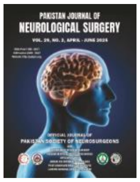

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Original Research

Comparison of Endoscopic Third Ventriculostomy and Choroid Plexus Cauterization Combined and Alone in Pediatric Hydrocephalus – A Prospective Cohort Study

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ABSTRACT

Objective: To evaluate whether combining endoscopic third ventriculostomy (ETV) with choroid plexus cauterization (CPC) improves treatment outcomes in pediatric hydrocephalus compared to ETV alone.

Materials and Methods: This prospective cohort study was conducted at the Department of Neurosurgery, DHQ Hospital, Rawalpindi, Pakistan, over 6 months. Pediatric patients diagnosed with hydrocephalus and meeting inclusion criteria were enrolled and assigned to two cohorts based on the procedure performed: Cohort A (ETV alone, n=35) and Cohort B (ETV + CPC, n=35). Patients were followed for three months postoperatively to assess treatment success, need for reoperation, and mortality. Relative risks (RR) with 95% confidence intervals (CI) were calculated to compare outcomes between cohorts.

Results: The success rate was significantly higher in the ETV + CPC cohort (85.7%) compared to the ETV-alone cohort (45.7%) (RR = 1.87, 95% CI: 1.31–2.66, p<0.001).** The reoperation rate was lower in the ETV + CPC group (8.6% vs. 34.3%, p=0.009), as was mortality (2.9% vs. 20.0%, p=0.024).

Conclusion: The addition of CPC to ETV is associated with significantly improved outcomes in pediatric hydrocephalus, reducing failure rates, need for reoperation, and mortality. These findings support CPC as an effective adjunct to ETV. Further long-term studies are warranted to confirm these benefits.

Keywords: Hydrocephalus, Cerebrospinal Fluid, Endoscopic Third Ventriculostomy, Choroid Plexus Cauterization, Shunt System, Cohort Study.

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INTRODUCTION

Hydrocephalus refers to brain fluid excess accumulation, divided into obstructive and communicating forms. Obstructive occurs due to blockage in the flow of cerebrospinal fluid (CSF), while communicating hydrocephalus results from CSF re-absorption defects.[1] Adams et al, 1965 defined hydrocephalus as a condition characterized by ventricle enlargement, normal CSF pressure, gait disturbance, dementia, and urinary incontinence, with secondary NPH induced by meningitis and trauma.[2]

Hydrocephalus is a common condition in infancy, particularly in premature babies, with a global prevalence of 85 per 100,000 individuals, with higher rates in Africa and South America.[3] Infantile cases range from 1 to 32 per 10,000 births. The choroid plexus generates CSF and it traverses through the ventricular system, arachnoid granulations, and dural venous sinuses.[4] It is absorbed into the systemic circulation and has an average volume of 150 ml.[5] CSF flows slowly and can be affected by any obstructions in the brain ventricular system, subarachnoid space, or the venous sinuses.[5] Following the Monro-Kellie doctrine the summation of volumes of brain, CSF, and intracerebral blood is always constant such that an increase in one compartment must always accompany a decrease in the other two compartments.[6]

The common treatment for hydrocephalus includes ventriculoperitoneal shunting but its failure is common.[7] Endoscopic procedures like ETV, aqueductoplasty, and scenting are gaining recognition for better outcomes. The success of ETV is determined by clinical and radiological criteria, such as improved consciousness, ocular movement abnormalities, and reduced head circumference. Simultaneous CSF absorption may be necessary to reduce CSF production and improve outcomes.[8,9] Postoperative decrease in ventricular size is inversely related to preoperative symptoms, while the size of ventricles after ETV may indicate success.

There is an inverse relation between the extent of the decrease in ventricular size postoperatively with both the severity as well as the duration of preoperative symptoms. On the other hand, a decrease in the size of the ventricles after ETV could indicate a possibility of being an effective approach as it has been established to lessen narrowly in both settings.[10] A study was conducted by Warf et al, and reported successful treatment with ETV alone in 48.6% of participants and 81.9% successful treatment with ETV + CPC group.[11,16]

No local study on a small sample size was conducted in this region on comparison between clinical findings of participants who underwent ETV alone and ETV with CPC for hydrocephalus hence this study was designed to bridge the local reference gap and we would be able to go for the procedure which given us better outcome and less morbidity.

MATERIALS AND METHODS

Study Design and Settings

This perspective was conducted at the Department of Neurosurgery, District Headquarters Hospital, Rawalpindi, Pakistan, over six months, from February 28, 2022 to August 29, 2022.

Inclusion Criteria

The determined sample size for this study consisted of 70 participants, with 35 participants allocated to each group. Regarding participant selection, inclusion criteria encompassed individuals falling within the range of 6 months to 18 years of age, irrespective of gender. Additionally, only the participants exhibiting symptomology of intracranial hypertension and evidenced radiographically by non-communicating hydrocephalus were included.

Exclusion Criteria

Individuals with indications of a potential infectious origin of hydrocephalus, based on either medical history or imaging findings at the time of ventriculoscopy, were excluded. Moreover, participants presenting with either patent or a membrane or cyst obstructed aqueduct of sylvius, rather than stenosis were also not included. Severe cerebral hemisphere malformations, such as hydranencephaly, extensive regions of underdeveloped brain, or schizencephaly, were additional factors leading to exclusion from the study. These criteria were vital in refining the participant selection and maintaining the study's intended scope and objectives.

Data Collection

The study was carried out in the Department of Neurosurgery at District Headquarters Hospital Rawalpindi, Pakistan. The hospital's ethics board granted the ethical approval. Non-probability consecutive sampling technique was employed to pick and choose the participants. They were then assigned to two cohorts i.e. group A (ETV alone) or group B (ETV plus CPC). In the right prefrontal area of the cranium, a burr hole was created, anteriorly to the coronal suture, and in the mid pupillary line. This provided the optimal trajectory for the endoscope to reach the third ventricle traversing through the interventricular foramina (foramen of Monro) and the interpeduncular cistern. A 0° rigid endoscope with a double irrigating sheath (4.6 mm) was introduced into the lateral ventricle, under video guidance, followed by a catheter. The patient was lying in a supine position with his head flexed to ensure that the burr hole is positioned at the topmost point. This helped to avoid excessive drainage of the CSF and the entrance of any air into the ventricles and subdural space. ETV was then performed. At the junction point of the thalamostriate vein, septal vein, and choroid plexuses, the formen joining the paired lateral ventricles and third ventricle was identified. Ringer's lactate solution at 90°F was used for irrigation. The endoscope was negotiated into the third ventricle. A cautery probe was then inserted between the mammillary bodies and the infundibular recess. It was then used to puncture the thinnest part of the floor of the third ventricle. A Fogarty catheter was inflated to dilate and fenestrate the opening. At the end of the procedure, a Gelfoam plug was inserted into the cortical tract. In group B, simultaneous cauterization of the choroid plexus was also performed. The study was recorded on a proforma designed beforehand. Participants were also followed for 3 months to ascertain the effectiveness of the procedure.

Data Analysis

Data was entered and analyzed on SPSS version 23. Mean and standard deviations were calculated for age, BMI, and duration of surgery. Frequencies and percentages were also calculated for qualitative variables. e.g. success (Yes/No) re-operation, other procedure, mortality. Effect modifiers like age, BMI, and surgery duration were assessed. The chi-square test was applied post-stratification. A p-value of ≤0.05 was taken as significant. Success between the groups was compared by the chi-square test.

RESULTS

Gender & Age Distribution

This study included 70 participants with a mean age of 9.90±5.83 years. The participants were assigned to Group A (ETV alone) or Group B (ETV plus CPC). The mean ages of the participants in groups A and B were 9.20±5.93 and 10.60±5.72 years respectively. The difference between their ages was not statistically significant (p-value = 0.319). There were 42 (60%) male and 28 (40%) female participants in the study with a male-to-female ratio of 1.5:1. In groups A and B, a total of 22 (62.9%) and 20 (57.1%) participants were male respectively. This difference was statistically insignificant also (p-value=0.626).

BMI Distribution

The mean value of body mass indexes (BMI) of the participants in this study was 21.69±3.02 kg/m2. The minimum BMI was 17.41 kg/m2 and the maximum BMI of 27.81 kg/m2. The mean BMI of the participants in groups A and B was 21.57±3.33 kg/m2 and 21.82±2.71 kg/m2 respectively. This difference was statistically insignificant (p-value= 0.741).

Success Rate

The cumulative success rate of ETV plus CPC was 65.71% (46 out of 70 participants) in this study. The success rate was greater in group B i.e. ETV plus CPC than in group A i.e. ETV alone, with 85.71% (30 out of 35 participants) and 45.71% (16 out of 35 participants) success rates respectively. This difference was significant statistically (p-value < 0.001).

In participants aged 10 years or younger, the success rate of ETV plus CPC was 86.7% (13 out of 15 participants) in comparison to 47.4% (9 out of 19 participants) for ETV alone (p-value = 0.017). In participants aged over 10 years, the success rate of ETV plus CPC was 85.0% (17 out of 20 participants) in comparison to 43.8% (7 out of 16 participants) for ETV alone (p-value = 0.009).

In male participants, the success rate of ETV plus CPC was 85.0% (17 out of 20 participants) in comparison to 40.9% (9 out of 22 participants) for ETV alone (p-value = 0.017). In female participants, the success rate of ETV plus CPC was 86.7% (13 out of 15 participants)in comparison to 53.8% (7 out of 13 participants) for ETV alone (p-value = 0.055).

In participants with a BMI of 25 kg/m2 or less, the success rate of ETV plus CPC was 87.1% (27 out of 31 participants) in comparison to 46.4% (13 out of 28 participants) for ETV alone (p-value = 0.001). In participants with a BMI of over 25 kg/m2, the success rate of ETV plus CPC was 75.0% (3 out of 4 participants) in comparison to 42.9% (3 out of 7 participants) for ETV alone (p-value = 0.303).

Rate of re-operation

In this study, 15 (21.4%) participants required re-operation, and 9 (12.9%) participants required other procedures. The rate of re-operation was higher in group A (ETV alone) as compared to group B (ETV plus CPC), with 34.3% (12 out of 35 participants) and 8.6% (3 out of 35 participants) re-operation rates, respectively. This difference was statistically significant (p-value = 0.009). The rate of other procedures done was also higher in group A than in group B, with 20.0% (7 out of 35 participants) and 5.7% (2 out of 35 participants) rates, respectively. This difference was however statistically insignificant (p-value = 0.074).

In participants aged 10 years or younger, the re-operation rate of ETV plus CPC was 0% (0 out of 15 participants) compared to 26.3% (5 out of 19 participants) for ETV alone (p-value = 0.031). In participants aged over 10 years, the re-operation rate of ETV plus CPC was 15.0% (3 out of 20 participants) compared to 43.8% (7 out of 16 participants) for ETV alone (p-value = 0.031).

In male participants, the re-operation rate of ETV plus CPC was 5.0% (1 out of 20 participants) compared to 40.9% (9 out of 22 participants) for ETV alone (p-value = 0.017). In female participants, the re-operation rate of ETV plus CPC was 13.3% (2 out of 15 participants) compared to 23.1% (3 out of 13 participants) for ETV alone (p-value = 0.639).

In participants with a BMI of 25 kg/m2 or less, the re-operation rate of ETV plus CPC was 6.5% (2 out of 31 participants) in comparison to 28.6% (8 out of 28 participants) for ETV alone (p-value = 0.025). In participants with a BMI of over 25 kg/m2, the re-operation rate of ETV plus CPC was 25.0% (1 out of 4 participants) in comparison to 57.1% (4 out of 7 participants) for ETV alone (p-value = 0.345).

In participants aged 10 years or younger, the rate of other procedures was 26.3% (5 out of 19 participants) in group A (ETV alone) and 13.3% (2 out of 15 participants) in group B (ETV plus CPC) (p-value = 0.426). In participants aged over 10 years, the rate of other procedures was 12.5% (2 out of 16 participants) in Group A and 0% (0 out of 20 participants) in Group B (p-value = 0.190). In male participants, the rate of other procedures was 18.2% (4 out of 22 participants) in group A and 10% (2 out of 20 participants) in group B (p-value = 0.665). In female participants, the rate of other procedures was 23.1% (3 out of 13 participants) in group A and 0% (0 out of 15 participants) in group B (p-value = 0.087). In participants with a BMI of 25 kg/m2 or less, the rate of other procedures was 25% (7 out of 28 participants) in group A and 6.5% (2 out of 31 participants) in group B (p-value = 0.048).

Mortality Rate

In this study, 8 (11.43%) participants succumbed to death. The mortality rate was higher in group A (ETV alone) than in group B (ETV plus CPC), with 20.0% (7 out of 35 participants) and 2.9% (1 out of 35 participants) mortality rates, respectively. This difference in mortality rates in both groups was significant statistically (p-value = 0.024). Comparison of mortality between both our study groups A and B, stratified by age, gender, and BMI showed be statistically insignificant difference (p-value>0.05).

Table 1: *Patient demographics and outcomes.*

Variables	Outcome	Group A (ETV)	Group B (ETV with CPC)	Total	P-value
Age (Years)	Mean±SD	9.20±5.93	10.60±5.72	9.90±5.83	0.319
BMI	Mean±SD	21.57±3.33	21.82±2.71	21.69±3.02	0.741
Gender	Males	22(62.9%)	20(57.1%)	42(60.0%)	0.626
	Females	13(37.1%)	15(42.9%)	28(40.0%)	
Success Rate	Yes	16(45.7%)	30(85.7%)	46(65.7%)	<0.001
	No	19(54.3%)	5(14.3%)	24(34.3%)	
Re-operation	Yes	12(34.3%)	3(8.6%)	15(21.4%)	0.009
	No	23(65.7%)	32(91.4%)	55(78.6%)	
Other Procedure	Yes	7(20.0%)	2(5.7%)	9(12.9%)	0.074
	No	28(80.0%)	33(94.3%)	61(87.1%)	
Mortality	Yes	7(20.0%)	1(2.9%)	8(11.4%)	0.024
	No	28(80.0%)	34(97.1%)	62(88.6%)	

Table 2: *Comparison of success between study groups A and B stratified by age, gender, and BMI.*

		Success	Study Groups		Total	p-value
			Group A	Group B		
Age (Years)	≤ 10	Yes	9(47.4%)	13(86.7%)	22(64.7%)	0.017
		No	10(52.6%)	2(13.3%)	12(35.3%)	
	>10	Yes	7(43.8%)	17(85.0%)	24(66.7%)	0.009
		No	9(56.2%)	3(15.0%)	12(33.3%)	
Gender	Male	Yes	9(40.9%)	17(85.0%)	26(61.9%)	0.003
		No	13(59.1%)	3(15.0%)	16(38.1%)	
	Female	Yes	7(53.8%)	13(86.7%)	20(71.4%)	0.055
		No	6(46.2%)	2(13.3%)	8(28.6%)	
BMI	≤ 25	Yes	13(46.4%)	27(87.1%)	40(67.8%)	0.001
		No	15(53.6%)	4(12.9%)	19(32.2%)	
	>25	Yes	3(42.9%)	3(75.0%)	6(54.5%)	0.303
		No	4(57.1%)	1(25.0%)	5(45.5%)	

Table 3: *Comparison of re-operation between study groups A and B stratified by age, gender, and BMI.*

Re-operation			Study Groups		Total	p-value
			Group A	Group B		
Age (Years)	≤ 10	Yes	5(26.3%)	0(0.0%)	5(14.7%)	0.031
		No	14(73.7%)	15(100.0%)	29(85.3%)	
	>10	Yes	7(43.8%)	3(15.0%)	10(27.8%)	0.073
		No	9(56.2%)	17(85.0%)	26(72.2%)	
Gender	Male	Yes	9(40.9%)	1(5.0%)	10(23.8%)	0.006
		No	13(59.1%)	19(95.0%)	32(76.2%)	
	Female	Yes	3(23.1%)	2(13.3%)	5(17.9%)	0.639
		No	10(76.9%)	13(86.7%)	23(82.1%)	
BMI	≤ 25	Yes	8(28.6%)	2(6.5%)	10(16.9%)	0.025
		No	20(71.4%)	29(93.5%)	49(83.1%)	
	>25	Yes	4(57.1%)	1(25.0%)	5(45.5%)	0.345
		No	3(42.9%)	3(75.0%)	6(54.5%)	

Table 4: *Comparison of other procedures between study groups A and B stratified by age, gender, and BMI.*

Other Procedure			Study Groups		Total	p-value
			Group A	Group B		
Age (Years)	≤ 10	Yes	5(26.3%)	2(13.3%)	7(20.6%)	0.426
		No	14(73.7%)	13(86.7%)	27(79.4%)	
	>10	Yes	2(12.5%)	0(0.0%)	2(5.6%)	0.190
		No	14(87.5%)	20(100.0%)	34(94.4%)	
Gender	Male	Yes	4(18.2%)	2(10.0%)	6(14.3%)	0.665
		No	18(81.8%)	18(90.0%)	36(85.7%)	
	Female	Yes	3(23.1%)	0(0.0%)	3(10.7%)	0.087
		No	10(76.9%)	15(100.0%)	25(89.3%)	
BMI	≤ 25	Yes	7(25.0%)	2(6.5%)	9(15.3%)	0.048
		No	21(75.0%)	29(93.5%)	50(84.7%)	
	>25	Yes	0(0.0%)	0(0.0%)	0(0.0%)	--
		No	7(100.0%)	4(100.0%)	11(100.0%)	

Table 5: *Comparison of mortality between study groups A & B stratified by age, gender, and BMI.*

Mortality			Study Groups		Total	p-value
			Group A	Group B		
Age (years)	≤ 10	Yes	4(21.1%)	1(6.7%)	5(14.7%)	0.355
		No	15(78.9%)	14(93.3%)	29(85.3%)	
	>10	Yes	3(18.8%)	0(0.0%)	3(8.3%)	0.078
		No	13(81.2%)	20(100.0%)	33(91.7%)	
Gender	Male	Yes	4(18.2%)	1(5.0%)	5(11.9%)	0.346
		No	18(81.8%)	19(95.0%)	37(88.1%)	
	Female	Yes	3(23.1%)	0(0.0%)	3(10.7%)	0.087
		No	10(76.9%)	15(100.0%)	25(89.3%)	
BMI	≤ 25	Yes	7(25.0%)	1(3.2%)	8(13.6%)	0.022
		No	21(75.0%)	30(96.8%)	51(86.4%)	
	>25	Yes	0(0.0%)	0(0.0%)	0(0.0%)	--
		No	7(100.0%)	4(100.0%)	11(100.0%)	

DISCUSSION

Endoscopic third ventriculostomy (ETV) and choroid plexus cauterization (CPC) are two minimally invasive procedures commonly used to treat hydrocephalus in children.[12] ETV creates a new opening in between the third and fourth ventricles of the brain, allowing cerebrospinal fluid (CSF) to flow more easily.[8,9] CPC cauterizes the choroid plexus, which is the tissue responsible for producing CSF.[13] There is not enough evidence to say how well ETV+CPC compares to other treatments for hydrocephalus in our local population. However, studies from other parts of the world have shown that it is a promising treatment.[14,15,16] Based on the available evidence, it appears to be a safe procedure, but the success rate varies.

Our study is a prospective cohort that compared the outcomes of the combined application of the ETV and CPC procedures (ETV+CPC) to ETV alone in pediatric hydrocephalus. The study found that combined ETV plus CPC application was associated with a higher success rate and lower re-operation rate than ETV alone. In this study, a significantly higher success rate was achieved in the ETV combined with the CPC group when compared to the ETV alone group (p-value=<0.001). Furthermore, other factors of morbidity including reoperation and other complications were also higher in the ETV alone group.

These findings are congruous with the findings of other studies that have compared ETV+CPC to ETV alone in children with hydrocephalus. For example, in a meta-analysis comprising 11 studies, it was found that ETV+CPC had a success rate of 75.2%, in comparison to 62.2% for ETV alone. The re-operation rate was also lower with ETV+CPC (12.3%) than with ETV alone (20.6%).[17] Similarly, a study by Benjamin C Warf et al, demonstrated that in infants of age, one year or less combined application of ETV-CPC was more efficacious than ETV application alone.[16] In developing countries where it is dangerous to depend on shunts, combined ETV plus CPC application is quite possibly the best treatment choice for infants with hydrocephalus, notably for those with myelomeningocele and non-post infectious hydrocephalus.

A prospective study was also carried out to determine whether the result for the application of CPC plus ETV combined bilaterally was preferable to the ETV procedure done alone. The study included 710 children who went through ventriculoscopy and were considered potential candidates for ETV application as the primary treatment for hydrocephalus.[16] In a total of 550 children in whom ETV was applied: 266 were subjected to a combined ETV and CPC procedure and 284 went through ETV alone. Among infants of age 1 year or less, the cumulative success rate for combined ETV plus CPC application (66%) was found to be superior to that of ETV alone (47%). Also, the combined ETV plus CPC application was more efficacious in participants with myelomeningocele (76% compared with 35% success) and non-postinfectious hydrocephalus (NPIH) (70% compared with 38% success). These findings are in concordance with our study findings of ETV with CPC having more favorable outcomes as compared to ETV alone.

On the other hand, some studies have found no significant difference between outcomes in patients undergoing ETV alone as compared to patients undergoing ETV and CPC.[18] A meta-analysis done on assessing the efficacy of ETV alone compared to ETV with adjunct CPC found no difference between the functional outcomes of the two groups but did notice the CPC adjunct patients having significantly better outcomes in studies originating from Sub-Saharan Africa.[19] Reasons for this difference in outcome between patients from nations with different financial and healthcare resources were analyzed in a risk-adjusted study by Kulkarni et al,[14] which highlighted patient prognostic factors, technical variation in the procedure, and intra-operatively aborted cases as major factors that affected postoperative outcomes in children undergoing ETV for hydrocephalus.

These findings propose that the combination of ETV and CPC application may positively offer improved outcomes in certain patient populations, but more research is advocated to fully understand the benefits and potential risks of this approach. It's important to note that individual patient characteristics and circumstances can significantly influence treatment decisions and outcomes. The results of these studies put forward that combined ETV and CPC application is a more efficacious treatment option in children suffering from hydrocephalus than ETV alone. It is also associated with a higher success rate, lower re-operation rate, and a shorter hospital stay. However, it is important to note that the ETV plus CPC combined is a more complex procedure than the ETV being done alone, and it carries a slightly higher risk of complications. Therefore, it is crucial to weigh the risks and benefits of ETV+CPC carefully before recommending it to a patient.

The study found that combining ETV and CPC was particularly effective in infants under 1 year of age, especially for congenital hydrocephalus and myelomeningocele. The results indicated a potentially successful strategy to offset the imbalance between cerebrospinal fluid (CSF) production and absorption, ultimately benefiting participants, particularly in regions where shunt dependency is challenging. Other studies have also mirrored these findings with studies indicating ETV and CPC to be significantly superior as a treatment modality compared to ETV alone in infants less than 1 year old with hydrocephalus due to aqueductal stenosis.[20]

However, the study also acknowledged the need for further research, including longer follow-up, to establish the long-term advantages of neuroendoscopic treatments like ETV–CPC, particularly regarding neurocognitive outcomes and late failures. It emphasized that while ETV–CPC could be a promising primary treatment for hydrocephalus, especially in resource-limited settings, more extensive studies are essential to validate its efficacy and safety, especially in comparison to traditional shunt insertion procedures.

RECOMMENDATIONS

The study authors recommend that combined ETV and CPC application be given thought to as the first line treatment for hydrocephalus, especially in infants and children. They also recommend that further studies be undertaken to compare the extended outcomes of ETV with CPC in the long run, with those of ventriculoperitoneal shunt placement.

LIMITATIONS

The study had a relatively small sample size, including a total of 70 participants only. It was a single-center study, which limits the result's generalizability. The follow-up period was only 3 months, which was relatively short.

CONCLUSION

Combined application of CPC and ETV showed significantly better outcomes as compared to ETV alone in the treatment of hydrocephalus.

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AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Nadeem Akhtar & Amna Yamin	1. Study design and methodology
2.	Saqlain Ghazanfar & Muhammad Naeem	2. Paper writing
3.	Amna Yamin & Rida Muneer	3. Data collection and calculations
4.	Amna Yamin & Umar Afzal	4. Analysis of data and interpretation of results
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