Original Research Article

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Prospective Nerve Conduction Studies among Patients with Guillain-Barre Syndrome

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Abstract

There is considerable geographical variation worldwide in the prevalence rates of the subtypes of GBS.AIDP is the most common subtype in the Europe and North America constituting for 90% cases, while in Japan and china it is the AMAN Subtype. In India there is disparity among the studies regarding the prevalence of subtypes. Serial nerve conduction studies (NCS) were done on the day of admission and in between 3-8 weeks from the onset of illness. Electrophysiology was performed according to conventional standard methods by a qualified senior technician trained and experienced in electromyography using Medelec synergy (VIASYS Health Care, USA) machine. In all the sub types men outnumbered women. Mean (SD) MRC sum score at admission of AIDP, AMAN, AMSAN patients at admission are 32 (9), 31 (11), 31 (11) respectively. At discharge the mean (SD) MRC sumscore at discharge of the AIDP, AMAN, and AMSAN patients are 47 (10) 41 (12) 43 (11) respectively (p=0.001).

Keywords: GBS; AIDP; NCS.

Introduction

Guillain-Barre syndrome (GBS) is a disorder of peripheral nerves which is mediated by autoimmunity. It is characterised by acute flaccid areflexic paralysis, cranial nerve innervated muscle weakness, varying degree of sensory and autonomic disturbances. GBS is due to auto-immune mediated damage to the nerve roots and peripheral nerves characterised by increased CSF protein and no pleocytosis. The incidence rate of GBSvaries between 1.2 to 2.3 per 100000 persons per year [1-2]. GBS is common after first decade of age and peak age of incidence is 5 th decade. Slightly more common in males than in females Based on clinical and electrophysiological studies GBS has been classified in to Acute inflammatory demyelinating polyradiculopathy (AIDP), Acute motor axonal neuropathy (AMAN), Acute motor and sensory axonal neuropathy (AMSAN), Miller fisher syndrome (MFS), Acute pandysautonomia, and pure sensory variant [3].

There is considerable geographical variation worldwide in the prevalence rates of the subtypes of GBS. AIDP is the most common subtype in the Europe and North America constituting for 90% cases, while in Japan and china it is the AMAN Subtype [3-4]. In India there is disparity among the studies regarding the prevalence of subtypes. AIDP is the most common subtype in many studies [5-6] while AMAN in some studies [7]. Reason for this geographical difference in the prevalence of subtypes is poorly understood, differences in the environmental factors, hygiene and genetic factors of the host are the probable explanation with little evidence to support it. There is seasonal clustering of AIDP cases in winter and AMAN in summer [8].

Nerve conduction studies play a vital role in establishing the diagnosis and classification in to subtypes. Electro-diagnostic criteria were first proposed with an assumption that GBS constitutes only AIDP. There are several criteria for AIDP with varying sensitivity. The sensitivity of different electrophysiological criteria in the diagnosis of Indian patients with GBS varied from 39.2% to 88.2% [6]. All of these criteria are based on the

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electrophysiological features like conduction block, prolonged distal latencies and slowing of conduction velocities which are the hallmarks of acquired demyelination and remyelination. In 1990 Ho et al. first reported the entity of AMAN and proposed the electro-diagnostic criteria for the same on the assumption that it only causes axonal degeneration. Kuwabara et al.1998 reported reversible conduction failure in 3 patients of AMAN who were initially labelled as AIDP later turned out to be AMAN on repeat nerve conduction study [9]. Uncini et al described length-dependent conduction failure in 3 cases of AIDP which on serial nerve conduction studies turned out to be AMAN [10]. The above studies brought out the pitfalls in the electrodiagnostic criteria for GBS. These criteria when applied in the early stages overestimated the prevalence of the AIDP. These studies underscore the importance of serial nerve conductions in the classification of GBS in to subtypes. A study done by Kokubun N et al. from Japan in 54 GBS patients with serial nerve conduction studies showed following changes in the prevalence of subtypes of GBS. The changes were AIDP reduced to 26% from 35%, AMAN increased from 24% to 57%, equivocal reduced from 41% to 17% [11]. There is paucity of the data regarding the serial nerve conduction studies in the patients of GBS in India.

This is a prospective observational study with 2 sets of nerve conduction studies performed one at admission and other at 3-8 weeks after the onset of weakness to establish subtype of GBS accurately and to study the outcome at discharge objectively by using MRC sum score and Hughes functional disability score.

Methodology

Written informed consent was obtained from all patients or responsible relative if the patient is not able to give the consent for participating in the study. In all the patients the following data were recorded: demographic data; season in which patient developed disease; detailed history of present and preceding (if any) illness; physical as well as neurological examination details; laboratory characteristics including CSF analysis (if done); electrophysiological findings, any need for assisted mechanical ventilation, duration of mechanical ventilation; duration of hospital stay; any complications; treatment given and outcome. All the details were recorded in a structured proforma. Patient's disability at admission and at discharge was evaluated using Hughes functional grading scale. Muscle power was expressed using MRC Sumscore.

Serial nerve conduction studies(NCS) were done on the day of admission and in between 3-8 weeks from the onset of illness. Electrophysiology was performed according to conventional standard methods by a qualified senior technician trained and experienced in electromyography using Medelec synergy (VIASYS Health Care, USA) machine. NCS were done on at least 4 motor (median, ulnar, common peroneal, and posterior tibial nerves) and 3 sensory (median, ulnar and sural nerves) nerves. The CMAPs were evoked from the median nerve (stimulating at wrist and elbow, and recording at the abductor pollicisbrevis muscle), ulnar nerve (stimulating at wrist and below elbow, and recording at the abductor digitiminimi muscle), common peroneal nerve (stimulating at ankle and fibular neck and recording at the extensor digitorumbrevis muscle) and tibial nerve (stimulating at ankle and popliteal fossa and recording at the abductor hallucis muscle). Shortest F response latencies were measured after 20 stimuli. Partial motor conduction block was calculated using the difference in amplitudes between stimulation sites. Parameters which were noted are: DML, motor and sensory conduction velocities, CMAP amplitude, F latencies, temporal dispersion, conduction blocks, and SNAP amplitude. The skin temperature was maintained over 32°C. The value of each variable was then compared with the upper or lower normal limits as set by our laboratory.

First and second nerve conduction studies are subjected to following electrophysiological criteria to classify into subtypes and compare the results of the both.

The patients were classified into demyelinating or axonal variants based on the Ho and Hadden criteria for AIDP and AMAN which are the most widely used criteria.Conduction block is defined as ratio of proximal to distal CMAP less than 0.5. Temporal dispersion was defined as the prolongation of the proximal CAMP duration more than 30% of distal CMAP duration. AMSAN were classified based on the Rees et al criteria. Classified inexcitable if d-CMAP absent in all nerves (or present in only one nerve with d-CMAP <10% LLN) and equivocal if does not exactly fit criteria for any other group and those of normal in early stage of the disease.

Follow up

On follow up, all the patients were for the clinically

examined and the power in the limbs is assessed using MRC sumscore. Outcome is measured using the Hughes functional disability score. Second NCS was done after 3–8 weeks following the onset of illness and electrophysiological criteria are applied and final electro-diagnosis of the patient was obtained and compared with the first one.

Results

The median Hughes GBS functional grading score at admission and at the time of discharge were 4 (IQR 2-5) and 3(2-4), respectively. Mean (± SD) MRC sum scores of patients at admission and at discharge were 32 ±11 and 43 ±12.

Nerve Conduction Studies and Electrophysiological Patterns

NCS were performed in all patients on the day of admission within the first week in 12, within 2 weeks in 43 and in 6 patients NCS were done within 3 weeks. Two (3.2%) patients had a normal nerve electrophysiology (conducted at 4 and 5 days, respectively, after onset of illness) at the time of admission.

Electrophysiological parameters of the NCS

Median, ulnar common peroneal and posterior tibial NCS were carried out in 122 nerves each. Median NCS was unrecordable in 6.6% ulnar in 13.2% peroneal in 16.4% posterior tibial in 19.6% of nerves. Distal latency was prolonged in the median nerve in 55%, in the ulnar nerve in 59%, in the common peroneal nerve in 51% and posterior tibial nerve in 41%. Conduction velocity was slowed in the median in 37%, in the ulnar in 37.7%, in the common peroneal in 44.3%, and in posterior tibial in 47.5% nerves. CMAP amplitude was reduced in the median in 52.5%, in the ulnar in 44.3%, in the common peroneal in 65.6% and in posterior tibial nerve in 51.9% of nerves. Mean±SD distal latencies, motor conduction velocities, distal compound motor action potentials of median, ulnar, common peroneal and posterior tibial nerves of the study population.

Conduction Blocks

Thirteen (16.3%) patients demonstrated conduction blocks out of 61 patients. In these thirteen patients 20 nerves showed conduction block. Right ulnar nerve was the most common nerve in which conduction block was seen in 6 patients (4.9%), followed by left ulnar nerve in 3 patients.

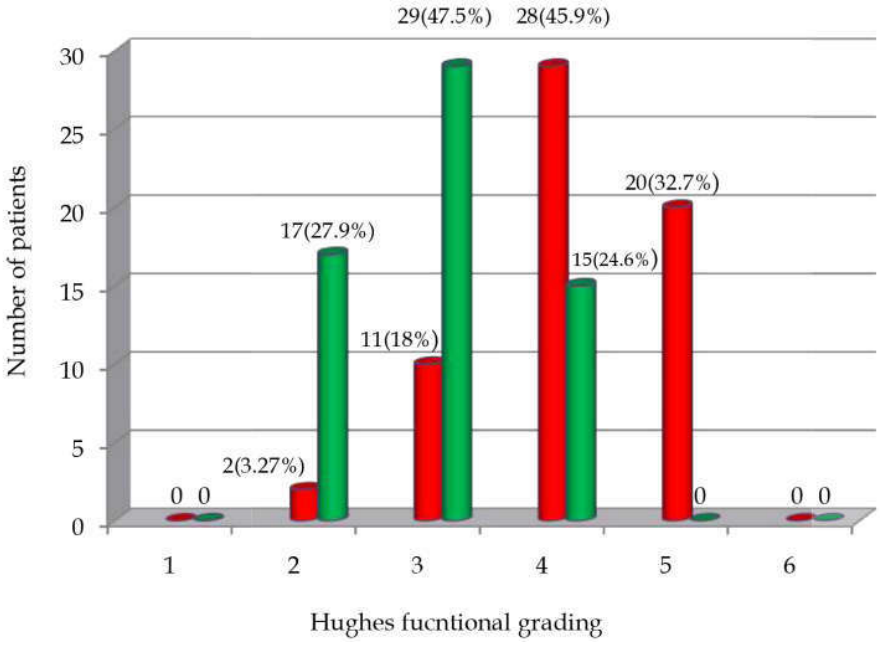

Fig. 1: Hughes functional grading at admission (red), at discharge (green)

Table 1: Nerve study statistics

Nerve (n=122)	DL (ms)	CV(m/s)	CMAPamp (MV)	F-Waves
Median				
Unrecordable	2(3.3%)	2(3.3%)	2(3.3%)	26(42.6%)
Normal	25(41%)	37(60%)	27(44.2%)	24(39.3%)
Abnormal	34(55%)	22(37%)	32(52.5%)	11(18.1%)
Mean(SD)	5.34(3.64)	45.8(11.9)	4.30(3.32)	-
Ulnar				
Unrecordable	4(6.6%)	4(6.6%)	4(6.6%)	25(41%)
Normal	21(34.4%)	37(60%)	27(44.2%)	24(39%)
Abnormal	36(59%)	22(37%)	32(52.5%)	12(18%)
Mean(SD)	3.13(1.85)	45.2(15.5)	5.40(7.4)	-
Common peroneal				
Unrecordable	5(8.2%)	5(8.2%)	5(8.2%)	50(81%)
Normal	25(41%)	29(47.5%)	16(26.2%)	7(11.4%)
Abnormal	31(50.8%)	27(44.3%)	40(65.6%)	4(6.6%)
Mean(SD)	5.40(2.76)	34.8(13.2)	1.52(1.43)	-
Posterior tibial				
Unrecordable	6(9.8%)	6(9.8%)	6(9.8%)	49(80%)
Normal	30(49.2%)	26(42.7%)	19(31.3%)	9(13.4%)
Abnormal	25(41%)	29(47.5%)	36(51.9%)	3(6.6%)
Mean(SD)	5.24(3.08)	34.5(13.7)	1.52(1.43)	-

DL (ms)=distal latency (milliseconds)
CMAP = Compound Muscle Action Potential amp(milivolts)
CV(m/s)= Conduction velocity (meters/sec)
SD=standard deviation

Table 2: Nerves showing conduction block in study population

Nerve	Number of Patients
RUN	3
RMN	1
LMN	1
LCP	1
RCP	1
RPTB	1
LPTB	1
RUN+LUN	1
RMN+LMN+RUN+LUN	1
RUN+RPTB	1
LUN+RCP+LPTB	1

RUN=Right ulnar nerve
LUN=left ulnar nerve
RCP=Right common peroneal nerve
LCP= left common peroneal nerve
RPTB=right posterior tibialnerve
LPTB= left posterior tibial nerve
RMN= Right median nerve
LMN=left median nerve

Temporal Dispersion

Thirteen patients (21.3%) out of 61 showed temporal dispersion. The right common peroneal showed temporal dispersion in 5 followed by right ulnar in 4 patients.

Normal Sural SNAPs are seen in 38 (62.3%) patients. Absent sural SNAPs are seen in 11 (18%) patients. Among the 25 AIDP patients normal sural SNAPs with decreased median and ulnar SNAPs are seen 7 (28%) patients.

Electrophysiological subtypes of GBS after first NCS

The first set of nerve conductions studies fulfilled diagnostic criteria of AIDP in twenty five (40.9%), AMAN in sixteen (26.2%) patients, AMSAN in sixteen (26.2%) patients, unclassified in two (3.3%) patients. In

Table 3: Nerves showing temporal dispersion in the study population

Nerve	Number of Patients
RUN	3
RCP	2
RPTB	2
LCP	1
RCP+LCP	1
LCP+RPTB	1
LCP+LPTB	1
LUN+RCP+LPTB	1
RMN+RUN+RCP+RPTB	1

RUN=Right ulnar nerve LUN=left ulnar nerve
RCP=Right common peroneal nerve
LCP= left common peroneal nerve
RPTB=right posterior tibial nerve
LPTB= left posterior tibial nerve
RMN= Right median nerve
LMN=left median nerve

Table 4: Sensory nerve conduction profile of the study population

Parameter	Mean ± S.D
Median sensory conductions	
DSL	2.12±1.19
SCV	37.97± 21.46
SNAP	11.94
Ulnar sensory conductions	
DSL	1.72±1.04
SCV	36.46±21.54
SNAP	8.22±8.69
Sural sensory conductions	
DSL	2.33± 1.19
SCV	39.22±19.17
SNAP	9.37±7.49

SCV=Sensory conduction velocity (m/s)
DSL= Distal Sensory latency (milliseconds)
SNAP = Sensory nerve action potential (microvolts)

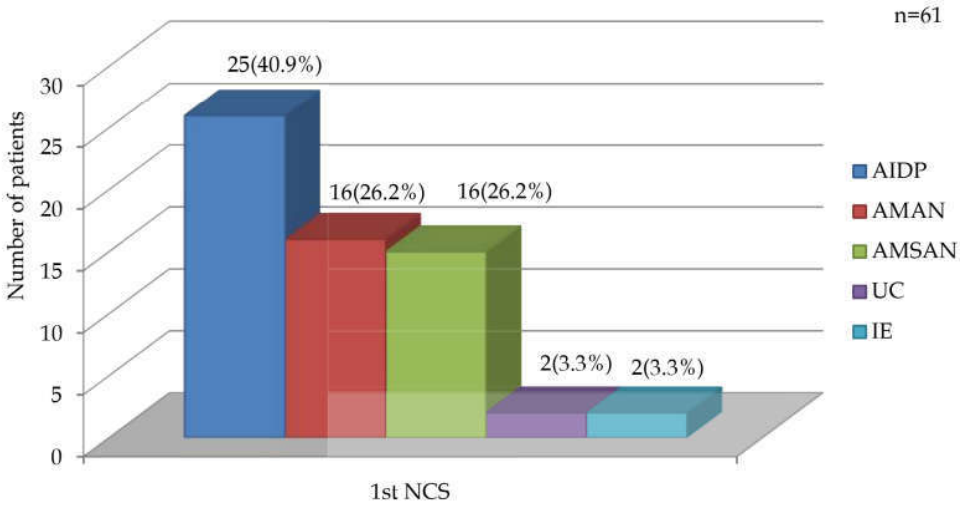

Fig. 2: Electrophysiological subtypes of study population after 1st nerve conduction study

NCS: Nerve conduction study AIDP: Acute inflammatory demyelinating polyneuropathy AMAN: Acute motor axonal neuropathy AMSAN: Acute motor and sensory axonal neuropathy UC: unclassified IE: Inexcitable

two (3.3%) patients the nerves are in-excitable.

Comparison of Clinical Parameters, Treatment and Outcome of Subtypes of GBS Patients

In all the sub types men outnumbered women. Mean (SD) MRC sumscore at admission of AIDP, AMAN, AMSAN patients at admission are 32 (9), 31 (11), 31 (11) respectively. At discharge the mean (SD) MRC sumscore at discharge of the AIDP, AMAN, and AMSAN patients are 47(10) 41(12) 43(11) respectively.(p=0.001).

Electrophysiological subtypes after 2nd NCS

The second nerve conduction study performed 3-8 weeks after the onset of illness, 2nd NCS satisfied the electro-diagnostic criteria for AIDP in 21 (34.4%)patients, AMAN in 19 (31.5%) patients, AMSAN in 18 (29.5%) patients, Unclassified in 1 (1.6%) patient and inexcitable in 2 (3.2%) patients, respectively.

Discussion

The interval between the onset of illness and to the electrophysiological studies at admission was 1 week in 12 (19.2%), 2 weeks in 43 (70.4%) and three weeks in 6 (10%) patients respectively.

NCS were performed in all patients on the day of admission within the first week in 12 (19.6%), within 2 weeks in 43 (70.4%) and in 6 (10%) patients NCS were done within 3weeks.

On the first nerve conduction study AIDP (40.9 %) was the most common subtype followed by AMAN (26.9%), AMSAN (26.9%), unclassified (3.27%) and inexcitable (3.27%).

Table 5: Comparison of clinical parameters of individual subtypes of GBS in the study population

Parameter	AIDP (n= 25)	AMAN (n=16)	AMSAN (n=16)	P value
Age (mean±SD)	38.20±16.50	34.56±12.91	39.94±10.22	0.387
Sex (male, female)	12,13	10, 6	14,2	0.674
Time to nadir (days) (mean±SD)	7.08±1.8	6.56±1.71	6.31±1.44	0.749
Hospital stay (days) (mean±SD)	19.48±8.6	18±12.62	17.31±8.23	
Ophthalmoplegia	2(8%)	0	0	0.265
Bilateral facial palsy	19(76%)	7(43%)	11(68%)	0.029
Bulbar weakness	12(48%)	3(18%)	7(43%)	0.477
Autonomic disturbance	8(32%)	2(16.5%)	6(37.5%)	0.486
Respiratory failure	10(40%)	2(16.5%)	6(37.5%)	0.151
Immunotherapy	21(84%)	11(68.7%)	14(87.5%)	0.001
MRCS1 (mean±SD)	32 ± 9	31±11	32±11	0.007
MRCS2 (mean±SD)	47 ± 10	41±12	43±11	0.001
HFG1 median(IQR)	4(3-5)	4(2-5)	4(2-5)	
HFG2 median(IQR)	3(2-4)	3(2-4)	3(2-4)	

MRCS1=Medical research council sumscore = at admission
MRCS 2=Medical research council sumscore at discharge
HFG1=Hughes functional grading at admission
HFG2=Hughes functional grading at discharge

Table 6: Shows Comparison of incidence of subtypes among the recently published studies

Parameter	Vengamma[2] (2011)	Alexander[4] (2011)	kalita[3] present study (2014)	(2016)
Place of study	Tirupathi	Vellore	Lucknow	Tirupathi
No. of subjects	59	115	328	61
AIDP	76.2%	38.2%	73.8%	40.9%
AMAN	3.4%	30.4%	13.4%	26.2%
AMSAN	12%	13.6%	4.6%	26.2%
UC	3.4%	17.4%	8.2%	3.3%

Our results are comparable with Alexander et al. [7] probable reason for this may be close proximity of these two centres and common geographical and environmental factors. Difference in the incidence among the different regions of the same country may be due to differences in the environmental factors, state of hygiene as the pathogenesis is to be correlated with the antecedent infection. Genetic factors of the people in this region may also be related to the difference.

In the present study thirteen (21.3%) patients demonstrated conduction blocks out of 61 patients. Total of 20 (16.3%) nerves in out of 122 nerves examined showed conduction block. Kalita et al. [3] reported in 24.5% of the cases while Alexander et al. [4] 14.1% which is similar to the present study.

In the present study thirteen (21.3%) patients demonstrated out of 61 patients. Total of 21 (17.2%) nerves in out of 122 nerves examined showed conduction block. Gordon et al. [12] reported in 58% of 31 patients of GBS. The disparity may be due to high incidence of the AIDP subtype in the Gordon study when compared to the present study.

Following the repeat nerve conduction study the patients satisfying the electrodiagnostic criteria of AIDP decreased from 40.9 to 34.4%. yet it was the most common sub type, those of AMAN increased from 26.2% to 31.2% and that of AMSAN increased from 26.2% to 29.50%. One of two unclassified changed to AMSAN and 2 of the inexcitable remained the same.

The neurophysiology changes of changed group of patients following the repeat conduction include rapid recovery of distal motor latencies and improved conduction velocities. Disappearance of conduction blocks due to length dependent conduction failure due to axonal degeneration.In contrast, patients with AIDP showed persistent demyelinating and remyelinationfeatures even after the repeat nerve conduction.

Conduction block refers to the condition in which saltatory conduction is stopped but the axon remains intact. In electrophysiological studies it is defined by anabnormal amplitude/area CMAP reduction on proximal stimulationas compared with CMAP on distal stimulation. Conduction blockis usually considered to be the electrophysiological correlate ofsegmental acquired demyelination. But the same electrophysiological finding can be seen in other conditions like reversibleconduction failure and length-dependent conduction failure in axonal pathology. Hence those with length dependent conduction failure and slowing of conductions across the axonal degeneration was satisfying the criteria of AIDP in the 1st NCS and reclassified in to AMAN following the 2nd NCS. In Kukubun study the changes from AIDP to the AMAN are attributed to the reversible conduction failure and length dependent conduction failure. In our study we found only length dependent conduction failure but not reversible conduction failure.

In our study the respiratory failure ($p = 0.015$) was significantly higher in theaxonal subtype patients who were reclassified after 2nd NCS (subtype 2) when compared to the previously axonal subtype (subtype 1). The median Hughes functional grading of the subtype 1 at admission and at discharge of the subtype one are 4 (range of 2-5) and 3 (range 2-4) respectively. In subtype 2 Hughes functional grading was 5 in four out of five patients and 3 in the other one at admission and at discharge it improved to 4 in four of the five and 2 in the other. There was no statistically significant difference ($p=0.98$ admission and $p=0.99$ discharge) in the MRC sumscore at admission and at discharge between the two groups.

Conclusion

In the early disease stage and basedon only one NCS, no electro-diagnostical distinction between demyelinating conduction block and these mimics cannot be made. This study highlights the need for serial nerve conduction studies to demonstrate serial electrophysiological changes that determine pathophysiological origin of abnormal CMAP amplitude reduction in GBS subtypes which leads to accurate electro -diagnosis of the GBS patients in to subtypes. It also highlights the need for revision of existing electro-diagnostic criteria to include the reversible conduction failure and length dependent conduction failure in axonal subtypes with serial nerve conductions.

- AIDP (40.9%) was the most common subtype followed by AMAN (26.9%), AMSAN (26.9%), unclassified (3.27%) and inexcitable (3.27%) on the first nerve conduction study performed at admission.
- Conduction blocks were seen in 16.3% of the nerves examined and temporal dispersion in 17.2% of the nerves.
- Normal Sural nerve conductions with impaired median and ulnar sensory conductions are seen in 7 (28%) AIDP patients.
- On repeat nerve conduction studies after 3-8 weeks after the onset of illness AIDP was still the most common subtype (34.4%) followed by AMAN

(31.5%), AMSAN (29.5%) inexcitable (3.2%) and unclassified (1.6%).

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