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An open multi-centre study to assess the efficacy of inhaled salmeterol in bronchial asthma in Nigeria

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Summary

An open multicentre clinical trial of inhaled B-agonist, salmeterol, was carried out to assess its efficacy in adult Nigerian asthmatic patients. Seventy-four patients were recruited to the trial and 64 (86.48%) completed the trials. 50mcg of inhaled salmeterol was administered to the patients twice a day over a period of 2 weeks. The patients were assessed on weekly basis, at week 1,2 and 3 subjectively and objectively using the protocol prepared by the sponsor of the study.

Salmeterol was found to reduce symptoms of asthma considerably, both at day time and at night. The patient's tolerance to exercise improved significantly. The lung function assessed using Peak Expiratory Flow Meter (PEFR) showed significant improvement. Side effects were not encountered during the duration of the study. It was conclusively shown that overall, salmeterol is effective in the management of asthma in adult Nigerian patients.

Résumé

On a effectué un essai ouvert à plusieurs centres cliniques sur le B-agoniste inhalé, salmeterol, pour évaluer l'efficacité de ce médicament à l'endroit des asthmatiques adultes Nigérians. Pour ce faire, on a recruté 74 (soixante-quatorze) malades dont 64 (soixante-quatre) ont complété l'essai. Une dose de 50 mcg du salmeterol a été administrée aux malades deux fois par jour pour une période de deux semaines. On a hebdomadairement examiné les malades, de façons subjective et objective, pendant les semaines 1, 2 et 3, en utilisant le protocole préparé par le parrain de l'étude.

L'expérience a révélé que le salmeterol réduisait considérablement les symptômes d'asthme durant la journée et la nuit. La tolérance des malades aux exercises physiques s'est améliorée d'une manière significative. La fonction des poumons, évaluée à l'aide d'un compteur respiratoire peak, a fait preuve d'amélioration substantielle. Aucune réaction secondaire ne s'est montrée pendant la période de l'étude. Tout cela a définitivement prouvé en général l'efficacité du salmeterol pour les soins des asthmatiques adultes Nigérians.

Introduction

Many clinical trials have shown that B_2 agonists have been of benefit in the treatment of acute episodes of asthma[1,2,3,4]. However, control of chronic asthma still remains unsatisfactory. One of the deficiencies of B agonists in clinical use is the brevity of their action. The introduction of salmeterol, a long acting, selective inhaled B agonist is likely to give considerable relief to the asthma patients. This drug has been designed to prove long term regular treatment for asthma[5,6]. Salmeterol has been found effective in all types of asthma in early clinical trials in Europe and America[7,14]. Side effects are also reported as few[5,6,14]. Salmeterol has also been found to have anti-inflammatory properties in clinical practice[15,16,17,18]. The efficacy of salmeterol has not been confirmed in Nigeria as no clinical trial has been undertaken before now. Before its introduction to clinical practice, it i necessary that the claims attributed to salmeterol in clinical trials elsewhere, also be confirmed in the local environment, as the subjects used for trials in Europe and America are not of the same ethnic origin as the people in the local environment. This study therefore sets out to assess the efficacy of salmeterol in the local population.

Patients and Methods

This study was conducted at four tertiary health care centres in Nigeria. The study was conducted at the medical outpatients department of the selected hospitals. All patients were Nigerians with an established history of asthma. All patients admitted to the trial were aged 16-70, had no previous

administration of corticosteroids, were not in acute attack and had not had respiratory tract infection in the last month. In addition, they were free from renal, cardiac or liver diseases. Informed consent in presence of a witness was taken from all the patients after the procedure has been explained to them.

Pretreatment evaluation included a full blood count, total eosinophil count, stool examination for parasites and skin (allergy) tests. The patients were seen on 3 occasions on weekly visit. The following assessments were made: presence of symptoms of asthma; evidence of night time waking during the last preceding week, and the number of times of waking per night were ascertained. Tolerance to exercise was also assessed through questions on walking; ability to perform daily work; and effects of running or sports on symptoms of asthma. A pretreatment Peak Expiratory Flow Rate (PEFR) was determined, the best of three readings being recorded.

Salmeterol inhaler (MDI) was given to the patients after explanation and demonstration of its use to the patients, in addition to previous medications. Patients were then instructed to inhale 2 puffs (50mcg) morning and evening, and to return to the clinic every week for the next 2 weeks, for assessment at weeks 2 and 3, repeating the pretreatment subjective and objective assessment, and other additional assessment as indicated in the protocol specially prepared by Glaxo, Allen and Hanbury Ltd, U.K. The open clinical assessment was the choice of the sponsor (Glaxo, Allenbury, U.K.).

Results

Seventy four patients were recruited to the trial from the 4 centres. Sixty four (86.48%) completed the trial at the end of 3 weeks. Two of the 10 patients developed acute episodes during the trial and were withdrawn from the study, while 8 defaulted between weeks 2 and 3.

Table 1 shows the age distribution of the patients. Majority were in the 21-40 age groups.

Table 1: Age distribution in years

Age group	No. of Cases
16-20	7
21-30	17
31-40	26
41-50	17
51-60	7
Total	74

Symptoms of Asthma

Table 2 shows the duration of symptoms of asthma in years. Fifty four (73%) of patients had symptoms for a period varying from 1 to 10 years. Symptoms were graded as mild, moderate and severe at week 1. However, symptoms after administration of salmeterol were graded at week 2 and 3 as worse, same as before, better, and much better. The pattern of symptoms before and after administration of salmeterol is shown in Table 3. Fifty nine (90%) of the patients had improvement in symptoms at week 3.

Table 2: Duration of symptoms of asthma before study

Duration	No. of cases
1 - 5 Years	39
6 - 10 Years	15
11 - 15 Years	9
16 - 20 Years	7
21 - 25 Years	2
26 - 30 Years	2
Total	74

Table 3: Patients subjective assessment symptoms of asthma

Symptoms	No. of cases		
	Visit (week)		
	1	2	3
1	2	2	1
2	31	1	5
3	36	48	33
4	3	18	26
Total	72	69	65

Key

Visit 1	Visits 2 and 3
1 - None	1 - Worse
2 - Mild	2 - Same as before
3 - Moderate	3 - Better
4 - Severe	4 - Much better

Waking at night

Tables 4 (a and b) show the waking pattern of patients at night. Fifty nine (89%) at week 2 and 52 (84%) at week 3 were able to sleep better with reduction in the frequency of waking at night.

Table 4a: Waking at night in the last week

	Visit (week)		
	1	2	3
	No. of cases		
1	22	3	—
2	39	14	10
3	10	59	52
Total	71	66	62

Key

Visit 1
1 - None
2 - 1-3
3 - > 3

Visits 2 and 3
1 - None
2 - Same as before
3 - Less

Table 4b: No. of times waking per night

No. of times waking	Visit 1
None	24
1 to 2	41
Most of the night	7
Total	72

Tolerance to exercise

This is illustrated in Table 5 (a, b, c). At the end of week 3, 52 (82%) could tolerate walking, while 51 (80%) could perform their daily duty. Forty one (76%) of the patients could tolerate running or sports.

Table 5a: Tolerance to exercise [Walking]

Effect on Symptoms	Visit (week)		
	1	2	3
1	26	1	—
2	40	16	11
3	5	45	48
4	—	10	4
Total	71	72	63

Key

Visit 1
1 - No effort
2 - Mild symptoms
3 - Severe symptoms
4 - Unable to do

Visits 2 and 3
1 - Worse
2 - Same
3 - Better
4 - Much better

Table 5b: Daily work

Effect on Symptoms	Visit (week)		
	1	2	3
1	28	—	1
2	34	14	12
3	11	48	40
4	—	8	11
Total	73	70	64

Table 5c: Running or sport

Effect on Symptoms	Visit (week)		
	1	2	3
1	7	2	2
2	40	18	21
3	19	41	36
4	4	7	5
Total	70	68	64

Patients preference for salmeterol

Only one (1.56%) patient out of 64 did not prefer salmeterol to drugs previously administered to him.

Peak expiratory flow rate

In majority of cases, there was a rise in level of PEFR after administration of salmeterol. This is illustrated in figures 1 and 2. There was significant improvement in the lung function of patients following salmeterol administration.

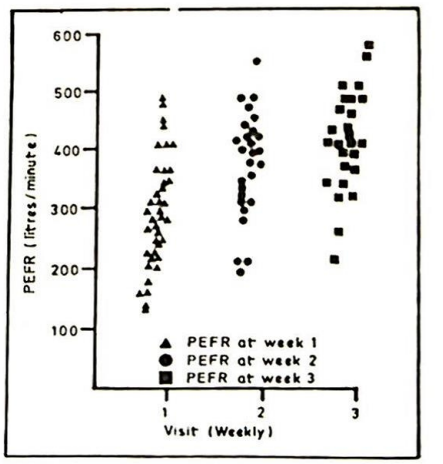

Fig. 1: Pattern of PEFR level during the study (3 weekly visit).

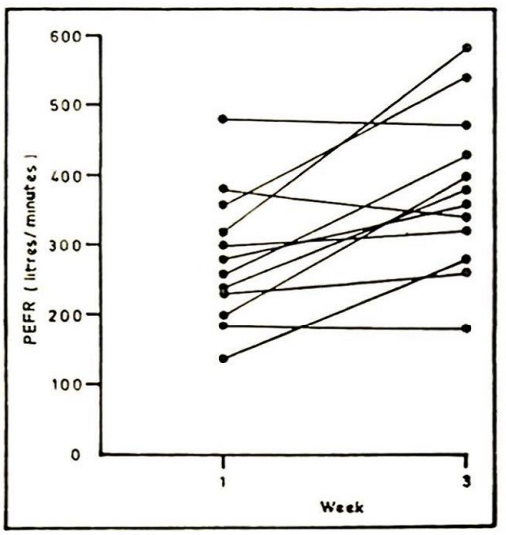

Fig. 2: PEFR values at weeks 1 and 3

The overall assessment of salmeterol in control of asthma by the investigators, shows that the drug was effective in 40 out of 64 (63%) cases and very effective in 22 (34%). Only in 2 (3.13%) patients was the drug reported as not effective. When subjective and objective assessment were put together, 61 out of 64 (95%) cases benefited from treatment with salmeterol.

Adverse effects

None was observed during the period of the trial.

Discussion

This study has shown that salmeterol at a dose of 50mcg twice a day is effective in the control of bronchial asthma.

The symptoms were improved in the majority of patients. This finding is in agreement with observations made on symptoms in studies undertaken in other centres[15,20,21]. The study also confirms findings in other studies that salmeterol allows patients to sleep better, with reduced waking[14]. Patients were also able to tolerate exercise better when salmeterol was added to their previous medications[21].

The lung function of the patients improved remarkably, confirming the findings in earlier studies[18,22]. The peak flow rate increased steadily at the third week of administration of salmeterol.

Side effects were not encountered in this study. The short duration of the study and the small number of patients used for the study might have been responsible for this finding. However, previous studies in other centres have reported occasional few side effects[4,5,6,14,21].

This limited clinical study, has conclusively shown that salmeterol in this environment is effective and safe for patients usage. Its long acting ability is an advantage for patients' compliance especially in our environment where defaulter rate, when patients are exposed to frequent administration of drugs daily, is notoriously high. Future studies with a much larger sample size will provide more information on claims which have been attributed to the drugs.

Acknowledgement

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