns, and trends in tranexamic acid usage. The planned sample size is 100 physicians, ensuring a diverse and representative sample for robust statistical analysis. Ethical approval will be obtained, and all responses will remain anonymous. In terms of treatment, the primary approach for managing AUB involves medical management. This includes an assessment of the patient's history, with first-line treatments such as tranexamic acid (500 mg, two to three times daily for up to three days) to reduce blood loss. Other treatments, such as NSAIDs or hormonal treatments, may also be used. Regular follow-up consultations are necessary to monitor and adjust treatment as needed. Data analysis will involve both descriptive and inferential statistics to explore the relationship between physician characteristics and clinical practices.

5 RESULTS

A total of 89 HCPs participated in the survey. Below is the summary of the responses.

1. In your clinical practice how many % of patients come with abnormal uterine bleeding (AUB)?

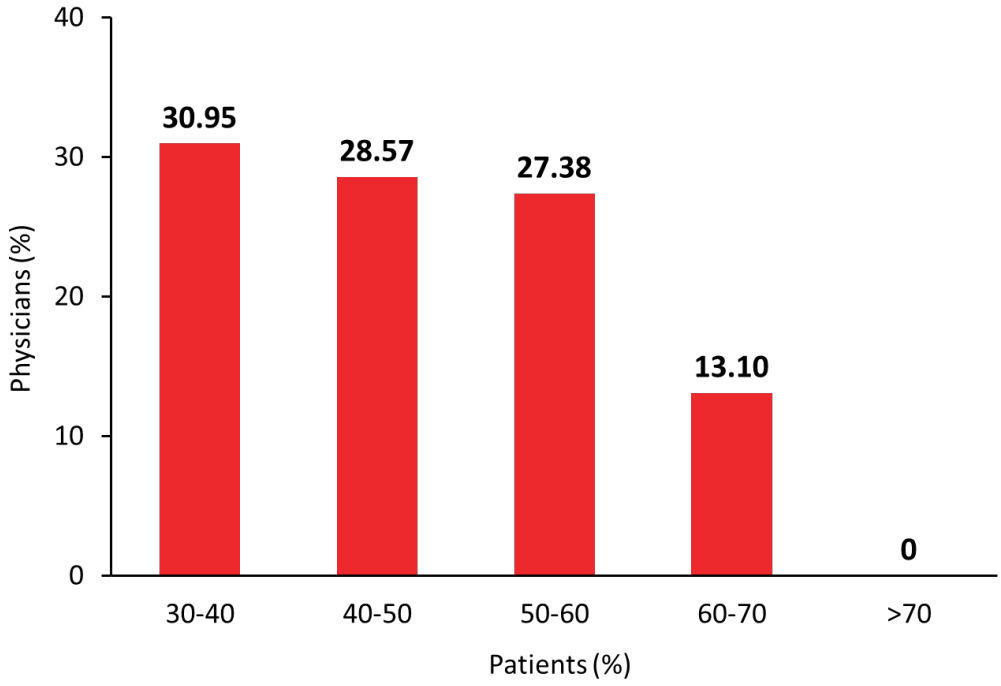
A. 30-40%

B. 40-50%

C. 50-60%

D. 60-70%

E. > 70%



- Approximately, 30.95% of physicians observed 30-40% of patients come with abnormal uterine bleeding (AUB).
- Around 28.57% and 27.38% of physicians noted more than 40-50% and 50-60% of patients respectively come with AUB.
- A small proportion (13.10%) of physicians has seen 60-70% of patients come with AUB.
- No physicians reported more than 70% patients present with AUB

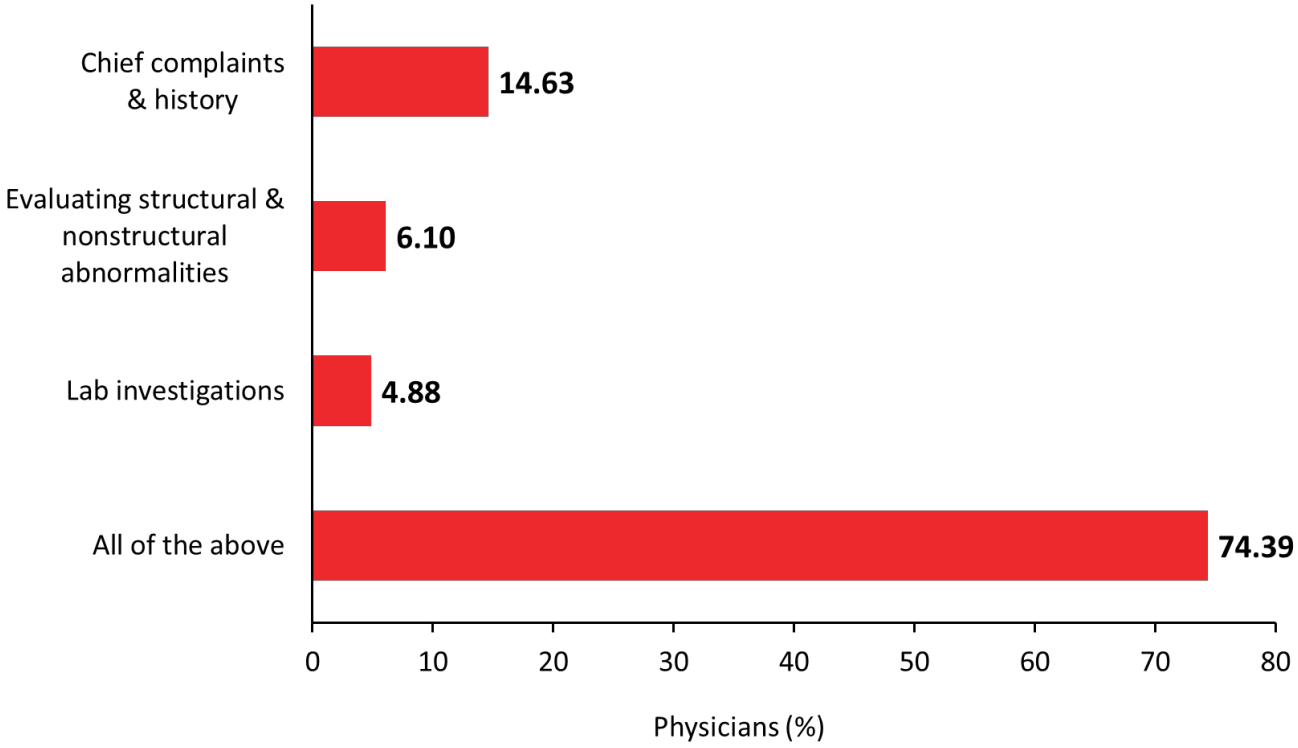
2. In your clinical practice how do you diagnose AUB?

A. Chief complaints & history

B. Evaluating structural & nonstructural abnormalities

C. Lab investigations

D. All the above



- Around 14.63% of physicians diagnose AUB through chief complaints & history.
- Approximately, 6.10% of physicians diagnose AUB through evaluating structural & nonstructural abnormalities.
- A small proportion (4.88%) of physicians diagnose AUB through lab investigations.
- The majority (74.39%) of physicians diagnose AUB through all the above mentioned criteria.

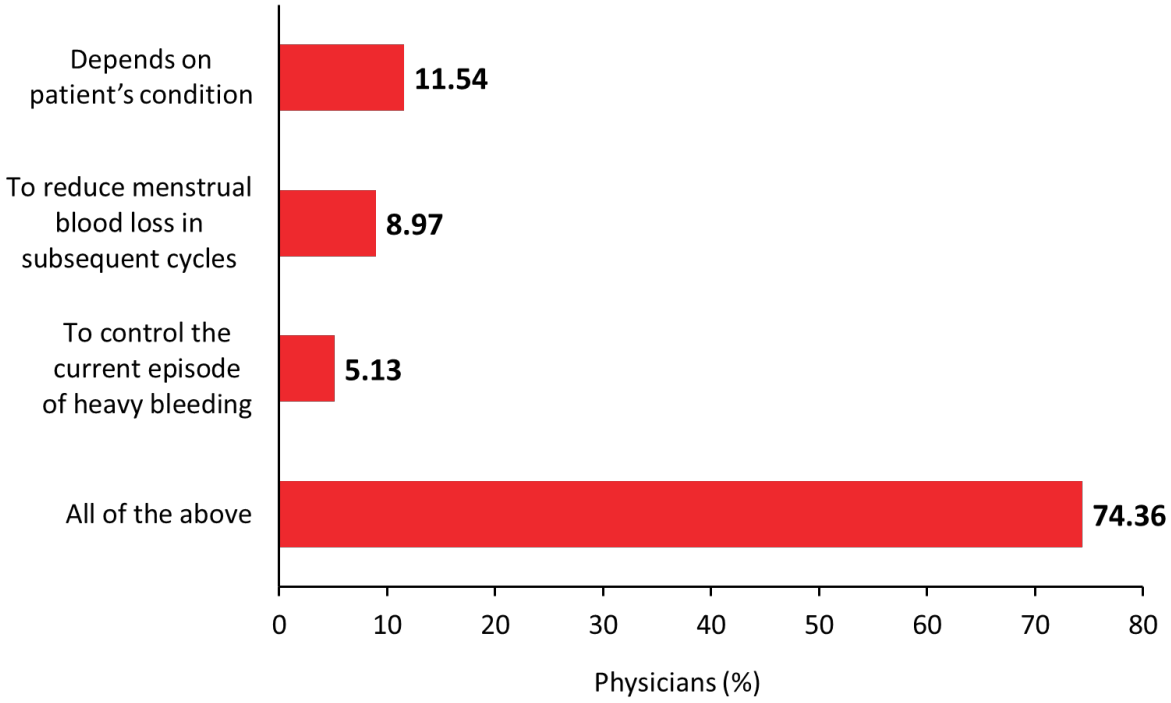
3. In your practice, what remains your objective in treating AUB

A. To control the current episode of heavy bleeding

B. To reduce menstrual blood loss in subsequent cycles

C. Depends on patient's condition

D. All the above



- Approximately, 11.54% of physicians objective depends on the patient condition in treating AUB.
- Around 8.97% of physicians had an objective to reduce menstrual blood loss in subsequent cycles while treating AUB.
- A small proportion (5.13%) of physicians had an objective to control the current episode of heavy bleeding while treating AUB.
- The majority (74.36%) of physicians all the above mentioned objective while treating AUB.

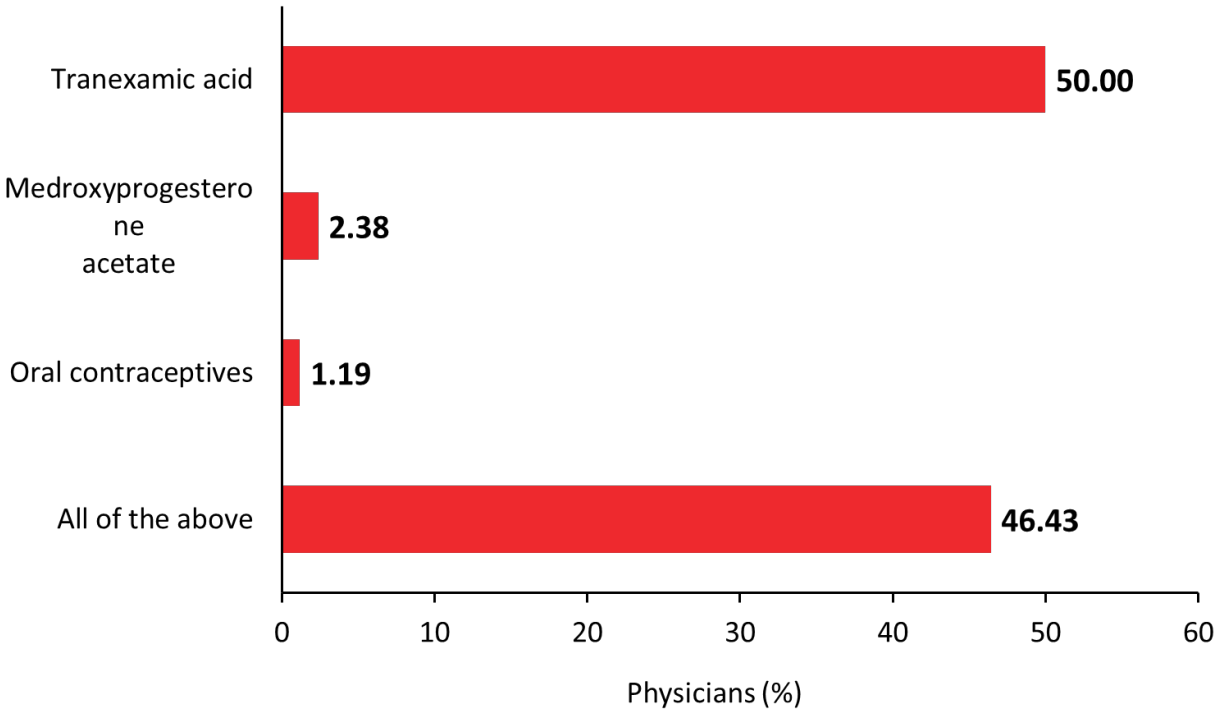
4. In your clinical practice, which drugs do you use to treat AUB?

A. Oral contraceptives

B. Medroxyprogesterone acetate

C. Tranexamic acid

D. All the above



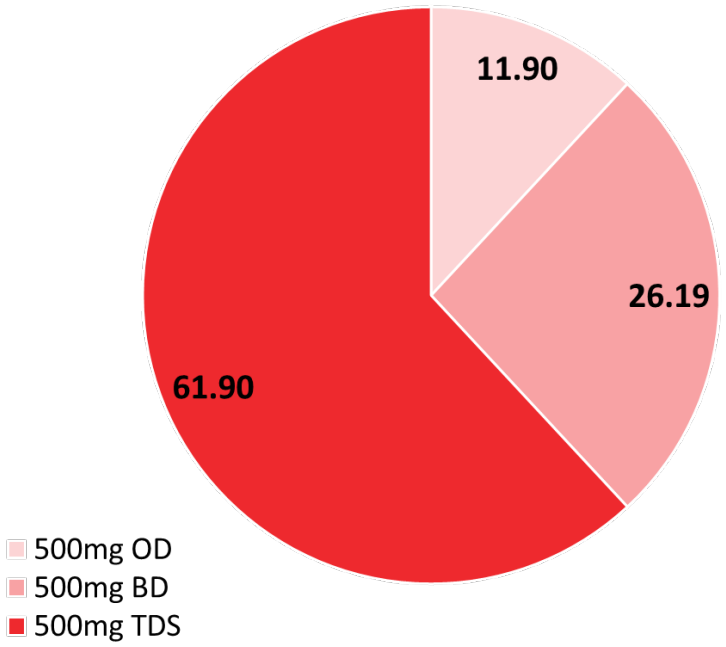
- The majority (50.00%) of physicians use tranexamic acid in treating AUB
- A small proportion (2.38%) of physicians use medroxyprogesterone acetate in treating AUB.
- Around 1.19% of physicians use oral contraceptives in treating AUB.
- Approximately, 46.43% of physicians use all of the above mentioned therapies to treat AUB.

5. In your clinical practice, what dose of oral tranexamic acid you use in treating AUB?

A. 500mg OD

B. 500mg BD

C. 500mg TDS



- The majority (61.90%) of physicians use 500 mg TDS dose of tranexamic acid in treating AUB.
- Approximately, 26.19% of physicians use 500 mg BD dose of tranexamic acid in treating AUB.
- Around 11.90% of physicians use 500 mg OD dose of tranexamic acid in treating AUB.

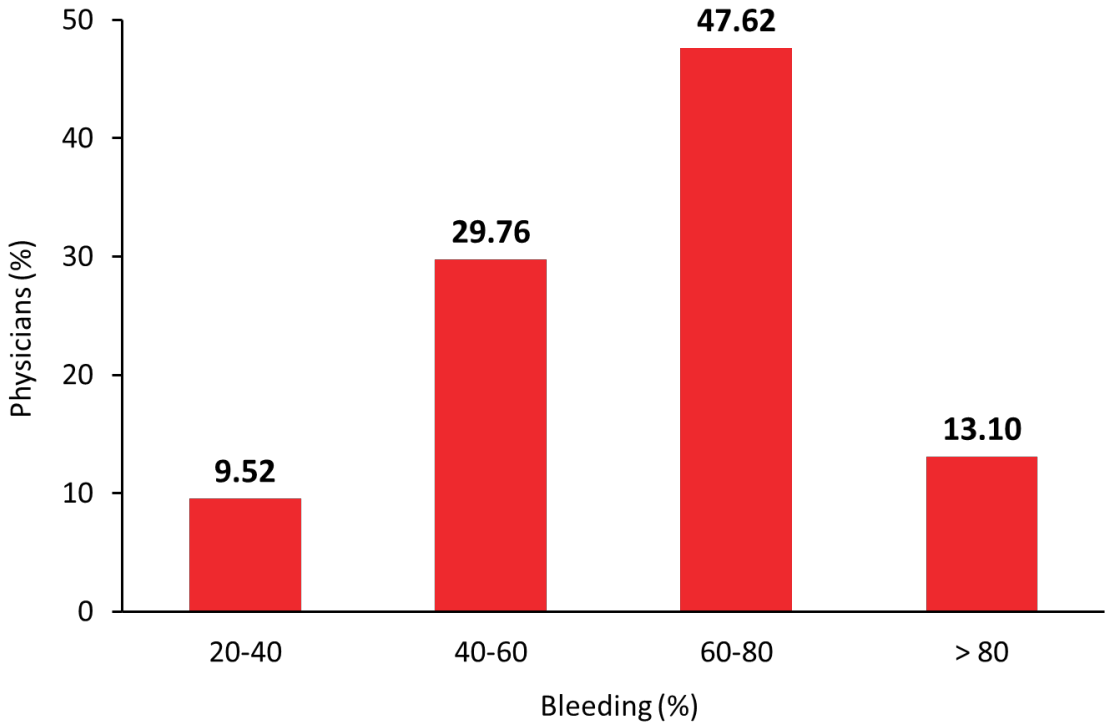
6. In your clinical practice what % of bleeding reduction is seen with tranexamic acid?

A. 20% - 40%

B. 40% -60%

C. 60%- 80%

D. >80%

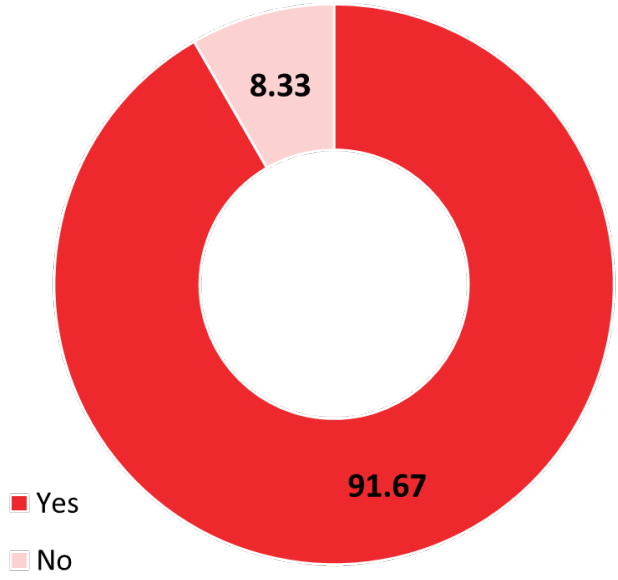


- Approximately, 47.62% of physicians observed 60-80% bleeding reduction with tranexamic acid.
- Around 29.76% of physicians noted 40-60% bleeding reduction with tranexamic acid.
- Meanwhile, 13.10% of physicians has seen more than 80% of blood reduction with tranexamic acid.
- A small proportion (9.52%) of physicians reported 20-40% bleeding reduction with tranexamic acid.

7. In your clinical practice do you use IV tranexamic acid?

A. Yes

B. No



- The majority (91.67%) of physicians use IV tranexamic acid whereas only 8.33% of physicians do not use IV tranexamic acid in their clinical practice.

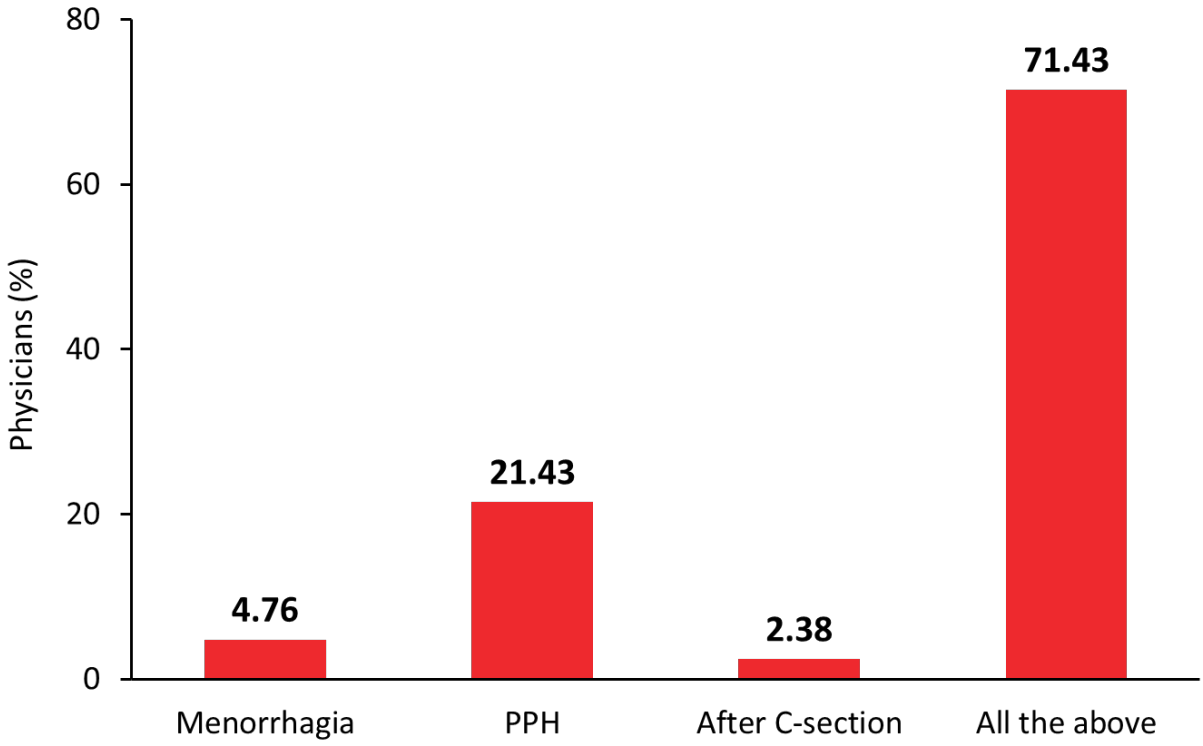
8. In your clinical practice in which condition, you use iv tranexamic acid

A. Menorrhagia

B. PPH

C. After C-section

D. All the above

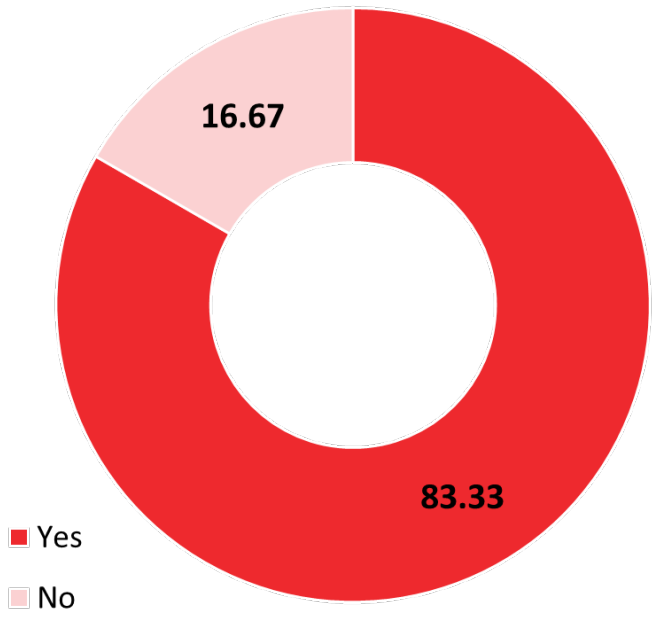


- Around 21.43% of physicians use IV tranexamic acid in the condition of PPH during their clinical practice.
- Approximately, 4.76% of physicians use IV tranexamic acid in the condition of menorrhagia during their clinical practice.
- A small proportion (2.38%) of physicians use IV tranexamic acid after C-section during their clinical practice.
- The majority (71.43%) of physicians use IV tranexamic acid in all the above mentioned condition during their clinical practice.

9. In your clinical practice do you use tranexamic acid prophylactically?

A. Yes

B. No



- The majority (83.33%) of physicians use tranexamic acid prophylactically whereas 16.67% do not use tranexamic acid prophylactically in their clinical practice.

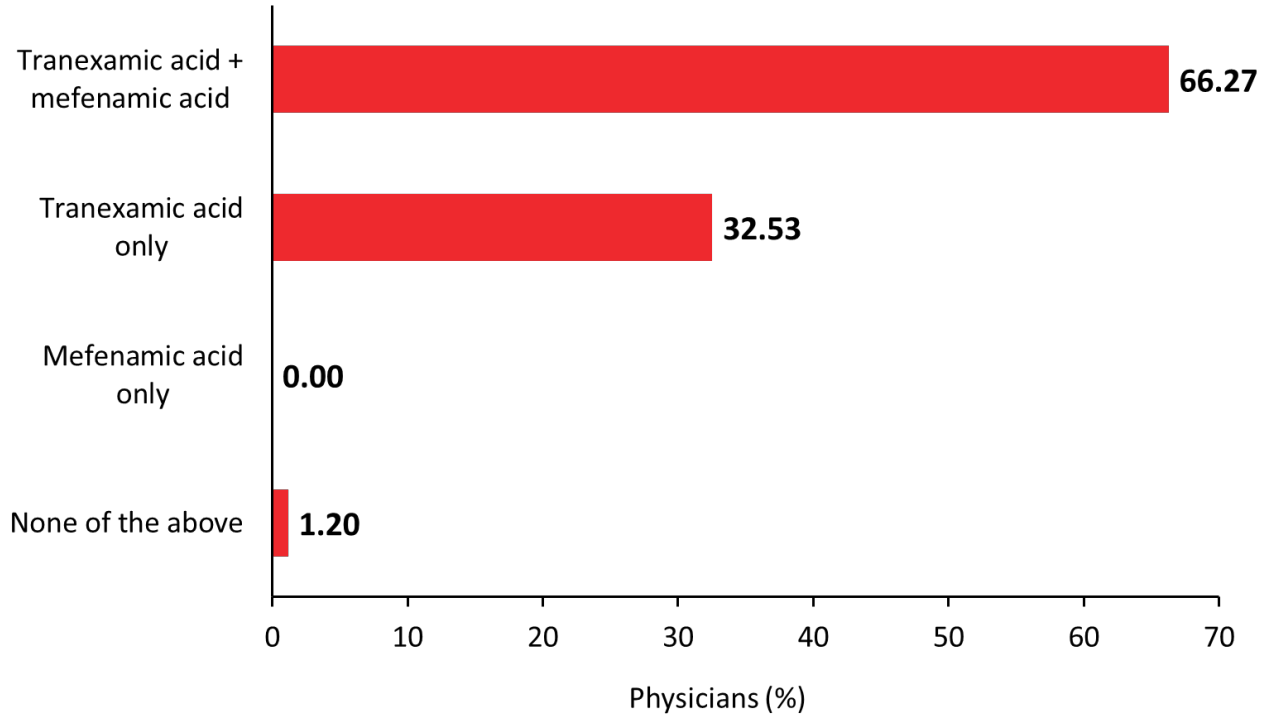
10. In your clinical practice which of the following you use more frequently for treatment of heavy menstrual bleeding?

A. Tranexamic acid only

B. Tranexamic acid + mefenamic acid

C. Mefenamic acid only

D. None of the above



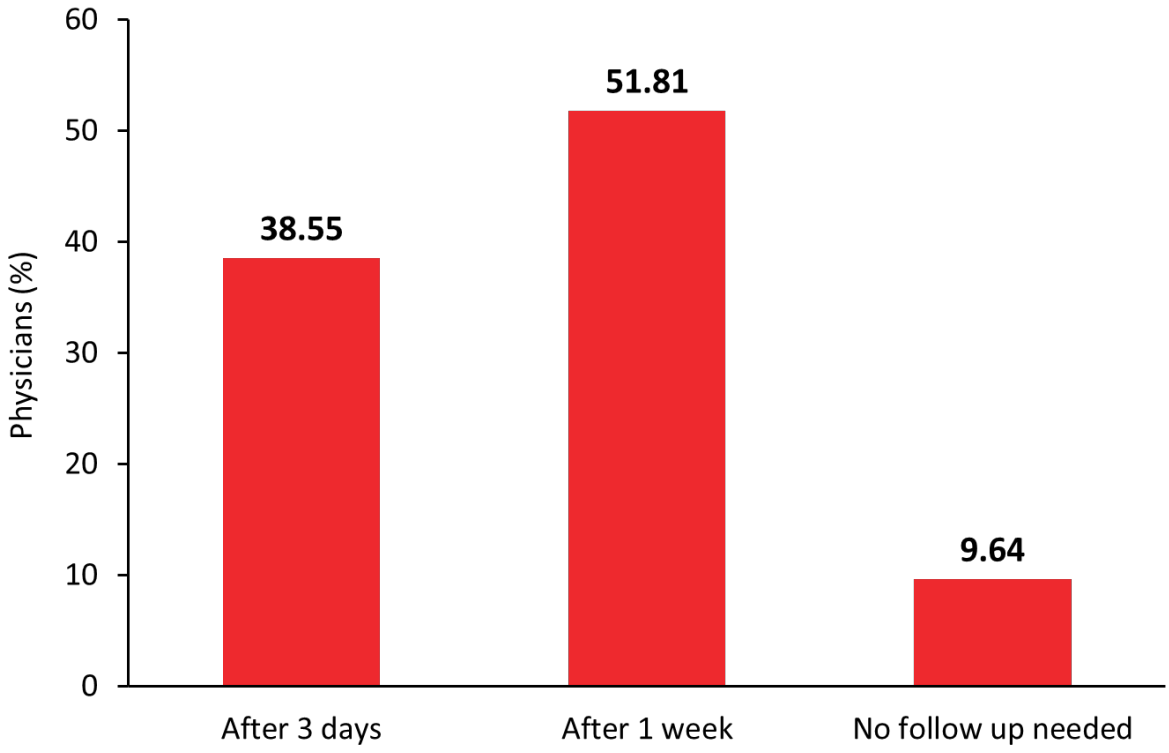
- The majority (66.27%) of physicians use tranexamic acid + mefenamic acid more frequently for the treatment of heavy menstrual bleeding.
- Around 32.53% of physicians use only tranexamic acid frequently for the treatment of heavy menstrual bleeding.
- A small proportion (1.20%) of physicians use none of the above drugs for the treatment of heavy menstrual bleeding and also no physician uses only mefanamic acid in the treatment of heavy menstrual bleeding.

11. In your clinical practice after how many days you ask for follow up in treating AUB in non -pregnant patients

A. After 3 days

B. After 1 week

C. No follow up needed



- The majority (51.81%) of physicians ask patients to get a follow up after 1 week in treating AUB in non -pregnant patients.
- Around 38.55% of physicians ask patients to get a follow up after 3 days in treating AUB in non-pregnant patients.
- A small proportion (9.64%) of physicians do not ask patients for the follow up in treating AUB in non -pregnant patients.

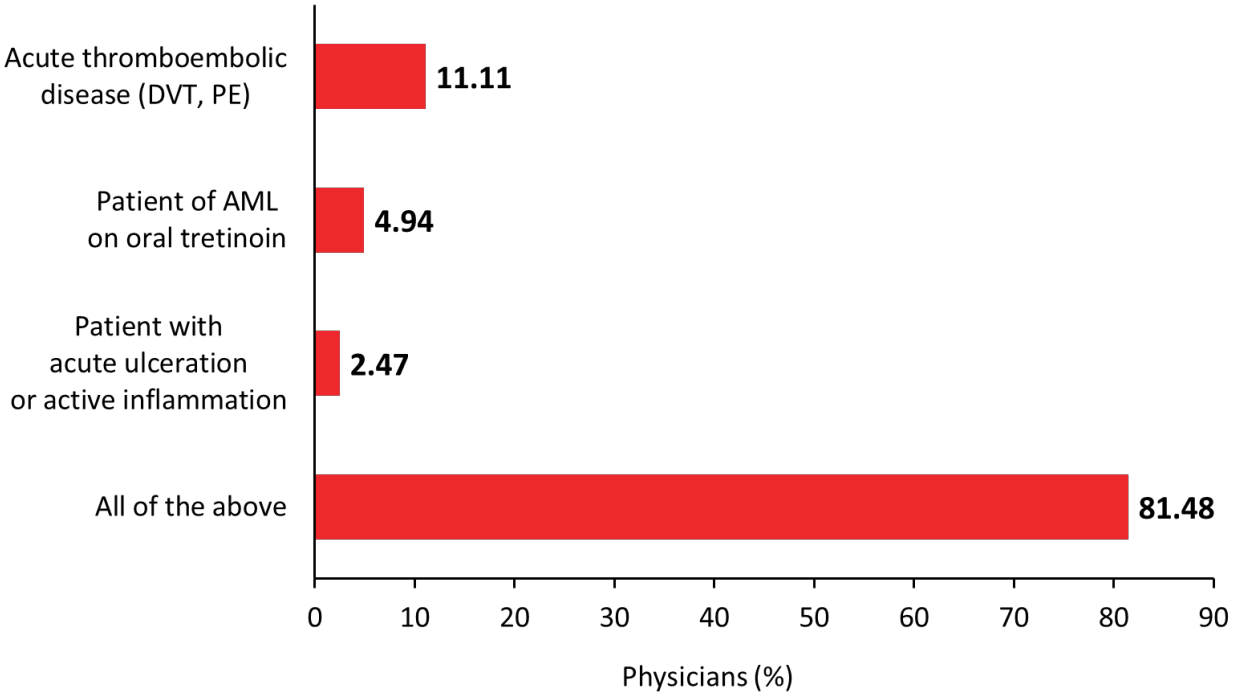
12. In your clinical practice, where you don't use tranexamic acid apart from hypersensitivity?

A. Patient with acute ulceration or active inflammation

B. Acute thromboembolic disease (DVT, PE)

C. Patient of AML on oral tretinoin

D. All of the above

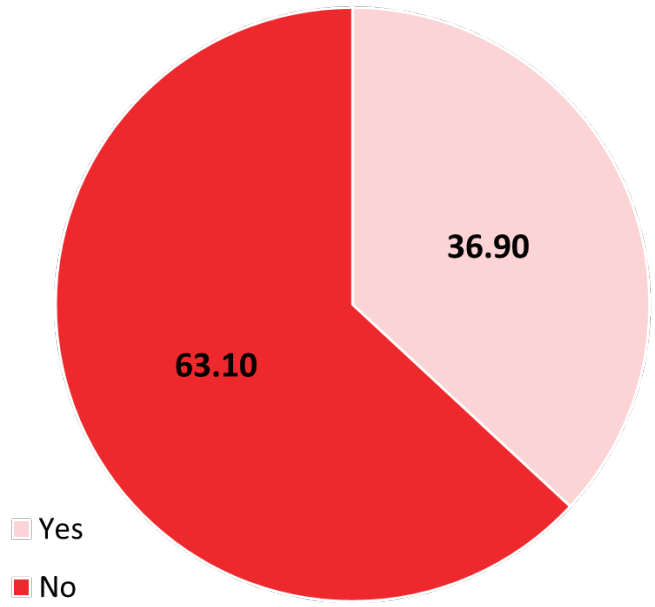


- Around 11.11% of physicians don't use tranexamic acid in acute thromboembolic disease (DVT, PE) apart from hypersensitivity.
- Approximately, 4.94% of physicians don't use tranexamic acid in patient of AML on oral tretinoin apart from hypersensitivity.
- A small proportion (2.47%) of physicians don't use tranexamic acid in Patient with acute ulceration or active inflammation apart from hypersensitivity.
- The majority (81.48%) of physicians don't use tranexamic acid in all the above mentioned patients apart from hypersensitivity.

13. In your clinical practice, have you noticed any adverse drug reaction with oral tranexamic acid

A. Yes

B. No



- The majority (63.10%) of physicians did not noticed any adverse drug reaction with oral tranexamic acid whereas significant portion (36.90%) of physicians have noticed adverse drug reaction with oral tranexamic acid.

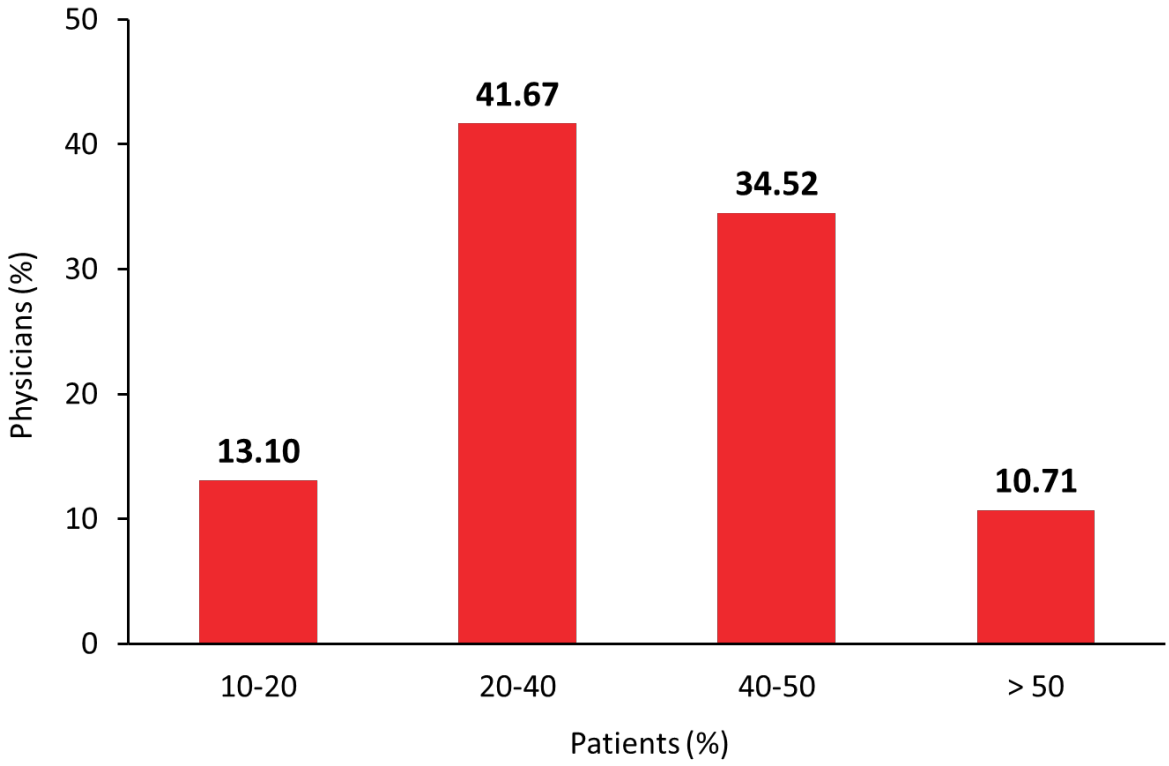
14. In your clinical practice in how many % of patients you use FDC of tranexamic acid & mefenamic acid?

A. 10-20%

B. 20-40%

C. 40-50%

D. >50%



- Around 41.67% of physicians have observed that 20-40% of patients use FDC of tranexamic acid & mefenamic acid.
- Approximately, 34.52% of physicians have noted 40-50% of patients using FDC of tranexamic acid & mefenamic acid.
- A significant portion (13.10%) of physicians have seen 10-20% of patients using FDC of tranexamic acid & mefenamic acid.
- A smaller portion (10.71%) of physicians reported more than 50% of patients using FDC of tranexamic acid & mefenamic acid.

15. In your clinical practice for what duration you prescribe tranexamic acid

A. 500 mg OD for 3 days

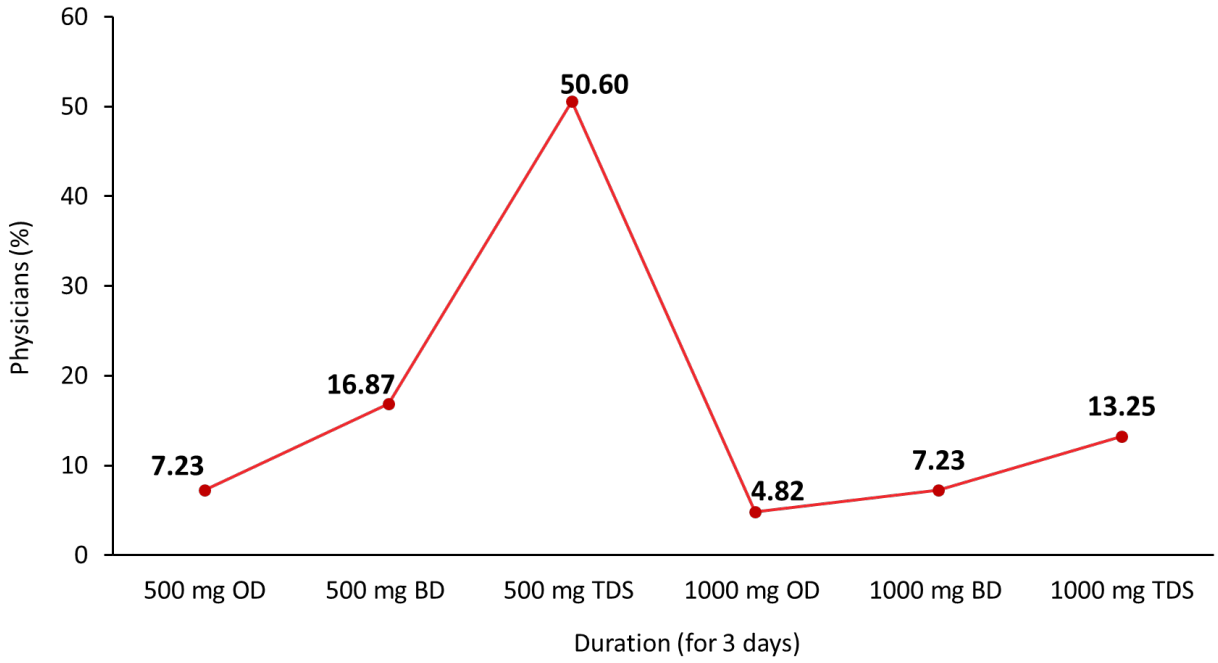
B. 500mg BD for 3 days

C. 500mg TDS for 3 days

D. 1000mg OD for 3 days

E. 1000mg BD for 3 days

F. 1000mg TDS for 3 days

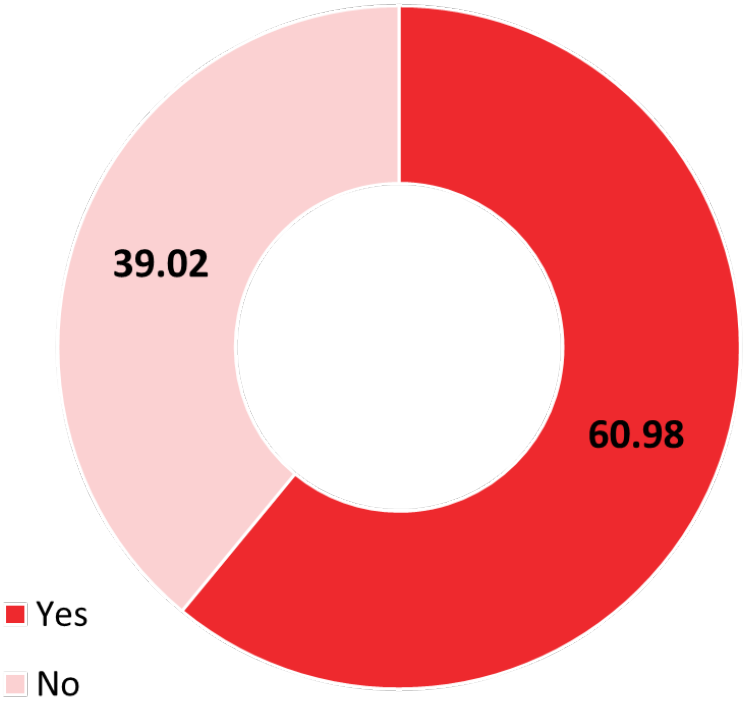


- The majority (50.60%) of physicians prescribe 500 mg TDS of tranexamic acid for 3 days.
- Approximately, 16.87% of physicians prescribe 500 mg BD of tranexamic acid for 3 days.
- Similarly, two groups of 7.23% of physicians prescribe 500 mg OD and 1000 mg BD of tranexamic acid for 3 days.
- A significant portion (13.25%) of physicians prescribe 1000 mg TDS of tranexamic acid for 3 days.
- A small portion (4.82%) of physicians prescribe 1000 mg OD of tranexamic acid for 3 days.

16. In your clinical practice do you use three times a day dose of 1000mg of tranexamic acid

A. Yes

B. No



- The majority (60.98%) of physicians use three times a day a dose of 1000mg of tranexamic acid whereas around 39.02% of physicians do not use three times a day a dose of 1000mg of tranexamic acid.

6 SUMMARY

The data shows that abnormal uterine bleeding (AUB) is a prevalent issue observed by physicians, with around 30.95% noting that 30-40% of their patients present with AUB, while approximately 28.57% and 27.38% report 40-50% and 50-60% prevalence rates, respectively. Diagnosing AUB often involves multiple approaches, with a significant majority (74.39%) of physicians relying on a combination of patient history, structural assessments, and lab investigations. Additionally, the primary treatment objectives vary, though the majority (74.36%) aim to control the current bleeding episode, reduce blood loss in subsequent cycles, and tailor interventions to patient-specific conditions.

Tranexamic acid is a frequently used treatment for AUB, with 50% of physicians prescribing it, and nearly half (46.43%) of them employ a combination of tranexamic acid with other medications, such as mefenamic acid. Dosage also varies, with the most common approach being a 500 mg TDS regimen. Efficacy of tranexamic acid is notable, as approximately 47.62% of physicians observed a 60-80% reduction in bleeding, while smaller groups reported varying levels of effectiveness. Prophylactic use is common (83.33% of physicians), and it's used in conditions like menorrhagia and postpartum hemorrhage (PPH).

Side effects of tranexamic acid are not commonly reported, as 63.10% of physicians did not notice any adverse reactions, though some observed mild effects. Fixed-dose combinations (FDC) of tranexamic and mefenamic acids are also widely prescribed. Follow-up practices generally involve check-ins after one week (51.81%) or three days (38.55%) for non-pregnant patients. Usage of tranexamic acid is avoided in patients with acute thromboembolic disease or other contraindicated conditions. This comprehensive approach reflects a balanced application of various medications, dosage adjustments, and patient monitoring to effectively manage AUB.

7 DISCUSSION

AUB is a prevalent condition encountered by physicians, with approximately 30.95% reporting that 30-40% of their patients present with this issue. About 28.57% see 40-50% of patients affected, and 27.38% report a 50-60% prevalence. Fewer physicians observe cases exceeding these rates, with only 13.10% encountering 60-70% of patients with AUB, and none reporting more than 70%.For diagnosing AUB, around 14.63% of physicians rely primarily on patient history and chief complaints, while 6.10% evaluate structural or non-structural abnormalities. Laboratory investigations are less common, utilized by 4.88% of physicians. However, a large majority (74.39%) use a comprehensive approach, combining all three diagnostic criteria to ensure accuracy.

Physicians' treatment objectives vary, with 11.54% adapting goals based on patient condition. Common objectives include reducing menstrual blood loss in subsequent cycles (8.97%) and controlling acute episodes (5.13%), while 74.36% pursue all these goals concurrently. Tranexamic acid is a primary treatment for AUB, used by 50% of physicians, while smaller percentages employ medroxyprogesterone acetate (2.38%) and oral contraceptives (1.19%). A broad approach involving multiple therapies is favored by 46.43% of physicians. Regarding dosage, 61.90% prescribe 500 mg of tranexamic acid thrice daily, and various dosing frequencies are used based on patient needs.

Bleeding reduction outcomes vary, with 47.62% of physicians observing 60-80% reduction in bleeding, while 29.76% report 40-60% and a smaller portion sees above 80% reduction. IV tranexamic acid is widely used by 91.67% of physicians, especially for postpartum hemorrhage (21.43%), menorrhagia (4.76%), and post-C-section (2.38%). In cases of heavy menstrual bleeding, 66.27% of physicians combine tranexamic acid with mefenamic acid, with 32.53% preferring tranexamic acid alone.Follow-up practices vary: 51.81% of physicians ask patients to return after one week, 38.55% after three days, while 9.64% do not require follow-ups. For contraindications, 81.48% avoid tranexamic acid in patients with conditions like thromboembolic disease, acute inflammation, or AML with oral tretinoin. Most physicians (63.10%) report no adverse reactions with oral tranexamic acid, though 36.90% have noted side effects. Combination therapy with fixed-dose formulations of

tranexamic and mefenamic acid is observed in 20-50% of patients, with 34.52% of physicians noting 40-50% usage among their patients. Prescribed doses and durations for tranexamic acid vary, with 500 mg thrice daily over three days being the most common regimen, followed by other combinations as appropriate.

8 CLINICAL RECOMMENDATIONS

- Abnormal uterine bleeding (AUB) is a common condition seen in many clinical practices. Approximately 30.95% of physicians report that 30-40% of their patients present with AUB, with other physicians observing larger proportions, ranging from 40-60% to 60-70% of patients.
- The diagnosis of AUB is usually based on a combination of patient history and clinical evaluations. A majority (74.39%) of physicians incorporate all criteria—chief complaints, structural abnormalities, and lab investigations—in diagnosing AUB.
- For treatment, tranexamic acid is the most commonly used therapy, with 50.00% of physicians relying on it. A large number of physicians observe a 60-80% reduction in bleeding with this medication.
- Tranexamic acid is often administered in doses of 500 mg TDS, and is used either orally or intravenously depending on patient condition. A significant portion of physicians also combines tranexamic acid with mefenamic acid for better outcomes in managing heavy menstrual bleeding.
- Clinical recommendations suggest using tranexamic acid for controlling heavy menstrual bleeding, with a follow-up recommended after 3-7 days to assess the patient's progress. For certain patients, like those with thromboembolic disease or active inflammation, the use of tranexamic acid should be carefully considered or avoided.

9 CONSULTANT OPINION

Abnormal uterine bleeding (AUB) refers to any deviation from the normal menstrual cycle, either in terms of frequency, volume, or duration of menstrual bleeding. It is categorized into two primary types: acute and chronic AUB. Acute AUB is often characterized by heavy bleeding that occurs suddenly and may be life-threatening, while chronic AUB refers to long-term or persistent irregular bleeding.

The causes of AUB can be broadly classified into functional causes, such as hormonal imbalances (anovulatory cycles), and structural causes, such as fibroids or polyps. Diagnosis typically begins with a thorough patient history and physical examination, followed by necessary tests like pelvic ultrasound, endometrial biopsy, or hysteroscopy. Depending on the findings, treatments vary.

For acute AUB, the first-line treatment is typically hormonal therapy, including oral contraceptives or intravenous conjugated estrogen, to control bleeding. In chronic cases, treatment may involve hormonal medications to regulate the menstrual cycle. Surgical options like dilation and curettage (D&C), endometrial ablation, or hysterectomy are considered if medical management is ineffective. Non-surgical therapies, such as tranexamic acid, mefenamic acid, or progestin, are used to reduce bleeding or regulate menstrual cycles when the underlying cause is not structural

For many patients, the condition can be managed effectively with a combination of medical therapies. However, when these measures fail, or if the bleeding is too severe, surgical treatments may be necessary

10 MARKET OPPORTUNITIES

- The data presents significant opportunities for marketing various treatments for abnormal uterine bleeding (AUB), particularly tranexamic acid. With approximately 50% of physicians using tranexamic acid for AUB treatment, there is a solid demand for its promotion.
- Tranexamic acid's efficacy in reducing bleeding (reported by 47.62% of physicians to achieve 60-80% reduction) positions it as a leading choice in managing AUB. This opens up marketing avenues focusing on its high efficacy and differentiation from other therapies like medroxyprogesterone acetate and oral contraceptives, which are used by much fewer physicians (2.38% and 1.19%, respectively).
- The data also highlights combination therapies, such as tranexamic acid with mefenamic acid, which 66.27% of physicians use for heavy menstrual bleeding. Marketing campaigns targeting the effectiveness of these combinations could appeal to physicians looking for more comprehensive treatment options.

- Another opportunity lies in the prophylactic use of tranexamic acid (used by 83.33% of physicians), which could be marketed for preventative care, particularly in high-risk scenarios like postpartum hemorrhage (PPH) or menorrhagia.
- Further segmentation could focus on IV formulations, as 91.67% of physicians use intravenous tranexamic acid in clinical settings, particularly for conditions like PPH. Promoting both oral and intravenous forms for varied use cases ensures broad market penetration.

11 MARKET POSITIONING

- Tranexamic acid is widely recognized by physicians as a leading treatment option for abnormal uterine bleeding (AUB), particularly in managing heavy menstrual bleeding. Its efficacy in reducing blood loss is well-documented, with a majority (47.62%) of physicians observing a 60-80% reduction in bleeding.
- Around 50% of physicians use tranexamic acid as a first-line treatment, emphasizing its role in controlling acute bleeding episodes and reducing menstrual blood loss in subsequent cycles.
- Physicians tend to prefer a 500 mg TDS (three times a day) dosage for optimal results, with 61.90% adopting this regimen for treating AUB.
- Additionally, tranexamic acid is often prescribed alongside mefenamic acid, as seen in 66.27% of physician practices, making it a preferred combination for enhanced treatment outcomes.
- Its prophylactic use is also common, as 83.33% of physicians include it in their clinical protocols for preventing excessive bleeding.
- Moreover, IV tranexamic acid is used in more acute conditions like post-partum hemorrhage (PPH), menorrhagia, and post-C-section bleeding, with 91.67% of physicians incorporating it into their clinical practices. These diverse uses position tranexamic acid as a versatile and critical drug in the management of AUB and related conditions.

12 REFERENCES

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