

## Comparison of Nifedipine and Captopril for the Control of Hypertension among Children with Acute Glomerulonephritis: A Randomized Control Trial

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### Abstract

**Background:** As control of hypertension is crucial in patients with acute glomerulonephritis (AGN) to avoid life-threatening complications and deaths. **Objectives:** This study was done to see the efficacy of captopril and nifedipine to control hypertension in AGN in respect to their clinical response, duration and cost of treatment. **Methodology:** This randomized clinical trial was done among children ages ranging from 3 to 12 years who were suffering from AGN with hypertension and/or its complications. After enrolment the patients were randomly divided into two groups as Group A and Group B. Both groups received the standard management of AGN. In addition, children in group-A received captopril (dose 0.5 up to 6 mg/kg/day) and children in group B received nifedipine (0.25 up to 0.5 mg/kg/day). Their effectiveness in relation to timing of response, duration of therapy, side effects and cost effectiveness of the drugs were assessed statistically and at p value of <0.05 the result was considered significant. **Results:** Mean systolic and diastolic blood pressure (BP) in group A were 134.8±9.31 and 94.97±6.33 mm Hg respectively and those in group B were 131.96±8.16 and 92.80±9.11 mm Hg respectively. After intervention both the drugs were found effective to normalize BP (BP <90th centile). The mean time/duration taken to normalize BP by captopril was 4.86 ± 1.73 days and that by nifedipine was 2.17 ± 1.73 days respectively and this difference is significant (p<0.01). The mean total duration of treatment required for captopril was 6.75 ± 2.04 days and that for nifedipine was 3.67 ± 1.24 days and this is highly significant (p<0.001). The average cost of captopril treatment was 11.95 ± 8.65 taka and that of nifedipine was 1.77±1.15 taka respectively and it is highly significant (p<0.001). The mean duration of hospital stay in captopril group was 8.59 ± 2.64 days and that in nifedipine group was 5.53 ± 1.49 days and it was very significant (p<0.005). **Conclusion:** Nifedipine is more effective to control BP in relation to its earlier clinical response, duration and cost of treatment than Captopril in children with AGN. [Journal of National Institute of Neurosciences Bangladesh, January 2022;8(1): 28-32]

**Keywords:** Acute glomerulonephritis; blood pressure; captopril; nifedipine

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### Introduction

Transient hypertension is observed in more than 80%

patients with AGN and many of them are at risk of death because of hypertensive encephalopathy and/or heart

failure<sup>1</sup>. The prognosis of AGN virtually depends on early and good control of hypertension<sup>2</sup>.

Reports on randomized clinical trials among the children with anti hypertensive drugs are limited<sup>1</sup>. However, the recommended anti-hypertensive agents are ACE inhibitor (captopril), Calcium channel blocker (nifedipine) and diuretics because they are generally effective and have minimum side effects. Some studies had shown the superiority of nifedipine in reducing BP in severe hypertension in children. Similarly captopril was also proved as effective in many studies. In clinical practice, sometimes there is dilemma about choosing the right anti-hypertensive agent. Therefore, the present study was designed to see the efficacy of these 2 drugs to control hypertension in children with AGN.

### Methodology

It was a randomized clinical trial done in the department of Paediatrics at Dhaka Medical College Hospital, Bangladesh from July 2005 to June 2006 for a period of one year. The children with the age ranging from 4 to 12 years who suffered from acute glomerulonephritis with hypertension (BP above 95<sup>th</sup> centile) and/or with heart failure or encephalopathy were enrolled in the study. Patients whose BP was  $\leq$  95<sup>th</sup> centile or who had acute renal failure were excluded from the study. After enrollment, the cases were fully assessed both clinically and with laboratory support. Blood pressure (BP) of the cases were measured following the standard procedure like appropriate sized cuff, lying posture and in calm and quite status of the patients. Along with other treatment and supports, anti-hypertensive drugs were selected randomly using a randomization table. Children received captopril was categorized as Group A (n=30) and those received nifedipine as Group B (n=30). The dose of captopril was ranging from 0.5 to 6 mg/kg/day in 2-3 divided doses as required<sup>3</sup> and that of nifedipine was (0.25 to 0.5 mg/kg/day)<sup>3</sup>. Blood pressure as well as other symptoms and signs including any complications were recorded every 2 hourly on the first day and every 6 hourly from the 2<sup>nd</sup> day onward till the patients remain in the hospital. Investigations like Urine for R/M/E, blood CBC, hemoglobin, Serum creatinine, electrolytes, x-ray chest, ASO titre, C<sub>3</sub> level were done and the results were recorded. The dose, efficacy, duration of therapy and adverse effects of the antihypertensive drugs, if any, in each group were noted. Antihypertensive drugs were discontinued when BP become normal (systolic and diastolic BP below 90<sup>th</sup>

centile for age and sex). If hypertension remained above 95<sup>th</sup> centile after 48 hours of any antihypertensive drug then the other one was decided to give. The time needed to bring BP below 90<sup>th</sup> percentile, the duration of antihypertensive therapy (i.e. the time for BP become <90<sup>th</sup> percentile), duration of hospital stay and outcome of patients in each group were recorded. The costing of each group was calculated. At the end of data collection, it was checked carefully. A master sheet was prepared first for the purpose of tabulation. Simple statistical analytical methods were used where necessary to process and present in data in table form. The patients were divided into the following age groups: <4 years, 4-7 years 11 months, 8-10 years and >10 years. AGN was defines as children aged 3-12 years suffering from gross hematuria, edema, hypertension and/or renal insufficiency<sup>4,5</sup> with or without history of sore throat or pyoderma were defined as AGN in this study. Hypertension was defined as an average systolic and/or average diastolic BP greater than or equal to the 95<sup>th</sup> percentile for age, sex and height, measured on admission<sup>6,7,8</sup>. Normal BP was defined as systolic and diastolic BP less than the 90<sup>th</sup> percentile for age, sex and height<sup>9,10</sup>. Prehypertension or borderline hypertension was again defined as average systolic or diastolic pressures between 90-95<sup>th</sup> percentile. Collected data were sorted and were screened for any discrepancy. The edited data were entered on to the template of SPSS version 11.0. For background variables and socio-demographic data descriptive statistics and relative frequency (percentage) was generated. Association between socioeconomic variables and related factors was assessed through chi square test. Level of significance was considered at p value less than 0.05. Multivariate analysis was done to determine individual risk factor adjusting for others Odds ratio and 95.0% CI was reported. Data were presented in the form of table and graphs. Descriptive statistics was presented with frequency table. Association was illustrated with cross tables and test statistics was added in the footnote of the table. Bar and pie charts were generated to illustrate descriptive statistics.

### Results

The mean age of the children (n=60) was 6.43 $\pm$ 2.33 years (age range 4 to 12 years). Among them more (48.3%) were in the 4 to 7 years age group than the 8 to 10 years (30.0%). The ratio between boys and girls was 2.53:1 (Figure I).

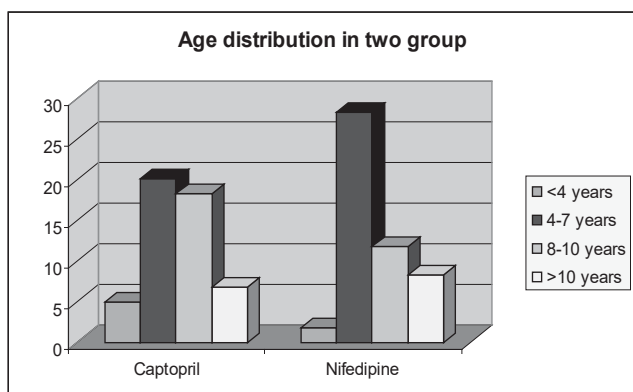


Figure 1: Age distribution in two groups (years)

Among the sixty patients, 39(65%) patients were having AGN without complications. However, the rest 21(35%) cases had various complications with AGN; 11(18.33%) cases had heart failure, 6(10.0%) cases had hypertensive encephalopathy and 4(6.67%) cases had hypertensive encephalopathy and heart failure (Figure II).

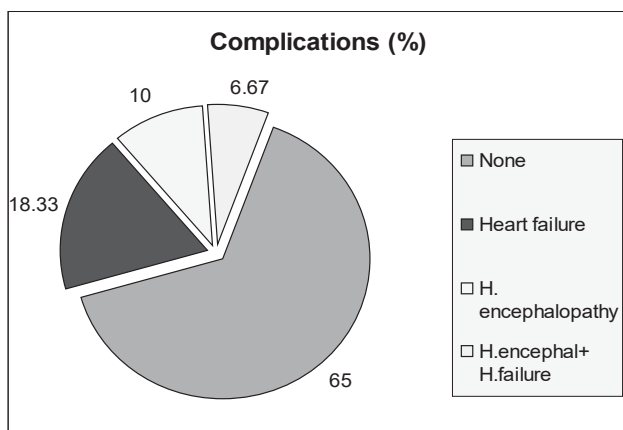


Figure II: Different Complications of AGN in the study

The mean systolic and diastolic BP in group A on admission were 133.37±8.81 and 93.88±7.90 mm of Hg respectively and those in group B were 134.67±7.56 and 93.63±8.11 and there was no statistical difference (p>0.05). Mean systolic BP in Captopril group became 128.2 mm of Hg on day 2 from 133.2 mm of Hg on day 1; whereas in Nifedipine group, it became 116.8 mm of Hg from 134.4 mm of Hg (Fig. 3). Similar difference was observed in diastolic BP; where mean DBP became 84.9 mm of Hg on day 2 from 93.9 mm of Hg on day 1 in Captopril group. In Nifedipine group, it became 76.4 mm of Hg from 95.1 (Figure III).

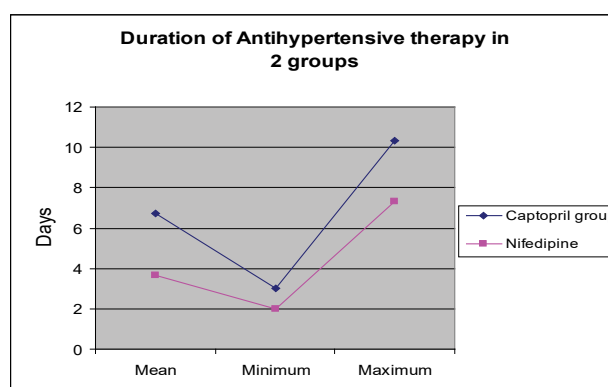


Figure III: Response of Antihypertensives in reducing SBP

The days (mean ± SD) required to bring BP < 95th centile in the captopril group was 4.86 ± 1.73 days (range: 1.66 to 7.66 days) and that in nifedipine group was 2.17 (±1.73) days (range: 0.66 to 5.66 days). The difference between two groups was significant (p<0.01, CI was 1.92 to 3.46). The mean duration of anti-hypertensive therapy required in the captopril group 6.75 ± 2.04 days (range: 3-10.33 days) and that in nifedipine group was 3.67 ± 1.24 days (range: 2.00 to 7.33 days). This difference was significant (p<0.001, CI 2.20 to 3.95) (Figure IV).

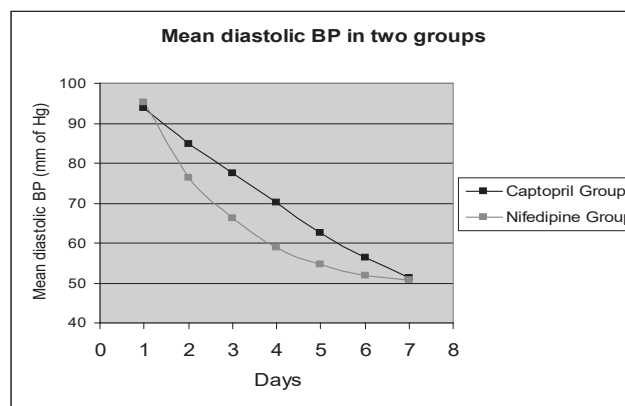


Figure IV: Response of Anti-hypertensive in reducing SBP

The mean with SD of the duration of anti-hypertensive drugs therapy was found difference in captopril and nifedipine groups (Figure V).

The mean cost of antihypertensive therapy was 11.95±8.65 taka in captopril group (range: 1.50 to 33.50 taka) and 1.77±1.15 taka (range: 0.40 to 5.00 taka). The confidence interval (CI) was 6.99 to 13.37. The statistical difference between two groups was highly significant (p<0.001) (Figure VI).

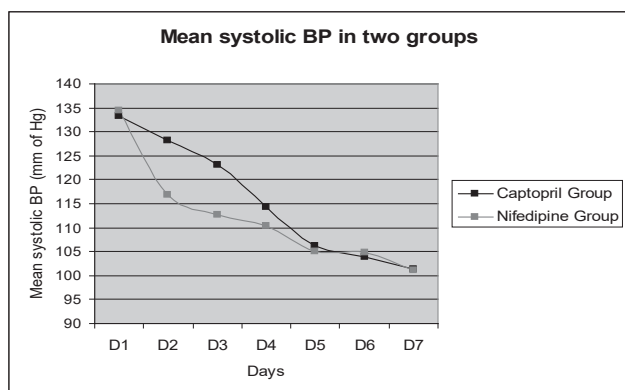


Figure V: Duration of Anti-Hypertensive (Days)

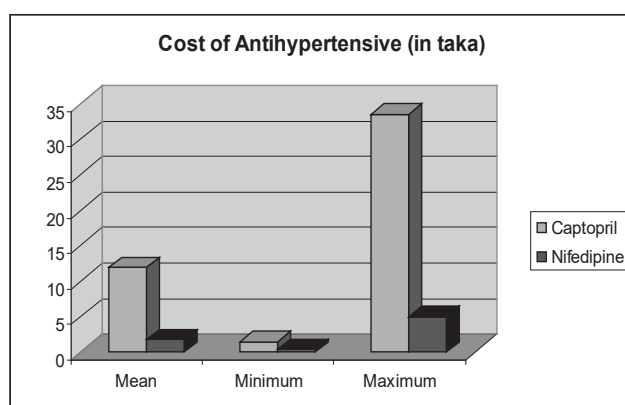


Figure VI: Cost of Antihypertensive (in taka)

There were no significant side effects of the antihypertensive given in both groups observed after therapy. Only one patient in captopril group complained of cough, two in the same group developed hyperkalemia after treatment had started. One from nifedipine group had constipation and 1 case complained of dizziness. The mean with SD of two groups stayed in the hospital were  $8.59 \pm 2.64$  days versus  $5.53 \pm 1.49$  days, minimum 3.00 versus 3.33 days and maximum 13.66 versus 9.0 days respectively in group A (Captopril) and group B (Nifedipine). The confidence interval (CI) was 1.95 to 4.17. The statistical difference between two groups was very significant ( $p < 0.005$ ).

## Discussion

AGN causes significant hospital load also in Bangladesh. On average, it is responsible for 2%-5% of Pediatric admission in Bangladesh<sup>11,12</sup>. A total of 60 (sixty) patients were enrolled in this study. None was withdrawn from the study as there was no clinical deterioration or new complications arose.

Acute PSGN is common in children aged 5 to 12 years and uncommon in less than 3 years<sup>3</sup>. The male-to-female

ratio range is 2:1<sup>13</sup>. The most patients in this study were between 4 to 10 years (78.3%) which was similar to many other studies. The ratio between boys and girls (2.53:1) was also correlated with most studies. Most patients had very high systolic (mean  $133.93 \pm 8.26$  mm of Hg) and diastolic (mean  $93.57 \pm 8.11$  mm of Hg) blood pressure. These were said to be very high as these values were much higher than 95<sup>th</sup> percentile of any age.

Patient may develop encephalopathy and/or heart failure due to hypertension or hypervolemia as a complication in AGN. Regarding complications, 5.0 to 10.0% patients may suffer from encephalopathy and 8.0 to 20.0% from heart failure<sup>14,15,16</sup>. In this study, 11(18.33%) had heart failure, 6 (10.0%) had hypertensive encephalopathy and 4(6.67%) had hypertensive encephalopathy with heart failure. The rate of heart failure only matched with one study, but most other studies shown much lower rate of complications than this study. Complications were most marked in more than 10 years age group (66.67%), next is less than 4 years (50.0%), 8 to 10 years (33.33%) and 4 to 7 years (24.13%) respectively in descending order.

There was an obvious difference between the effects of the two antihypertensives. Nifedipine reduced both SBP and DBP much earlier than Captopril, thus reducing the morbidity of the patient as well as duration and cost of therapy. There were no significant side effects of the antihypertensive given in both groups (10.0% in captopril and 6.0% in nifedipine group) observed after therapy.

As in other studies, our patients tolerated nifedipine well despite a sometimes large and unpredictable fall in BP. The even lower incidence of adverse events observed in our patient group compared with other studies of children, may be related to the presumed rapid rise in BP in APSGN. Regarding the hospital stay between two groups, Captopril group had a longer hospital stay than that of nifedipine group ( $p < 0.005$ ). There was no significant difference between two groups statistically in outcome ( $p > 0.05$ ).

As we have already mentioned that we found very high rate of complications (35.0%) of AGN than many other studies which might be due to the fact that all our cases were hypertensives ( i.e. BP > 95<sup>th</sup> percentile). Another important reason for high rate of complications is that we could start treatment much later than expected due to the late arrival of the patients to the hospital. Poverty, ignorance, negligence, lack of health seeking behaviour are the additional factors for this apart from poor health education. As a result we also got very high systolic and diastolic BP in most cases ((86.67% and 73.33% respectively). Though we were very fortunate that there

were no fatalities in our study, but to reduce morbidity and mortality from AGN, early effective control of BP is always essential. Most important factors responsible for the failure to control HTN are selection of inappropriate antihypertensive drug, improper dose, unavailability of drugs, higher cost, poor response and non-compliance. In this particular study, nifedipine clearly stands ahead captopril in terms of early control of HTN, shorter duration of therapy, much cheaper and shorter hospital stay. Nifedipine is very useful to control the worst of the hypertension until an effective diuresis is established. It is also the only oral drug recommended for use in hypertensive crises. Ease of administration (no intravenous access or infusion pumps) and wide availability make it appealing in secondary and primary hospitals in our setting.

### Conclusion

It was obvious from the study that Nifedipine controlled BP earlier; so that was given for a shorter period of time, much less costly and reduced the duration of hospital stay than did Captopril. By its less cost, early control of BP, shorter dosing and shorter hospital stay, it can reduce the morbidity of the patients; reduce the expenses of the family as well as the nation. So for the control of hypertension in AGN patients, Nifedipine is better drug at least in terms of activity, cost and morbidity.

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