COMPARING PERFORMANCE OF AMOXICILLIN AND INTRAMUSCULAR BENZATHINE PENICILLIN IN RELIEVING MANIFESTATIONS OF STREPTOCOCCAL PHARYNGITIS IN CHILDREN

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SUMMARY

Objective: To compare clinical and bacteriologic responses to intramuscular benzathine penicillin G (BPG) and single dose of amoxicillin in Group A streptococcal (GAS) pharyngitis.

Design: This study included 571 children from 6 to 15 years old age, with pharyngitis, who were admitted to 45 elementary and guidance schools from 7 regions of Education Organization in North-East of Iran, Mashhad. They were screened for enrollment and if he/she presented pharyngitis with clinical criteria of sore throat, erythema, exudate and tender or enlarged anterior cervical lymph nodes. Exclusion criteria included reports of antibiotic use, negative throat culture for GAS and history of allergy to the drugs. Clinical and bacteriologic responses to BPG and once daily orally amoxicillin were considered and compared.

Results: In the amoxicillin group, treatment failure was more than the penicillin group (18.9% vs. 6.4%, respectively) but the difference was not statistically significant ($p < 0.05$). Both drugs were significantly effective in reducing pharyngitis manifestations but penicillin was significantly more effective in reducing exudate than amoxicillin.

Conclusion: Our study was in line with studies comparing the two drugs. The results show that once-daily therapy with amoxicillin is as effective as intramuscular benzathine penicillin G for the treatment of GAS pharyngitis, but penicillin was significantly more effective in reducing exudate and concurrent signs vs. amoxicillin.

Keywords: Streptococcal Pharyngitis, Erythema, Lymph nodes, Amoxicillin, Penicillin

INTRODUCTION

Recent reports from low-income countries indicate an incidence rate of Acute Rheumatic Fever 50 to 100 times higher than in high-income countries. Therefore, diagnosis and treatment of GAS pharyngitis is very important. Many studies have shown that amoxicillin taken once a day may be as effective as oral penicillin V. There had been trials about once-daily therapy for strep throat with amoxicillin.[6-8] We aimed to compare efficacy of once-daily orally amoxicillin and BPG in relieving various clinical manifestations and their bacteriologic response to the pharyngitis.

SUBJECTS AND METHODS

The study was a prospective randomized controlled clinical trial included 571 children from 6 to 15 years old age who were admitted to 45 elementary and guidance schools from 7 regions of Education Organization in North-East of Iran, Mashhad. The children were screened for enrollment if they presented pharyngitis with clinical criteria of sore throat, erythema and exudate, tender or enlarged anterior cervical lymph nodes, performing throat culture before the initiation of drug prescription, GAS positive throat culture. Exclusion criteria included reports of one or more of the following: oral antibiotic use within preceding week or intramuscularly administered antibiotics within 28 days prior to the visit, no signs of pharyngitis, and negative throat culture for GAS, history of allergy to the drugs.

When we considered P-value <0.05, Confidence level 95% and permissible error 1%, at least 97 children with GAS positive throat culture were expected as sample size.

The studied clinical signs included objective signs (tonsillar erythema, exudate, tender and enlarged anterior cervical lymph nodes) and one subjective sign (sore throat) which were recorded after physical examination. Concurrent signs, cough, coryza and abdominal pain were considered as well. The children in two treatment groups were compared with respect to age, gender and other variables. For making and confirming diagnosis, we used throat culture, which is the gold standard method with 90-95% sensitivity. The samples were sent to a selected reference laboratory. We did not use rapid antigen detection test, which the negative results should be confirmed by culture. [9]

Sampling

The method of sampling was non-probability, easy sampling. Ninety-nine patients had throat swabs that yielded positive results on culture. They were assigned in two groups by random allocation. As the children usually abstained from injection, we preferred to consider two patients in amoxicillin group by chance and the third one in penicillin group who were sent to an appointed clinic for injection.

Therefore, sixty- eight of throat culture positive children were randomly assigned to receive 750 mg orally once-daily amoxicillin for 10 days and thirty- one of throat culture positive children were randomly assigned to receive a single shot of BPG 600.000 IU and 1.200.000 IU for children weighed less than 27 kg and those who weighed more, respectively. Eleven of the amoxicillin-treated patients refused to take the drug, and were noncompliant.

Three of amoxicillin-treated group, had residual positive culture 48 hours after treatment, and had bacteriologic failure with intramuscular penicillin. They were excluded as carriers or existence of beta-lactamase producing microorganisms in their throat or were fallowed as infectious mononucleosis and diphtheria; leaving 54 amoxicillin-treated patients.

Amoxicillin Group received orally amoxicillin by a health worker and compliance was monitored. For preventing school outbreak, the patients were sent home. Health worker in the school gave the second dose of amoxicillin at the next morning.

After 48 hours, the same physician reevaluated signs, symptoms in the patients with first negative and positive throat culture, compared them in two groups and recorded. The effects of the two drugs on various signs and symptoms in positive throat culture patients were assessed and recorded to compare as well. Then, second throat culture was performed.

The patients with first negative throat culture were excluded at the end. After 48 hours, results of second throat cultures were evaluated. They were re- examined by the same physician and effects of the two drugs on the signs and symptoms in two groups were assessed and recorded again. Outcomes were measured by impact on the clinical course and response, eradication of GAS within 48 hours and compliance.

Amoxicillin was considered as a generic drug and there presents no conflict of interest in this study. This study was conducted according to the Proposed International Guidelines for Biomedical Research involving Human Subjects issued by CIOMS.

There was no moral inconsideration, and all the cooperators and the parents were well explained about the study method and we received informed consent and ethical approval from all cases and from Education Organization as well.

The patients were sent home to prevent school outbreak, after beginning treatment, and also, amoxicillin treated patients and their families were asked to continue antibiotic for 10 days and the health worker monitored compliance of oral amoxicillin as well.

For comparison of results, t-test was used and for the quality variants, Fisher and Chi-Square tests were used with p-value <0.05 through SPSS software. RCT code: NCT01310361

RESULTS

Five hundred and seventy-one children (225 males and 346 females) with pharyngitis met the enrolment criteria and participated in the study. Of these, 472 patients had negative throat culture and in 99 patients throat swabs yielded positive results on culture.

The percentage of positive throat culture was 17.3% of which 51 (51.5%) were males and 48 (48.5%) were females. Male to female ratio was 1.8 in positive culture group (p =0.07).

The mean age of the positive culture group was 8.4±1.6 of which was significantly 8 months less than negative throat culture group (p=0.01) (Tables 1 and 2).

Distribution of group with positive cultures was significantly lower in higher social classes vs. lower or middle class ones (p = 0.01) (Table 3).

There was no significant difference between clinical signs in throat negative and positive culture group patients.

Erythema and sore throat were each one the most common signs in both groups. Negative throat culture patients, featured concurrent cough and coryza each one at percentage of 50% .In positive culture group, concurrent cough and coryza were7% and 0% respectively.

Table 1 Age based frequency distribution of groups with positive and negative cultures

	Sex	No.	Mean age	S.D	Interval (95%)	Confidence Probability
Positive First Culture	Male	51	8.3	1.7	(7.84-4.33)	0.7
	Female	48	8.5	1.5	(7.84-8.33)	
Negative First Culture	Male	174	9.1	1.5	(8.84-9.07)	0.9
	Female	298	9.1	1.4	(8.92-9.24)	
Total	Male	225	8.9	1.6	(8.84	0.4
	Female	346	9.0	1.5	(8.84-9.15)	
Total	Positive culture	99	8.4	1.6	(8.06-8.39)	0.000
	Negative Culture	472	9.1	1.5	(8.94-9.08)	

Table 2 Sex based frequency distribution of groups with positive and negative Cultures Groups

Negative culture				Positive Culture		Total	
Frequency			Percent	Frequency	Percent	Frequency	Percent
Sex	Male	174	36.9	51	51.5	225	39.4
	Female	298	63.1	48	48.5	346	60.6
Total		427	100.0	99	100.0	571	100.0

Test Statistic Probability Square =7.35, p-Value =0.007

Table 3 Frequency distribution to group with positive and negative cultures based on the socioeconomic status of patients Groups

Socioeconomic Status	Negative Culture		Positive Culture		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Low	266	56.4	23	23.2	289	50.6
Intermediate	144	30.5	56	56.6	200	35.0
Good	23	4.9	11	11.1	34	6.0
Very Good	39	8.2	9	9.1	48	8.4
Total	472	100.0	99	100.0	571	100.0

Test Statistic Probability Chi-Square =39.0, p-Value=0.0001

The results showed that both penicillin and amoxicillin were effective in reducing cough, and abdominal pain (p =0.00) but penicillin was more effective (p =0.01). Both penicillin and amoxicillin were significantly effective in reducing exudate (p = 0.00), but penicillin was significantly more effective vs. amoxicillin (p =0.01). Both penicillin and amoxicillin were significantly effective in reducing erythema (p=0.01), but there was no significant difference between efficacies of two drugs in reducing erythema (p > 0.05).

Both drugs were significantly effective in reducing severity of cervical lymph nodes, tenderness and enlargement (p=0.03), but there was no significant difference between efficacies of two drugs in reducing cervical lymph nodes (p> 0.05).

Both drugs were significantly effective in reducing sore throat (p =0.00), but there was no significant difference between efficacies of two drugs in reducing sore throat (p> 0.05) (Table 4).

Table 4 Effects of Penicillin and Amoxicillin on different signs and symptoms of patients with GAS Pharyngitis Drugs

		Sore throat N (%)	Erythema N (%)	Exudate N (%)	Lymph nodes N (%)
Penicillin	Before administration	29(35.8)	30(37.5)	24(38.1)	22(32.4)
	After administration	3(42.9)	12(27.9)	0(0.0)	15(53.6)
Amoxicillin	Before administration	52(64.2)	51(63.0)	39(61.9)	46(67.6)
	After administration	4(57.1)	31(72.1)	18(100.0)	13(46.4)
Total	Before administration	81(100.0)	81(100.0)	63(100.0)	68(100.0)
	After administration	7(100.0)	43(100.0)	18(100.0)	28(100.0)

There was no significant difference between clinical and bacteriological response, bacteriologic failure and residual positive cultures between the two groups, once-daily therapy with amoxicillin and intramuscular benzatine penicillin G, after 48 hours. In the amoxicillin group, 18.9% failed to respond to treatment compared to 6.4% in the penicillin group. The difference was not statistically significant (p-value = 0.1).

DISCUSSION

In this study, the percentage of 17.3% for positive throat culture was comparable with other studies. In various sources, averagely 15%-30% of patients with sore throat had GAS positive cultures.[2] Steinhoff et al reported percentage of 24.6% positive throat culture. [6] Similar studies have reported 39% and 29% percentage.[7,10] In a WHO study this report in children with sore throat was 24.6% in Brazil and 42.0% in Croatia.[11]

In our study, the mean age of the group with first positive throat culture was 8.4 years. In similar studies this mean age is reported similarly (i.e. 9.9 years), and 6.7 ± 3.9 years .[6, 10] It is estimated that approximately10.0% to 30.0% of patients who have a positive throat culture for GAS may be carriers.[12]

In a study, Immunofluorescence analysis using anti-GAS antibody was positive in 37% of children who had tonsillectomy and about one-third of children who underwent tonsillectomy revealed presence of GAS within their tonsillar reticulated crypts.[13]

Three of amoxicillin-treated group, were considered as carriers. As they were symptomatic, they were probably GAS carriers super infected with viral pharyngitis. Of course, serologic confirmation is necessary to make difference between a carrier state and acute GAS infection, but it is impractical and expensive for GAS diagnosis.

In the Lioyd et al study, the percentage of asymptomatic GAS carriers was 8.4 per cent.[14] In this study, sore throat, erythema, exudate, tender or enlarged anterior cervical lymph nodes were included as streptococcal pharyngitis clinical criteria. In similar trials, all beta-hemolytic streptococci were susceptible to penicillin and amoxicillin.[15]

CONCLUSION

Our study was in line with studies comparing the two drugs. In most of similar trials, amoxicillin is compared with oral penicillin. Present study reported that once-daily therapy with amoxicillin is as effective as intramuscular benzathine penicillin G that is drug of choice for treatment of GAS pharyngitis in lower-income countries, but penicillin was significantly more effective in reducing exudate and concurrent signs vs. amoxicillin.

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