MONTELUKAST AND MANAGEMENT OF ADENOID HYPERTROPHY

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ABSTRACT

Objective: evaluation effect montelukast (anti-inflammatory drugs) in management of adenoid hypertrophy among children to give optional noninvasive alternative non-surgical strategy for adenoid hypertrophy.

Methodology: Sixty children between the ages of 3–12 years with grade 3 or 4 nasopharyngeal obstruction, is divided in to 2 groups: 30 patients (study group) was treated with montelukast 5 mg daily for 3months while other 30 patients (control group) received placebo for the same period. Both groups were evaluated using (a) questionnaire completed by each child's parent/guardian for evaluation of snoring, mouth breathing, and sleep discomfort before and after therapy **(b)** Radiological assessment by plain x-ray nasopharynx lateral view for reduction of adenoid size**.**

Results: study group showed a statistically significant improvement compared with the placebo group in snoring, mouth breathing and sleep discomfort (p=0.000). Adenoid size showed significant reduction the study group compared with the placebo group after 3months (p=0.000).

Conclusion: Montelukast has significant reduction in adenoid size and significant improvement of related obstructive symptoms and therefore can be considered an effective alternative to adenoidectomy in children with (AH).

Key Words: Adenoid hypertrophy (AH), Montelukast, Mouth breathing, snoring, Sleep discomfort.

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1. Introduction

Adenoid hypertrophy (AH) is a very common disease in children [1]. Symptoms produced by AH could significantly affect the quality of children life [2]. These symptoms include snoring, mouth breathing, nasal obstruction, hyponasal speech, and obstructive sleep apnea (OSA) [3].

Adenoid hypertrophy diagnosis depends mainly on history and physical examination [4]. However, lateral head and neck radiography is usually needed especially in fussy or non-cooperative children [5].

The adenoid surgery may give long-lasting improvement but it is invasive, expensive and postoperative complications are considerable. Therefore, the second option is drug therapy, which is usually cheaper, less invasive [2].

Montelukast is cysteinyl-leukotriene receptor antagonist .It is effective, safe, oral and bioavailable [6]. It is well tolerated [8], [7] and approved by the US Food and Drug administration (FDA) for preventive therapy of the inflammatory component in asthma and allergic rhinitis in children aged ≥1year. montelukast has not induced tolerance in long-term studies [8] .

In this study we aimed to evaluate the Montelukast therapy in (AH) and its associated obstructive symptoms

2. Methodology

Approval of this study obtained from Ethical Committee of the Faculty of medicine of Al-Azhar University This study was conducted at Otorhinolaryngology Department of Al-Zahraa University Hospital between December 2019

2.1. and September 2020. In total, 60 children 60 patients with adenoid hypertrophy with grade 3 or4 nasopharyngeal obstructions were included in this study. 29 were female and 31 were males. The age ranged from 3 to 12 years. Informed consent was obtained from their parents prior to study. Patient with body over weight, craniofacial, neuromuscular, syndrome, genetic abnormalities, are excluded from the study. Also patients had received montelukast, any corticosteroids or antibiotics or having

2.2. acute upper respiratory tract infection within one month preceding the initial study was excluded from the study. Any child underwent adenotonsillectomy in the past were excluded as well.

Patients were divided into two groups (group A and group B) each including 30 patients. Group (A) patients (study group) received montelukast 5mgd and 10mg (for child less than 12 and more than 12 year respectively) for 3 months. Group B (control group) received placebo for 3 months

All patients were subjected to undergo Pre and post treatment clinical assessment including:

Taking history from the patient or his/her parents and complete ENT clinical examination. The main symptoms included in questionnaire. These symptoms are snoring, mouth-breathing, and obstructive sleep breathing. The score evaluated as; absent (0), mild (1), moderate (2), and severe (3). The final clinical score then calculated and categorized as; Mild: (<1), Moderate: (1:4) and Severe :(> 4).The scoring considered the most common patients symptoms [8].

Radiological assessments (plain x-ray nasopharynx lateral view open mouth were taken with a mild neck extension) for better visualization of AH. Calculation the thickness evaluated bythe ratio of the adenoid thinking over the all nasopharyngeal thinking (A/N) based on Fujioka method [9] (figure1).

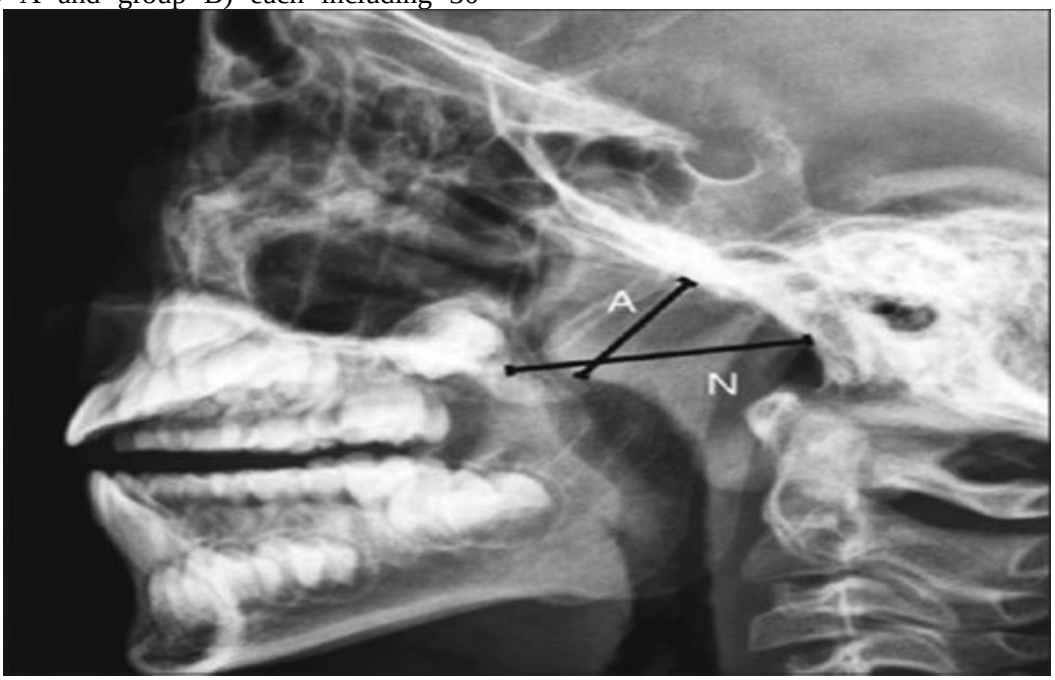

Fig. 1: Calculation of the A/N ratio according to Fujioka et al., 1979.

2.3. Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric. Also qualitative variables were presented as number and percentages. The comparison between groups with qualitative data was done by using ***Chi-square test***. The comparison between two groups with quantitative data and parametric distribution were done by using ***Independent t-test***. The comparison between two paired groups with

quantitative data and parametric distribution was done by using ***Paired t-test***. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P > 0.05: Non significant, P < 0.05: Significant and P < 0.01: Highly significant.

3. Results

Of The 60 patients fulfilling the inclusion and exclusion criteria and underwent a clinical examination and radiological investigations, Demographic data collected in table (1).

Table (1): demographic data of (group A) and (group B) including age and sex

Demographic Data		Patients group No. = 30	Control group No. = 30	Test value	P-value	Sig.
Age	Mean ± SD Range	5.20 ± 1.80 3 – 10	5.75 ± 2.33 3 – 12	-1.025•	0.310	NS
Sex	Female Male	13 (43.3%) 17 (56.7%)	16 (53.3%) 14 (46.7%)	0.601*	0.438	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

*:Chi-square test; •: Independent t-test

3.1. As regard to symptoms

In (Group A); there were highly statistically significant improvement in snoring, Breathing difficulty and Sleeping discomfort post montelukast therapy (p = 0.00) table (2)

In (Group B); there were with no statistically significant improvement in snoring, Breathing difficulty and Sleeping discomfort between pre and post placebo therapy (p = 1.00, p=0.074, p= 0.864 respectively) table (3)

On comparing post therapy effect between (Group A) and (Group B); we found highly statistically significant difference as regarding to three symptoms (p=0.000) table (4)

Table (2): pre and post montelukast effect on snoring, Breathing difficulty and sleeping discomfort in (Group A):

(Group A) Study group		Pre- medication		(3month)Post-medication		Test value	P-value	Sig.
		No.	%	No.	%			
Snoring	Never exist	0	0.0%	12	40.0%	44.348	0.00	S
	Occasional	5	16.7%	18	60.0%			
	Present at most time	12	40.0%	0	0.0%			
	Always present	13	43.3%	0	0.0%			
Breathing difficulty	Never exist	0	0.0%	9	30.0%	56.333	0.000	HS
	Occasional	0	0.0%	20	66.7%			
	Present at most time	11	36.7%	1	3.3%			
	Always present	19	63.3%	0	0.0%			
Sleeping discomfort	Never exist	0	0.0%	14	46.7%	36.960	0.000	HS
	Occasional	9	30.0%	16	53.3%			
	Present at most time	20	66.7%	0	0.0%			
	Always present	1	3.3%	0	0.0%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table (3): pre and post montelukast effect on snoring, Breathing difficulty and sleeping discomfort in (Group B):

(Group B) Control group		Pre		Post		Test value	P-value	Sig.
		No.	%	No.	%			
Snoring	Never exist	0	0.0%	0	0.0%	0.000	1.000	NS
	Occasional	9	30.0%	9	30.0%			
	Present at most time	17	56.7%	17	56.7%			
	Always present	4	13.3%	4	13.3%			
Breathing difficulty	Never exist	0	0.0%	0	0.0%	5.219	0.074	NS
	Occasional	0	0.0%	4	13.3%			
	Present at most time	17	56.7%	18	60.0%			
	Always present	13	43.3%	8	26.7%			
Sleeping discomfort	Never exist	0	0.0%	0	0.0%	0.292	0.864	NS
	Occasional	11	36.7%	13	43.3%			
	Present at most time	17	56.7%	15	50.0%			
	Always present	2	6.7%	2	6.7%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table (4) comparison between group (A) and group (B) in snoring after 3months montelukast therapy

Post		study group		Control group		Test value	P-value	Sig.
		No.	%	No.	%			
Snoring	Never exist	12	40.0%	0	0.0%	36.000	0.000	HS
	Occasional	18	60.0%	9	30.0%			
	Present at most time	0	0.0%	17	56.7%			
	Always present	0	0.0%	4	13.3%			
Breathing difficulty	Never exist	9	30.0%	0	0.0%	42.877	0.000	HS
	Occasional	20	66.7%	4	13.3%			
	Present at most time	1	3.3%	18	60.0%			
	Always present	0	0.0%	8	26.7%			
Sleeping discomfort	Never exist	14	46.7%	0	0.0%	31.310	0.000	HS
	Occasional	16	53.3%	13	43.3%			
	Present at most time	0	0.0%	15	50.0%			
	Always present	0	0.0%	2	6.7%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

3.2. <u>As regard to radiological finding in A/N ratio</u>

Using fujioko method for measuring the A/N ratio there was marked decrease of adenoid size after 3 month of montelukast therapy

In (group A), Pretreatment the A/N ratio ranged from 0.65 to 0.9 (mean 0.77 ± 0.07) while post treatment A/N ratio with range from o.4 to 0.75 (mean 0.55 ± 0.10) with mean total reduction of (28.74 ± 8.74) which was highly significant (p<0.001). Fig. 2

In (group B), before placebo the A/N ratio ranged from o.6 to 0.85(mean .73 ± 0.07) while post treatment A/N ratio ranged from o.6 to 0.85 (mean 0.72 ± 0.07 1.15 ± 2.61) with mean total reduction of (1.15 ± 2.61) which was non-significant (p =0.184). Fig. 3

On comparing post therapy effect on adenoid thickness between (Groups A) and (Group B), we found highly statistically significant difference between the two groups (p=0.000). Table 5, Fig.4

Table (5) comparison A/N ratio between in (group A) and (group B) after therapy

A / N ratio		Patients group No. = 30	Control group No. = 30	Test value•	P-value	Sig.
Post	Range Mean ± SD	0.4 – 0.75 0.55 ± 0.10	0.6 – 0.85 0.72 ± 0.07	-7.482	0.000	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

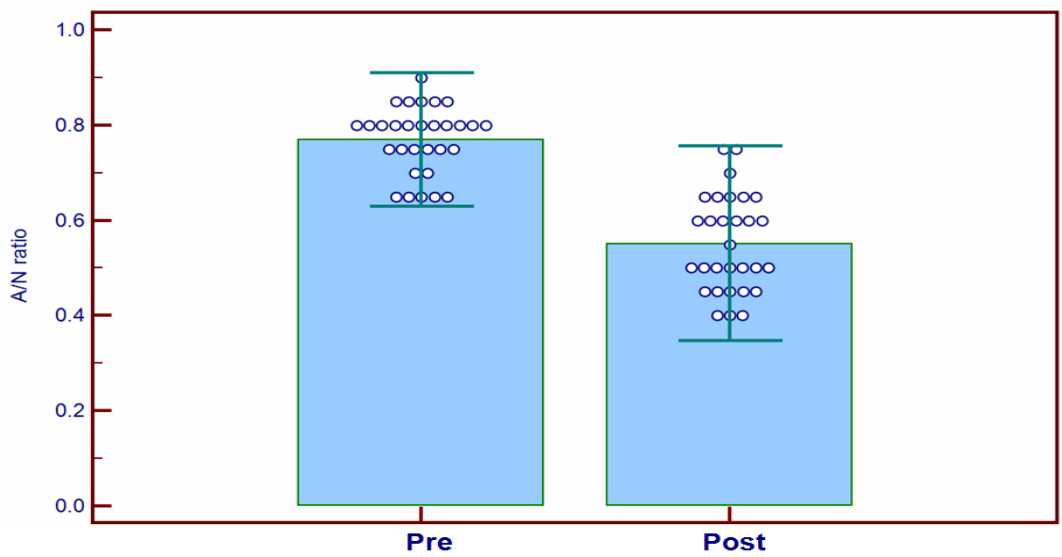

Fig. 2: bare chart comparing montelukast effect on A/N ratio in (group A)

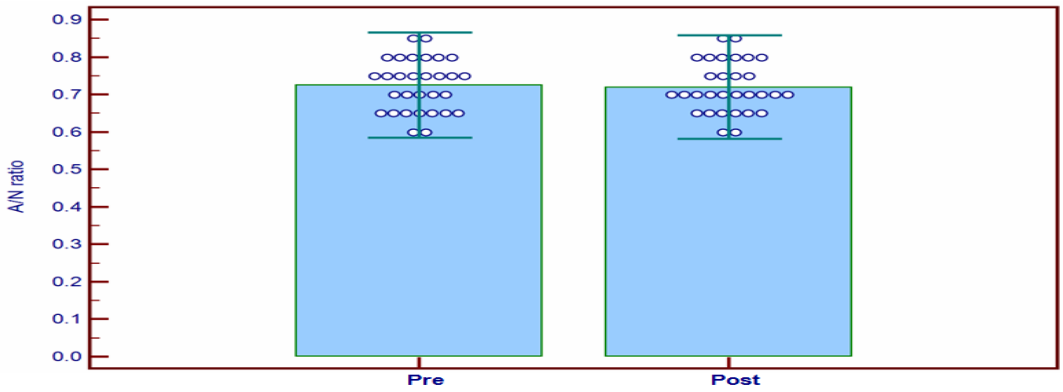

Fig.3: Bare chart comparing montelukast effect on A/N ratio in (group B)

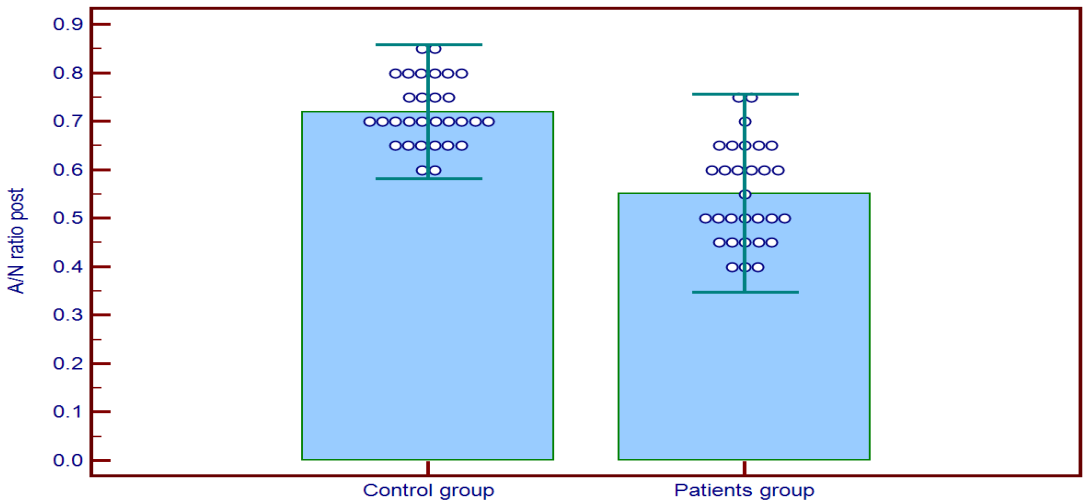

Fig. 4: Bare chart comparing adenoid size in (group A) and(group B) after montelukast therapy

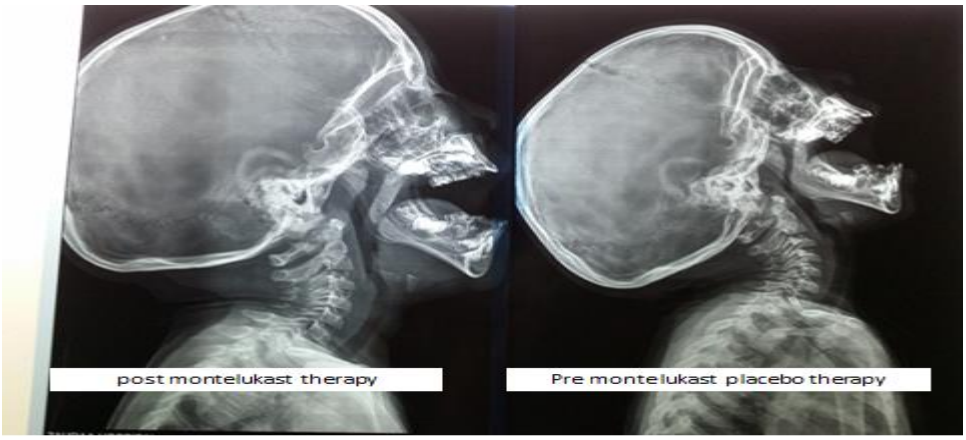

Fig. 5 Plain x-ray nasopharynx showing marked decrease of adenoid size pre and post treatment by montelukast in study group

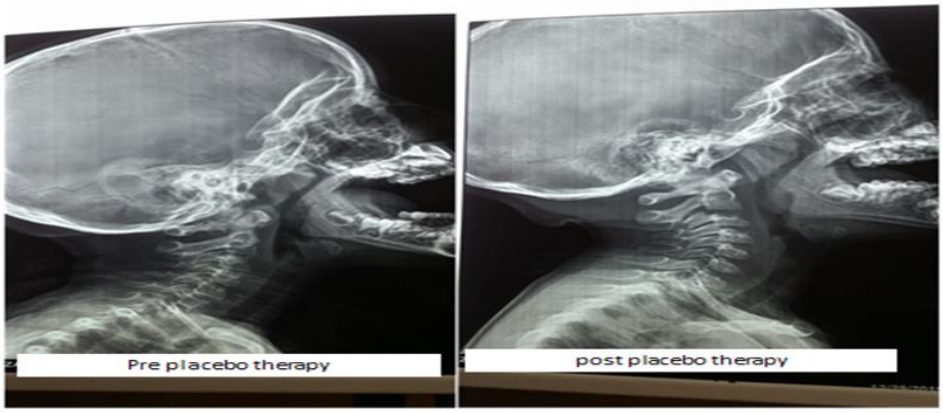

Fig. 6: Plain x-ray Nasopharynx showing no change in adenoid size pre and post treatment by placebo drug in the control group

4. Discussion

AH is a common disease of childhood and is the cause of most surgical procedures during the early years of life. This study showed that montelukast effect after 3month therapy pediatric with AH, concerning the severity of snoring, sleep discomfort, and mouth breathing as well as reducing the size of the adenoid tissue

This study included 60 patients with (AH); regarding to demographic data, there were no statistically significant different between the two group (Table 1). This agree with **Yang et al., [6]** who show no considerable statistical difference as regard to gender and age

In this study, the obstructive symptoms (snoring, breathing difficulty and sleeping discomfort) showed high significant improvement after for 3 months montelukast therapy (p value = 0.00) in(group A) (table 2), while in (group B) receiving placebo drug showed no significant improvement in snoring, breathing difficulty and sleeping discomfort (p value were 1.000, 0.074 and 0.292 respectively) (table3).There were high significant difference between(group A) and (group B) with (p value =0.00) (table 4) .

This agree with **Shokouhi et al., [8]** in which, the symptoms total score markedly dropped from 7.7 to 3.3 in the study group, while changed only from 7.4 to 6.7 in the placebo group.

As well, our results agree with **Yang et al., [6] who** investigate the clinical effect of montelukast sodium on 30 children (using Telephone questionnaire surveys) before and at 12 weeks after treatment and found that obstructive symptoms statistically improved at 12 weeks after treatment compared with before ($P<.01$)for snoring and($p< 0.01$) for breathing difficulty and sleeping discomfort.

In this study, children in (group A) had highly significant reduction of A/N (p =0.00) (Fig.2), while no significant reduction observed in (group B) (p =0.184))((Fig.3), and so, there were highly significant difference between the two groups(p =0.000) (table 5)(Fig.4)

Shokouhi et al., [8] were in agreement to our study and showed Adenoid size decreased in 76% of the study group compared with 3% of the placebo group after 12 weeks which is highly statistically significant

As well, This agree with the finding of Lateral x-ray radiographs of the cervical spine by [6]**Yang et al., 2017** .they revealed significant reduction adenoidal/nasopharyngeal ratio ($P<.05$) comparing pretreatment montelukast and at 12 weeks after treatment

This improvement could be attributed to target effect of montelukast in decreasing the inflammation present in children, decreasing tonsil and adenoid size **[10]**. Other considerable factor was Increased expression of leukotriene C4 synthase as well as leukotriene receptors 1 and 2 on adenotonsillar tissue in patient with tonsil hypertrophy & AH compared to healthy controls as reported by **Tsaoussoglou et al., [11]**. In vitro studies have also shown increased tonsillar tissue proliferation with exposure to leukotriene D4 (LTD4) and a reduction with leukotriene receptor antagonists, e.g., montelukast **[12]**. Several clinical studies have demonstrated the efficacy of leukotriene receptor antagonists in children with OSA **[10].**

Kumar [13] slightly differ from our study**,** as he reported no distinction in snoring between the two groups (P=0.111). However, a significant difference was seen between the two groups regarding to sleep discomfort and mouth breathing after treatment (Following 3 months of treatment, p value was (P<0.007) and (P<0.0001) respectively. Also **Kumar [13] reported a** marked decrease of ≥25 adenoid size after treatment. This was 76% in the treated group and 3.3% in placebo group (P<0.0001)

However, **Isil & Ayla** [14] doesn't agree with our study and reported no identified statistically significant difference in terms of sleep quality before and after treatment (p=0.91) in the group which adenoid hypertrophy obstructing more than 50% of the choana. Also, **Isil & Ayla** [14] reported no statistically significant difference identified between the A/N-R ratio before and after treatment (p=0.304) in the same group.

5. Conclusion and recommendation

montelukast treatment may be an alternative to surgical treatment for adenoid hypertrophy in patients with adenoid tissue obstructing more than 50% of the nasopharyngeal air way. The limitation of our study is the small number of patients due to discontinue follow up or discontinue treatment course.

No declarations of interests

Acknowledgements

For radiology department of ALzhraa university hospital .

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