

Artificial Intelligence and Systemic Isotretinoin: Patient Education on Ophthalmological Side Effects

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ABSTRACT

Purpose: Isotretinoin is frequently utilized in the treatment of skin disorders such as acne vulgaris and rosacea, with its associated side effects occurring relatively often. The most prevalent ophthalmological adverse effects include conjunctivitis, hordeolum, chalazion, blepharitis, and xerophthalmia. In light of the growing integration of artificial intelligence within healthcare, this study aims to evaluate the capability of ChatGPT to enhance patient education regarding these conditions.

Materials and Methods: A questionnaire consisting of fifteen frequently asked questions concerning the ophthalmological side effects of systemic isotretinoin was developed. Eight questions, selected by dermatologists and ophthalmologists, were posed to ChatGPT version 4.0. The responses were assessed using a four-point rating scale. Answers were independently categorized as “excellent,” “satisfactory with minimal explanation required,” “satisfactory with moderate explanation required,” or “unsatisfactory.”

Results: ChatGPT provided accurate and informative responses to all eight questions presented. Six responses were rated as “excellent,” while two were categorized as “satisfactory with minimal explanation required.” Inter-rater reliability was assessed using Cohen’s kappa analysis, resulting in a kappa value of 0.413 (95% confidence interval, 0.007 to 0.825).

Conclusion: ChatGPT exhibited a significant capacity to effectively address patient inquiries related to the ophthalmological side effects of systemic isotretinoin. Following a review by dermatologists and ophthalmologists, it may serve as a valuable complementary tool for patient education.

Keywords: Artificial intelligence; ChatGPT; Isotretinoin; Ophthalmological side effects; Patient education

ÖZET

Amaç: İso tretinoin, akne vulgaris, rozasea gibi deri hastalıklarında sık kullanılmaktadır, yan etkileri de relatif olarak sık görülür. En yaygın oftalmolojik yan etkiler konjonktivit, hordeolum, şalazyon, blefarit ve göz kuruluğudur. Yapay zekanın sağlık alanında artan kullanımını göz önüne alarak, bu çalışma ChatGPT’nin bu hastalıkla ilgili hasta eğitime katkı sağlama kapasitesini incelemektedir.

Gereç ve Yöntem: Sistemik isotretinoinin göz üzerine yan etkileri hakkında sıkça sorulan onbeş soruluk bir listeden, dermatolog ve göz hastalıkları uzmanı tarafından seçilen sekiz soru, ChatGPT 4.0 sürümüne yöneltilmiştir. Verilen yanıtlar dört basamaklı bir derecelendirme sistemi kullanılarak değerlendirilmiştir. Yanıtlar, bağımsız olarak “mükemmel”, “asgari açıklama gerektiren tatmin edici”, “orta düzeyde açıklama gerektiren tatmin edici” veya “tatmin edici olmayan” olarak derecelendirilmiştir.

Bulgular: ChatGPT, sekiz sorunun tamamına doğru ve bilgilendirici yanıtlar vermiştir. Altı yanıt “mükemmel” olarak, iki yanıt ise “asgari açıklama gerektiren tatmin edici” olarak değerlendirilmiştir. İncelemeler arası güvenilirlik kappa analizi ile hesaplanmış, Cohen k, 0.416 (95% güven aralığı, 0.007, 0.825) olarak bulunmuştur.

Sonuçlar: ChatGPT sistemik isotretinoinin oftalmolojik yan etkileri ile ilgili hasta sorularına etkili bir şekilde yanıt verebilecek güçlü bir kapasite sergilemiştir. Öncesinde dermatolog ve göz hastalıkları uzmanlarının gözden geçirmesinin ardından, hasta eğitimi için tamamlayıcı bir araç olarak kullanılabilir.

Anahtar Kelimeler: ChatGPT; Hasta eğitimi; İso tretinoin; Oftalmolojik yan etkiler; Yapay zeka

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Artificial Intelligence (AI) is a set of algorithms that exhibit human skills such as reasoning, learning, classification and creativity through a machine (1). ChatGPT is an advanced AI-powered language model that uses deep learning techniques to generate human-like responses to natural language inputs. It is a member of the generative pre-training transformer (GPT) model family developed by OpenAI and is currently one of the largest publicly available language models. There is also a free trial version (2). This makes it a powerful tool for communication, information dissemination and problem solving on a wide range of topics, including health care (3). The integration of artificial intelligence (AI) into dermatology and ophthalmology offers capabilities ranging from diagnostic accuracy to improved patient interaction (4,5).

Isotretinoin, a retinoid derivative, was approved by the FDA in 1982 for the treatment of acne (6). It is also indicated for severe (nodular, cystic or active scarring) acne and moderate (papulopustular) acne that does not respond to conventional treatment (7). Isotretinoin is the only drug that can treat all pathogenic causes of acne (8). It has side effects on the mucocutaneous, ophthalmic and musculoskeletal systems. The most common side effects on the eyes are conjunctivitis, hordeolum, chalazion, blepharitis and dry eyes (6). Like all artificial intelligence tools, with the increasing use of ChatGPT in the health field, it is known that patients turn to these sources before consulting a physician about their health problems (4). With this in mind, in our planned study, we aimed to evaluate ChatGPT's responses to patient questions about the ophthalmological side effects of isotretinoin.

Materials and Methods

"Ophthalmological side effects of systemic isotretinoin" was searched on Google (www.google.com). The "frequently asked questions" sections and patient information forms of numerous clinics and medical associations were examined. From a comprehensive list of 15 questions, the most common eight questions were

selected by one dermatologist and one ophthalmologist. The questions were submitted to ChatGPT (version 4.0), the latest premium version with limited free access, on November 1, 2024, and no follow-up questions or repetitions were made. A 4-level grading system previously used in medical articles to evaluate ChatGPT's responses to patient questions was used for grading (9). Each response was independently reviewed by two ophthalmologists (reviewer 1 and reviewer 2) using an evidence-based approach. In this grading system, scores of 1, 2, 3, and 4 corresponded to "excellent response requiring no explanation," "satisfactory response requiring minimal explanation," "satisfactory response requiring moderate explanation," and "unsatisfactory response requiring significant explanation," respectively.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0; IBM Corp. Subsequently, inter-rater reliability and confidence interval were calculated by k analysis.

Results

ChatGPT 4.0's questions and answers are shown in Table 1. Reviewer 1 rated six responses as "excellent" and two responses as "satisfactory requiring minimal explanation." Reviewer 2 rated six responses as "excellent" and two responses as "satisfactory requiring minimal explanation." None of the questions were rated as "satisfactory requiring moderate explanation" or "unsatisfactory" by the reviewers. The question "What are the side effects of isotretinoin on the eyes?" was rated as "satisfactory requiring minimal explanation" by reviewer 1 and the response to the question "Can I have refractive surgery while taking isotretinoin?" was rated as "satisfactory requiring minimal explanation" by reviewer 2. In this study, inter-rater reliability was calculated by k analysis. Cohen's k was calculated as 0.71 (95% confidence interval, 0.19, 1.24).

Table 1: Questions asked to ChatGPT, answers and reviewer scores

QUESTIONS	ANSWERS	ANSWER ACCURACY SCORE
1. How does isotretinoin show its effect?	<p>Isotretinoin, a derivative of vitamin A (retinoid), shows its effects primarily by targeting and reducing sebum production in the skin. It works through multiple mechanisms:</p> <p>Sebum Reduction: Isotretinoin significantly reduces the size and activity of sebaceous (oil) glands, which decreases the amount of sebum (oil) production. Since excess sebum contributes to acne, its reduction helps to prevent clogged pores and bacterial growth.</p> <p>Normalization of Skin Cell Shedding: Isotretinoin normalizes the process of skin cell turnover. In acne-prone skin, cells that line the follicle can shed irregularly and stick together, contributing to pore blockage. Isotretinoin helps prevent this by promoting normal desquamation (shedding of cells).</p> <p>Anti-inflammatory Effects: Isotretinoin has anti-inflammatory properties, which help to reduce the redness and swelling associated with inflammatory acne lesions.</p> <p>Inhibition of Bacterial Growth: By reducing sebum, isotretinoin indirectly inhibits the growth of Cutibacterium acnes (formerly Propionibacterium acnes), the bacteria associated with acne, which thrives in an oily environment.</p> <p>Isotretinoin is unique in its ability to affect multiple factors involved in acne development, making it one of the most effective treatments for severe, resistant acne. However, due to its strong effects, it also has significant side effects and risks, including potential teratogenicity (risk of causing birth defects), so it is typically reserved for severe cases.</p>	1-1
2. What are the side effects of isotretinoin on the eyes?	<p>Isotretinoin, a medication primarily used to treat severe acne, can have several side effects on the eyes. These ocular side effects are often related to its impact on the body's oil glands, as isotretinoin reduces sebum production, which affects tear production and ocular surface lubrication. Here are some common eye-related side effects associated with isotretinoin:</p> <p>Dry Eyes (Keratoconjunctivitis Sicca): Reduced tear production can lead to dry eyes, resulting in discomfort, redness, and a gritty feeling in the eyes. This is one of the most common side effects and may require artificial tears or lubricating eye drops.</p> <p>Conjunctivitis: Some individuals may experience inflammation or irritation of the conjunctiva (the white part of the eye), which may cause redness, itching, or swelling.</p> <p>Blepharitis: This is an inflammation of the eyelids, often due to a combination of dryness and irritation. Blepharitis can cause redness, itchiness, and flakiness around the eyelids.</p> <p>Contact Lens Intolerance: People who wear contact lenses may experience discomfort or difficulty wearing them while on isotretinoin due to decreased tear film stability and dryness.</p> <p>Corneal Opacities: In rare cases, isotretinoin can lead to changes in the cornea, such as small opacities, which may cause visual disturbances if they are significant.</p> <p>Night Vision Impairment: Isotretinoin can sometimes reduce the ability to see in low light, which is known as night blindness. This side effect is generally reversible once the medication is discontinued.</p> <p>Photophobia (Light Sensitivity): Increased sensitivity to bright lights can occur, making outdoor exposure or exposure to screens uncomfortable for some individuals.</p> <p>Optic Neuritis: Though extremely rare, there have been reports of optic neuritis (inflammation of the optic nerve) linked to isotretinoin use, which can lead to visual disturbances or vision loss.</p> <p>Most ocular side effects are temporary and tend to improve after discontinuing the medication.</p>	2-1

<p>3. Can I wear contact lenses while taking isotretinoin?</p>	<p>Yes, you can wear contact lenses while taking isotretinoin, but many people find it uncomfortable due to the eye dryness isotretinoin often causes. This dryness occurs because isotretinoin reduces the production of oil in the meibomian glands, which affects the tear film's stability and leads to dry eyes—a key factor in contact lens discomfort.</p> <p>If you plan to continue wearing contact lenses, here are a few tips to help manage any discomfort:</p> <p>Use Lubricating Eye Drops: Artificial tears or lubricating drops can help keep your eyes moist. Make sure to use preservative-free drops, as they are gentler on the eyes, especially with frequent use.</p> <p>Consider Lens Type: Some people find that daily disposable lenses are more comfortable than extended-wear lenses because they provide a fresh, clean surface each day, which may help reduce irritation.</p> <p>Take Breaks: If possible, reduce the amount of time you wear your contacts each day, especially if you start experiencing dryness or discomfort.</p> <p>Stay Hydrated and Avoid Irritants: Staying well-hydrated and avoiding smoky, dry, or windy environments can help reduce eye dryness.</p> <p>Consult Your Eye Doctor: If you experience significant discomfort or other eye symptoms, it's best to discuss alternatives with your eye doctor. They may suggest switching to glasses during your isotretinoin treatment or may recommend specific treatments for dry eyes.</p> <p>Most people find their eye comfort improves after they stop taking isotretinoin, but adjusting your contact lens routine while on the medication can make wearing them more comfortable in the meantime.</p>	<p>2-2</p>
<p>4. Can I have refractive surgery while taking isotretinoin?</p>	<p>It is not recommended to undergo refractive surgery (such as LASIK or PRK) while taking isotretinoin. Isotretinoin can affect the corneal healing process, increase the risk of post-surgery complications, and cause or worsen dry eyes, which are significant considerations for refractive surgery outcomes. Here's why it's generally advised to wait:</p> <p>Dry Eye Exacerbation: Isotretinoin can reduce tear production, leading to dry eyes. This is a common side effect that may worsen post-surgery, as LASIK and PRK can also induce dryness due to the disruption of corneal nerves that contribute to tear production.</p> <p>Delayed Healing and Corneal Epithelial Changes: Isotretinoin can interfere with the corneal epithelium (the outermost layer of the cornea), delaying healing and potentially leading to irregular healing patterns. This may affect visual clarity and the overall success of the surgery.</p> <p>Increased Risk of Corneal Scarring: The effects of isotretinoin on tissue healing can raise the risk of corneal scarring post-surgery, which can result in lasting vision impairment.</p> <p>To minimize these risks, most eye surgeons recommend waiting at least six months after stopping isotretinoin before undergoing any form of refractive surgery. This waiting period allows the medication to fully clear from your system and for your eyes to return to a more stable, healthy state. Always consult with your ophthalmologist or refractive surgeon regarding your medical history and medications to determine the best timing for surgery.</p>	<p>1-2</p>
<p>5. Will the dry eyes caused by isotretinoin be permanent?</p>	<p>In most cases, the dry eyes caused by isotretinoin are not permanent. Typically, dry eye symptoms improve and eventually resolve after the medication is discontinued, although the recovery time can vary from person to person. Many people experience relief within a few weeks to months after stopping isotretinoin, while others may take longer for their tear production and eye surface to fully stabilize.</p> <p>However, in rare cases, isotretinoin may lead to persistent dryness that can continue even after treatment ends. Factors that may increase the risk of prolonged dry eye symptoms include preexisting dry eye, long-term isotretinoin use, or other health conditions affecting the eyes.</p> <p>To manage dry eyes effectively while on isotretinoin and minimize any potential long-term impact, you might consider the following:</p> <p>Regular Use of Artificial Tears: Lubricating eye drops, especially preservative-free options, can help maintain moisture and reduce discomfort.</p> <p>Stay Hydrated: Drinking plenty of water can support overall eye hydration.</p> <p>Environmental Adjustments: Avoiding dry, windy, or smoky environments can reduce dryness. Using a humidifier at home can also help.</p> <p>Discuss with Your Doctor: If dryness is severe, your doctor may recommend treatments like omega-3 supplements, punctal plugs, or prescription eye drops designed to improve tear production.</p> <p>In most cases, these proactive measures, along with time, allow the eyes to recover from the effects of isotretinoin once treatment has stopped.</p>	<p>1-1</p>

<p>6. Which professions should not use isotretinoin?</p>	<p>Certain professions where vision, skin integrity, and environmental exposure are crucial may need to avoid or carefully consider using isotretinoin. Here are some examples of professions where isotretinoin might pose challenges:</p> <p>Pilots and Professional Drivers: Isotretinoin can impair night vision, which could be risky for those who need to operate vehicles or aircraft at night or in low-light conditions. Night vision disturbances may affect safety, and some aviation authorities advise caution or restrict isotretinoin use for pilots.</p> <p>Military Personnel and Police Officers: These professionals often work in demanding environments that require sharp vision and physical endurance. Dry eyes, skin sensitivity, or other visual side effects from isotretinoin can interfere with duties, especially in harsh or outdoor settings.</p> <p>Outdoor Workers (e.g., Construction, Agriculture): Isotretinoin increases sun sensitivity, making it easier to sunburn or develop skin irritation, which can be particularly challenging for people who work outdoors for extended periods. These workers may need more frequent breaks, strong sun protection, and protective clothing.</p> <p>Athletes: Professional and recreational athletes, especially those involved in contact sports, may be more prone to issues from isotretinoin's effects on skin fragility, leading to easier bruising or skin damage. Dry eyes and visual disturbances can also impact performance, especially in sports requiring quick visual focus and coordination.</p> <p>Healthcare Workers (e.g., Surgeons, Nurses): Long hours in dry, air-conditioned environments may exacerbate isotretinoin's drying effects, potentially causing eye discomfort and skin sensitivity. Surgeons or those who rely on steady hands and precise vision may find that isotretinoin's effects on tear film and ocular comfort impact their performance.</p> <p>Contact Lens Wearers: Professions that involve prolonged screen time, such as IT professionals, graphic designers, or writers, may face increased eye strain and dry eye discomfort if they wear contacts while on isotretinoin.</p> <p>Individuals in these professions might benefit from alternative acne treatments if isotretinoin poses significant challenges, or they could consider postponing isotretinoin treatment to a period when their professional demands are less intensive.</p>	<p>1-1</p>
<p>7. What can be used to reduce the side effects of isotretinoin on the eyes?</p>	<p>To help manage and reduce the eye-related side effects of isotretinoin, several strategies and treatments can be beneficial. These focus on maintaining moisture, minimizing irritation, and protecting the eyes from additional stress or environmental factors. Here are some of the most effective ways to reduce isotretinoin's impact on the eyes:</p> <p>Lubricating Eye Drops (Artificial Tears): Regularly using preservative-free artificial tears can help combat dryness and provide immediate relief. These drops are gentle enough for frequent use and help restore the tear film.</p> <p>Warm Compresses: Applying warm compresses to the eyelids can stimulate the oil glands (meibomian glands), which may help improve tear film quality and reduce dryness. Compresses can be done once or twice a day, especially if dry eyes are noticeable.</p> <p>Omega-3 Fatty Acid Supplements: Omega-3 supplements, such as fish oil or flaxseed oil, can help improve tear production and reduce inflammation. They may take a few weeks to show effects, so they're best used consistently over time.</p> <p>Hydration: Staying hydrated by drinking plenty of water throughout the day can support overall tear production and keep the eyes more comfortable.</p> <p>Environmental Adjustments: Using a humidifier, especially in dry indoor environments, can help maintain moisture in the air and reduce tear evaporation. Avoiding direct airflow from fans or air conditioning can also help.</p> <p>Prescription Eye Drops: If dryness is severe, your doctor may prescribe medicated eye drops, such as cyclosporine (Restasis) or lifitegrast (Xiidra), which can improve tear production and reduce inflammation in the eyes.</p> <p>Eyelid Hygiene: Regularly cleaning the eyelids with a gentle eyelid cleanser or wipes can help reduce any buildup that may irritate the eyes, especially if blepharitis (inflammation of the eyelids) occurs.</p> <p>UV Protection: Since isotretinoin increases light sensitivity, wearing sunglasses with UV protection can help shield the eyes from sun exposure, reducing strain and discomfort, especially in bright conditions.</p> <p>Breaks from Contact Lens Use: If you wear contact lenses, consider switching to glasses more frequently, or try using daily disposable lenses, which can be less drying than extended-wear lenses.</p> <p>Consult an Eye Doctor: For persistent symptoms, an ophthalmologist can assess the dryness severity and recommend personalized treatments, such as punctal plugs (small devices inserted into tear ducts to retain tears) for more severe cases.</p> <p>With these steps, most people find they can manage isotretinoin's effects on their eyes and experience improved comfort.</p>	<p>1-1</p>

8. Will the vision loss caused by Isotretinoin be permanent?	<p>Vision loss from isotretinoin is generally rare, and most visual side effects are temporary, resolving after discontinuing the medication. However, certain vision-related side effects may be more concerning, particularly if they go unaddressed. Here's a look at the potential vision issues and their typical outcomes:</p> <p>Night Vision Impairment: Isotretinoin can cause temporary night vision disturbances, which may include difficulty seeing in low light or at night. For most people, night vision improves once they stop the medication. In rare cases, it may persist for a while after discontinuation but typically improves over time.</p> <p>Dry Eyes and Visual Blurriness: Dryness can cause intermittent blurred vision, which can improve with lubricating eye drops or other dry eye treatments. Once isotretinoin is stopped, tear production usually returns to normal, alleviating the associated blurry vision.</p> <p>Corneal Opacities: Small corneal opacities or deposits may develop but are generally rare. If they occur, they are often reversible after stopping isotretinoin. If they do not resolve, an eye doctor may recommend specific treatments.</p> <p>Optic Neuritis: Optic neuritis (inflammation of the optic nerve) is extremely rare but can cause serious vision problems if it occurs. It requires immediate medical attention, as it can potentially lead to permanent vision loss if left untreated. Fortunately, this side effect is exceedingly uncommon.</p> <p>In almost all cases, any vision loss or impairment due to isotretinoin is temporary and reversible after stopping the medication. If you notice any sudden or lasting changes in vision, consulting an eye doctor promptly is crucial. They can help address symptoms and monitor any recovery needed, ensuring that any potential complications are managed early.</p>	1-1
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Discussion

Ophthalmological side effects are an important clinical issue in patients receiving isotretinoin therapy. Visual disturbances, including changes in visual acuity, refractive vision problems, night blindness, and abnormal color perception, have an overall reported prevalence of 3%. Inflammatory conditions of the eyelids, such as blepharitis, blepharoconjunctivitis, eyelid scaling and crusting, meibomitis, chalazion, and hordeolum, are observed with a prevalence of 10%. Moreover, dry or irritated eyes are among the most common ophthalmologic side effects, with an overall prevalence of 27%. In other words, the occurrence of ophthalmologic side effects in approximately one out of four patients underscores the critical importance of providing accurate information and patient education on this matter.(10)

The most important finding of this study was that ChatGPT 4.0 could generate accurate responses that could assist in patient education about the ophthalmological side effects of isotretinoin. Artificial intelligence has become popular among the general population in recent years, and more patients have started using artificial intelligence tools instead of internet searches to seek information (11). This has led to publications evaluating the role of artificial intelligence tools in patient education. In a study examining ChatGPT's responses to questions about acne and atopic dermatitis, 78% of the responses were evaluated as correct (12). Similarly, in this study, 75% of the responses were evaluated as excellent. The answer to the question "What are the side

effects of isotretinoin on the eyes?" was described as "satisfactory requiring minimal explanation" by reviewer 1. This was because it did not mention the side effects of isotretinoin on color vision (13). The answer to the question "Can I wear contact lenses while taking isotretinoin?" was described as "satisfactory requiring minimal explanation" by both reviewers. Whether a person can wear contact lenses or not can be decided after an ophthalmological examination. Although it makes correct recommendations to reduce the side effects of isotretinoin, it was evaluated in this way because it made definite suggestions such as 'you can wear lenses' (14). The answer to the question "Can I have refractive surgery while taking isotretinoin?" was described as "satisfactory requiring minimal explanation" by reviewer 2. This was because it did not mention more up-to-date surgical methods such as 'Small Incision Lenticule Extraction (SMILE)' and 'Transepithelial Photorefractive Keratectomy (trans PRK)' (15).

A notable limitation of ChatGPT is its reproducibility problem, which manifests in the capacity to generate divergent responses to identical queries. Consequently, the integrity of the input data is paramount in determining the precision and dependability of the system's outputs. Incorrect, incomplete, or ambiguous inputs can yield erroneous results, and the heightened sensitivity of AI to input alterations can result in minute variations leading to starkly divergent answers. This is particularly problematic for users who lack subject-specific knowledge, as it can lead to potentially misleading and risky results (16).

ChatGPT is prone to errors; consequently, it issues a warning to users by stating 'check important information'. However, it discloses its sources for topics that necessitate contemporary information, as determined by the algorithm. It did not provide references for any of the questions posed in our study, which hinders the verification of information accuracy. Additionally, ChatGPT can generate entirely unrealistic information, a phenomenon termed 'AI hallucination'. It has been suggested that ChatGPT-4 exhibits a significant reduction in AI hallucination in comparison to previous ChatGPT-3.5 models. However, it should be noted that the free ChatGPT-4 version imposes a usage limit, and upon its expiration, the system redirects to older versions that generate more unrealistic information, which may also have an impact on the accuracy of the information (17).

Our findings showed that the latest version, ChatGPT 4.0, which is the free form, could answer common patient questions about the side effects of systemic isotretinoin on the eyes with high accuracy. ChatGPT is an increasingly popular, promising technology. Although more research is needed for its role in patient education, it can serve as an adjunct method for patient education.

Conclusions

ChatGPT 4.0 provides highly accurate answers to patient questions regarding Ophthalmological side effects of systemic isotretinoin. After review by dermatologists and ophthalmologists, it can be used as a complementary tool for patient education.

Declarations

Conflict of Interest

The authors have declared no conflicts of interest or financial support.

Funding

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Ethics Approval

Since no patient data was used during this study, ethics committee approval is not required.

Availability of data and material

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author's Contributions

Motivation / Concept: S.Y.İ., İ.İ.

Study Design: S.Y.İ.

Control / Supervision: S.Y.İ., İ.İ.

Data Collection and/or Processing: S.Y.İ., İ.İ.

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