



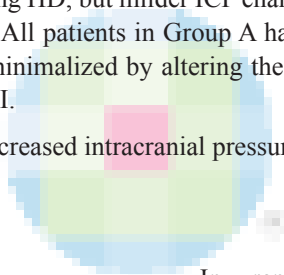
Preventing Intracranial Pressure Fluctuation in Severe Traumatic Brain Injury During Hemodialysis

Shih-Hao Yeh^{1,4}, Chen-Yu Wang², Chien-Min Lin^{1,3}

Departments of ¹Neurosurgery and ²Neurology, Taipei Medical University, Shuang Ho Hospital, ³School of Medicine, College of Medicine, Taipei Medical University, Taipei, ⁴Department of Surgery, Taoyuan Armed Forces General Hospital, Taoyuan, Taiwan, Republic of China

Background: Past studies have observed rises in intracranial pressure (ICP) during hemodialysis (HD) in the neurosurgical patient. This phenomenon may cause secondary brain injury and further compromise the patients' recovery. While continuous renal replacement modalities can theoretically be more beneficial for the brain-injured patient, this option is often not available due to limited resources. Modified prescriptions of intermittent HD may be the more easily accessible method. The purpose of this study is to clarify whether a less aggressive HD regimen in patients with severe traumatic brain injury (TBI) will prevent ICP fluctuation during HD. **Patients and Methods:** We present a single center experience with the enrollment of nine uremic patients with severe TBI who underwent decompressive surgery with ICP monitoring via external ventricular drain (EVD) between January 2003 and December 2006. These patients were divided into two groups based on different HD methods. In Group A, four patients received standard intermittent HD every other day, and in Group B, five patients received a modified, daily dialysis procedure that cut the amount of fluid removed per session and the dialysate flow rate by half. **Results:** All patients in both groups experienced an increased ICP during HD, but milder ICP changes were found in all five patients ($P < 0.05$) who had received the modified procedure (Group B). All patients in Group A had expired, but there were only two mortalities in Group B. **Conclusion:** ICP fluctuation may be minimized by altering the HD protocol. A less aggressive HD procedure is recommended for uremic patients with severe TBI.

Key words: Dialysis disequilibrium syndrome, increased intracranial pressure, severe traumatic brain injury, uremia



INTRODUCTION

As the prevalence of acute and chronic renal failure rises, it is increasingly common for clinicians to encounter patients with traumatic brain injury (TBI) who require hemodialysis (HD). In the head injured patient, secondary brain injury may be detrimental and one of the causes is cerebral ischemia resulting from inadequate cerebral blood flow (CBF). CBF can be estimated by cerebral perfusion pressure (CPP), which is related to intracranial pressure (ICP) and mean arterial pressure. Hence, either elevated ICP and/or shock may lead to poor CPP and worsened prognosis. Recent evidence has identified ICP > 20 mm Hg as a cut point between patients with potentially good or poor outcomes.^{1,2}

In uremic patients with TBI, who requires HD, this necessary procedure aimed to clear waste, correct fluid, and electrolyte imbalance may be a trigger for further brain injury. In a preliminary study performed on uremic dogs and uremic human, patients had concluded that HD could raise the ICP in dogs and the intraocular pressure in humans, respectively (intraocular pressure changes are known to be closely correlated to changes in ICP³). This phenomenon was further demonstrated in neurosurgical patients: significant ICP fluctuation was observed during HD in uremic patients who had received brain surgery with ICP monitoring;⁴ furthermore, another study found that this fluctuation not only resulted

Received: March 07, 2016; Revised: May 25, 2016;
Accepted: July 11, 2016

Corresponding Author: Dr. Chien-Min Lin, Department of Neurosurgery, Taipei Medical University, Shuang Ho Hospital, No. 291, Chung-Jan Road, Chung-Ho City, Taipei, Taiwan, Republic of China. Tel: 886-2-2490088 Ext. 8120; Fax: 886-2-29347054. E-mail: m513092004@tmu.edu.tw

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Yeh SH, Wang CY, Lin CM. Preventing intracranial pressure fluctuation in severe traumatic brain injury during hemodialysis. J Med Sci 2016;36:152-7.

in observable neurological deterioration but it also seemed to be correlated to the amount of fluid removed and the frequency of the HD.⁵ A different study has also postulated that exacerbation of brain injury during HD may be due to excessive ultrafiltration leading to reduced cerebral perfusion.⁶ Hence, attempts to limit further brain injury that dialysis may potentially impose by tailoring standard HD protocols to accommodate the traumatic-brain-injured patient is very important in facilitating recovery.

Strategies to prevent exacerbation of brain injury include reducing fluctuations in ICP and hemodynamic changes during HD. Ideally, continuous modalities of renal replacement therapy (RRT) such as continuous venous-venous hemodialysis (CVVH) are a better choice for patients with brain injury due to gradual solute and fluid removal, which will result in less risk of hypotension and cerebral edema, as well as milder changes in ICP.⁷ However, in clinical practice, due to limitations in the available equipment and resources, altering the prescription of intermittent HD may be the more feasible and easily accessible option in many clinical settings. Dialysis dosing for intermittent modalities is the function of dose per session and the frequency of treatment. In this study, we will investigate whether a less aggressive regimen, which includes reduction of dialysate flow and reduced fluid removal per HD session will have an impact of ICP fluctuation during and after the dialysis compared to the conventional HD protocol.

PATIENTS AND METHODS

Inclusion criteria

Patients with severe TBI who were admitted to Taipei Medical University, Wan Fang Medical Center during a 48-month period between January 2003 and December 2006 were considered for enrollment. Severity of head injury was categorized as mild, moderate, or severe based on the Glasgow Coma Scale (GCS, mild: GCS ≥ 13 , moderate: GCS 9–12 or severe: GCS ≤ 8). Out of these patients, we included uremic patients undergoing HD due to either acute or chronic renal failure who sustained a severe head injury (admitting GCS scores ≤ 8), for which they received decompressive brain surgery by either craniectomy and craniotomy or external ventricular drainage placement alone. We monitored the hourly ICP level via the accurate placement of EVD in all the cases.

Patient management and dialysis protocol

Patients were randomly assigned to two groups after their cranial surgery and consultation with a nephrologist: Group A received standard dialysis procedure every other day with a 4 h session until the amount of fluid removed was 5% of the body

weight (Model number: TORAY TR-321 EX). The blood flow was set at 200 mL/min. Group B received daily 4 h-session dialysis, with the flow rate controlled at 100 mL/min; the total amount of dialyzed fluid was controlled at 2.5% of body weight. In both groups, no heparin was used for the fear of rebleeding. Blood pressure maintenance was achieved during HD via infusion of inotropic agents. Dialysate solution A and B (HD concentrate NO.11, Ca 3.0 and Hemodialysis solution 300GB, Taiwan Biotech Co. Ltd., Taiwan) were used in this both protocols. Of the nine patients fulfilling the inclusion criteria, four patients were assigned to Group A and another four to Group B. One patient received continuous venous-venous hemodialysis (CVVH) for 24 h. We decided to include this patient in our study to determine if modified HD could produce similar results to that of CVVH. The CVVH was done by the GAMBRO PRISMA CRRT system and solution A and solution B (Taiwan Biotech Co. Ltd., Taiwan) were applied with 120 mL/min flow rate. The total amount of dialyzed fluid was 5% of the patient's body weight.

Intracranial pressure measurement

The primary endpoint of this study was ICP; the measurements taken via EVD at 1 h before dialysis at the beginning of dialysis and then every hour for the successive seven measurement hours.

Statistical analysis

Univariate analysis was performed for assessing if a statistically significant difference exists between the ICP levels of both groups; the one-tailed *t*-test was employed. Values for continuous parameters are presented as a mean $\pm$ standard deviation. Multivariate logistic regression analysis was performed using a backward conditional approach and variables with a statistically significant univariate association. Statistical significance was based on a $P < 0.05$.

RESULTS

Nine patients met our inclusion criteria and were enrolled in this study [Table 1]. The mean age was 44.78 ± 22.96 . The male to female ratio was 6:3. The patients all had a GCS level of equal or < 8 with the mean GCS score upon admission of 6.33 ± 1.41 . Of the nine patients, five (55.56%) had received HD because of end-stage renal disease (ESRD) and the other four (44.44%) due to acute renal failure. Three had subdural hemorrhage (SDH), three had concurrent intracerebral hemorrhage (ICH) and intraventricular hemorrhage (IVH), one had subarachnoid hemorrhage (SAH), one patient had concurrent SDH and epidural hemorrhage, and another one had SAH and SDH. They were randomly assigned to either

Preventing ICP fluctuation, TBI, HD

Table 1: Characteristics of nine uremic patients with severe brain injury

Case number	Age	Body weight (kg)	Sex	Diagnosis	Surgical procedure	Duration of previous dialysis (years)	Dialysis type	Renal failure	GCS on admission (E, M, V)	Outcome
A										
1	56	67	Male	SDH	Craniectomy	10	HD	Chronic	7 (2, 4, 1)	Death
2	67	60	Male	SDH	Craniectomy	6	HD	Chronic	6 (1, 4, 1)	Death
3	6	26	Male	SDH; EDH	Craniectomy	-	HD	Acute	3 (1, 1, 1)	Death
4	56	38	Female	ICH; IVH	EVD	7	HD	Chronic	6 (1, 4, 1)	Death
B										
5	24	53	Male	SAH; SDH	Craniectomy	-	CVVH	Acute	8 (1, 5, 2)	Alive
6	46	72	Male	ICH; IVH	EVD	4	Modified HD	Chronic	7 (1, 4, 2)	Alive
7	53	66	Male	SDH	Craniectomy	-	Modified HD	Acute	8 (1, 5, 2)	Death
8	43	48	Female	ICH; IVH	Craniectomy	2	Modified HD	Chronic	6 (1, 4, 1)	Alive
9	52	55	Female	SAH	Craniectomy	-	Modified HD	Acute	6 (1, 4, 1)	Death
Mean±SD	44.78±22.96	53.89±13.95				3.22±3.52			6.33±1.41	

SDH = Subdural hemorrhage; EDH = Epidural hemorrhage; ICH = Intracranial hemorrhage; IVH = Intraventricular hemorrhage; SAH = Subarachnoid hemorrhage; EVD = External ventricular drain; HD = Hemodialysis; SD = Standard deviation; GCS = Glasgow Coma Scale

Group A, which followed a conventional HD or Group B, which received a modified HD procedure. There was no significant difference in the initial ICP between the two groups ($P = 0.39$).

As seen in Table 2, in the patients of Group A, ICP had begun to rise during the 1st h following HD and reached a peak level at the 2nd h of HD. Mean ICP rose from 16.5 ± 2.4 mmHg before HD up to 36.5 ± 9.8 mmHg at the 2nd h of HD ($P = 0.012$). ICP returned to the original value after 4 h after the dialysis [Figure 1]. All the patients of Group A had expired within 3 days after surgery due to central failure. In the patients of Group B, ICP also began to rise during the 1st h following HD and peaked at the 2nd h of HD. Mean ICP from 16.0 ± 2.2 mmHg before HD up to 24.0 ± 1.6 mmHg at the 2nd h of HD ($P = 0.00015$). ICP in all patients were slightly elevated to around 20 mmHg [Figure 2]. There were two mortalities in Group B, in both cases, the cause of death was also a central failure. Whereas the initial ICPs were not statistically different between Group A and Group B, we saw a higher mean ICP value in Group A, 36.5 ± 9.8 mmHg compared to Group B, 24.0 ± 1.6 mmHg ($P = 0.028$). The mean ICP values of both groups are shown in Figure 3. In the single patient who underwent CVVH, the ICP remained relatively stable [Figure 4]. However, due to having only one data set in this group, further interpretation is of limited value.

DISCUSSION

Rises in ICP during HD had been previously observed in uremic animals and humans.¹ This phenomenon poses an important risk for patients with head injury and brain

Table 2: Mean intracranial pressure before and 2 h after hemodialysis

Group	Mean ICP before HD (mmHg)	Mean ICP 2 h after HD (mmHg)	P
A	16.5 ± 2.4	36.5 ± 9.8	0.012
B	16.0 ± 2.2	24.0 ± 1.6	0.00015

ICP = Intracranial pressure; HD = Hemodialysis

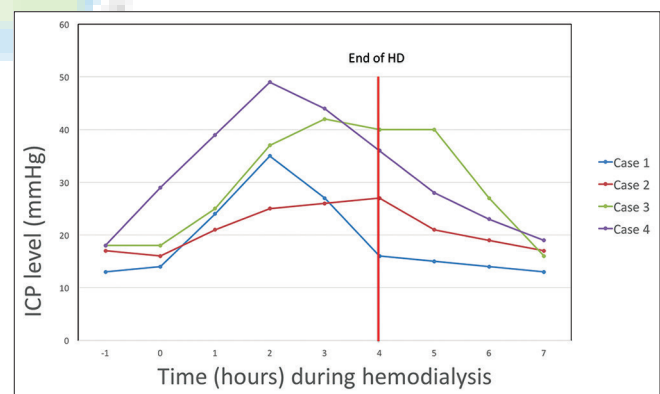


Figure 1: Intracranial pressure changes in Group A during hemodialysis

hemorrhage because IICP leads to higher mortality and worse outcome. In this study, we examined whether prescribing a less aggressive HD could prevent excessive ICP rise during the procedure.

In our study, the patients of both Group A and Group B experienced a rise in their ICP following HD and peaked at the 2nd h; however, whereas Group A's mean ICP went from 16.5 ± 2.4 mmHg before HD to 36.5 ± 9.8 mmHg and Group B's mean ICP increased from 16.0 ± 2.2 mmHg to

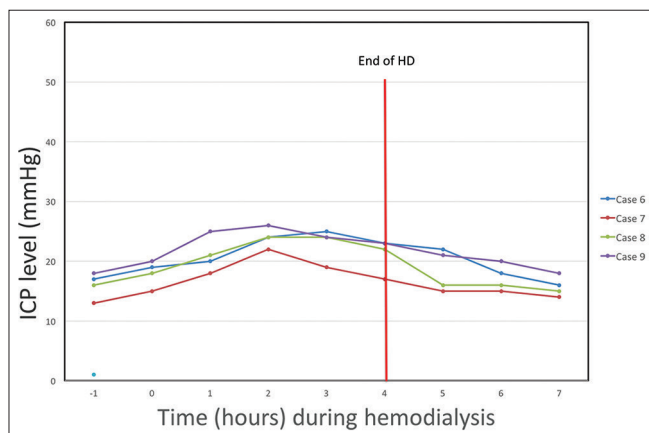


Figure 2: Intracranial pressure changes in Group B during hemodialysis

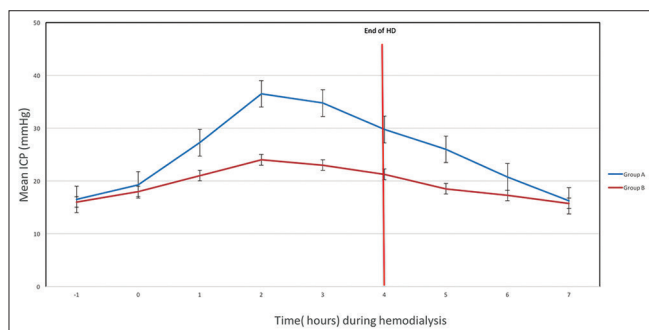


Figure 3: Mean intracranial pressure changes in Groups A and B patients

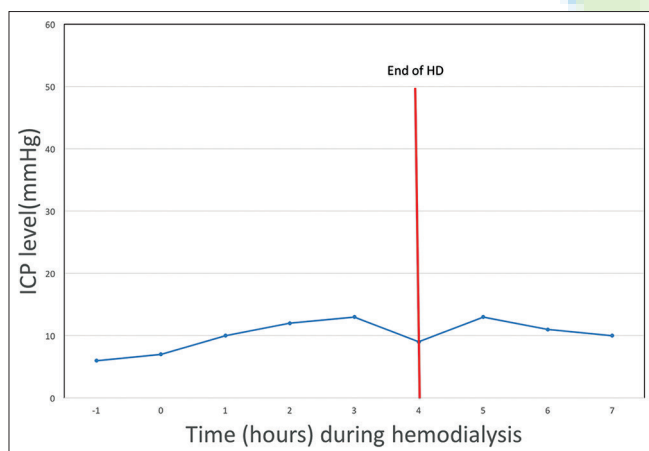


Figure 4: Intracranial pressure changes in patient who received CVVH

24.0 ± 1.6 mmHg at the 2nd h of HD. It is notable that both groups had higher ICPs compared to the patient who had received CVVH. Of course, there is only one patient who underwent CVVH, therefore making further interpretation and analysis from this single data set difficult. However, since keeping ICP level at <20 mmHg is the general goal in TBI patients, it is likely that the rise ICP levels during HD

in the other two groups contributed to the patients' outcomes. A larger sample size and perhaps extensive workup including CT scanning for patients who deteriorate after the HD to rule out other confounding factors contributing to post-TBI mortality such as delayed bleeding, hydrocephalus, or other metabolic abnormalities would provide stronger evidence regarding the relationship between this rise in ICP during HD and outcome.

The limitations of this study include small sample size due to the difficulty in enrolling uremic patients with severe TBI. Although we tried to include patients who were determined to be cases of severe TBI (which was defined by their initial GCS upon admission), there was still heterogeneity among the enrolled patients with regards to hemorrhage type, hemorrhage location, and extent of the brain injury. Their indication for HD was also different, with some patients requiring HD due to ESRD while others due to acute renal failure; this is important because these patients therefore have different preexisting comorbidities with those already receiving HD due to ESRD before the traumatic event possibly having poor compliance of cerebrovascular structures after long-term HD. Another limitation is that we only recorded data for ICP before, during, and after the patient's first HD session postoperatively. Perhaps we will see a different outcome during subsequent HD sessions as the patients' clinical conditions progresses. Finally, assuming that a gentler HD is indeed beneficial in these TBI patients, there is the question of whether these alterations can provide adequate HD (such as adequate urea toxin removal) as the number of subsequent HD session increase, and if it will affect that patient's long-term mortality and morbidity. In other words, other than preventing ICP fluctuation, we do not know whether the changes in these parameters will yield the best patient outcome. While we focused on the flow rate and the amount of fluid removed, there are other ways of potentially limiting the harmful effects of HD in SDH and ICH patients, including using minimally bio-incompatible small surface area dialyzers with lower blood flows, shorter dialysis sessions, in combination with higher sodium and cooled dialysate.⁸

When discussing ICP changes during HD, many existing papers further relate to the topic of dialysis disequilibrium syndrome (DDS). DDS is a clinical phenomenon of acute neurological symptoms that varies in severity, which includes symptoms of headache, nausea, disorientation, restlessness, blurred vision, and asterixis. In general, symptoms of DDS are self-limited. Some patients, however, may progress to confusion, seizures, coma, and even death. It is thought to be attributable to cerebral edema that occurs due to a reversed osmotic shift induced by urea removal.^{9,10} Several predisposing factors have

been described to be associated with DDS, including the first HD, severe uremia, age, preexisting neurological disorders, and metabolic acidosis.¹¹ While the evidence of ICP changes in cases with DDS had been lacking, there are now a few case reports and case studies have directly observed ICP changes in patients with DDS.^{5,12-14} Despite that the relationship between IICP and DDS and its mechanism require further elucidation, these studies show us that ICP monitoring during HD may help guide management and that measurements to prevent DDS, especially in high risk, neurosurgical patients, may also aid in preventing ICP fluctuation and thus warrant our consideration. In the prevention of DDS during HD, a slow and gentle start of HD (slow removal of urea) and/or adding an osmotically active agent such as increasing dialysate sodium levels or administering mannitol or glycerol may help.¹⁵ Some authors also suggest that CVVH or sustained low-efficiency dialysis (SLED) may also be used to prevent DDS.^{12,13} Although we did not statistically analyze whether regular HD or modified HD was inferior to CVVH in terms of ICP stability due to only having one participating patient in the CVVH group, we hypothesize that as an RRT modality, CVVH would be even more suited in the TBI patient than our modified HD due to smaller changes in plasma osmolality and cardiovascular stability offered by convective transport rather than diffusion. Future studies should enroll more patients with CVVH to clarify this.

Similarly, SLED, in which conventional HD machines are used to provide extended duration RRT (8–12 h), has emerged as an alternative to CRRT in terms of providing the same hemodynamic stability as CRRT while demanding fewer resources. However, in a cross-over study comparing the effects of hemodynamic parameters and ICP between SLED and CVVH in ten dialysis patients with brain hemorrhage, the authors found that regardless of which modality, there was an increased ICP 3 h after dialysis and there was no evidence to show an advantage of CVVH over SLED in regarding to stability of ICP.¹⁶ These results were similar to ours in terms of observing an increase in ICP after dialysis, but we further demonstrated that the HD prescription could potentially affect the magnitude of the ICP fluctuation. Larger prospective studies are required to further compare these modalities to intermittent HD or to modified HD.

CONCLUSION

In uremic patients with TBI, HD may potentially lead to poor ICP control and worsen prognosis; the risk of DDS is also increased due to their neurological lesions. In this report, we suggest that physicians should tailor the prescription of the HD in accordance to the needs of these patients, aiming for

gentler and slower HD session to prevent poor ICP control and possibly DDS.

Financial support and sponsorship

Nil.

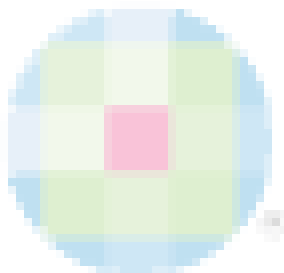
Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Bullock R, Chesnut RM, Clifton G, Ghajar J, Marion DW, Narayan RK, *et al.* Guidelines for the management of severe head injury. Brain Trauma Foundation. Eur J Emerg Med 1996;3:109-27.
2. Czosnyka M, Balestreri M, Steiner L, Smielewski P, Hutchinson PJ, Matta B, *et al.* Age, intracranial pressure, autoregulation, and outcome after brain trauma. J Neurosurg 2005;102:450-4.
3. Sitprija V, Holmes JH. Preliminary observations on the change in intracranial pressure and intraocular pressure during hemodialysis. Trans Am Soc Artif Intern Organs 1962;8:300-8.
4. Bertrand YM, Hermant A, Mahieu P, Roels J. Intracranial pressure changes in patients with head trauma during haemodialysis. Intensive Care Med 1983;9:321-3.
5. Lin CM, Lin JW, Tsai JT, Ko CP, Hung KS, Hung CC, *et al.* Intracranial pressure fluctuation during hemodialysis in renal failure patients with intracranial hemorrhage. Acta Neurochir Suppl 2008;101:141-4.
6. Davenport A, Will EJ, Losowsky MS. Rebound surges of intracranial pressure as a consequence of forced ultrafiltration used to control intracranial pressure in patients with severe hepatorenal failure. Am J Kidney Dis 1989;14:516-9.
7. O'Reilly P, Tolwani A. Renal replacement therapy III: IHD, CRRT, SLED. Crit Care Clin 2005;21:367-78.
8. Davenport A. Changing the hemodialysis prescription for hemodialysis patients with subdural and intracranial hemorrhage. Hemodial Int 2013;17 Suppl 1:S22-7.
9. Silver SM, DeSimone JA Jr., Smith DA, Sterns RH. Dialysis disequilibrium syndrome (DDS) in the rat: Role of the "reverse urea effect". Kidney Int 1992;42:161-6.
10. Silver SM, Sterns RH, Halperin ML. Brain swelling after dialysis: Old urea or new osmoles? Am J Kidney Dis 1996;28:1-13.
11. Arieff AI. Dialysis disequilibrium syndrome: Current concepts on pathogenesis and prevention. Kidney Int 1994;45:629-35.
12. Esnault P, Lacroix G, Cungi PJ, D'Aranda E, Cotte J, Goutorbe P. Dialysis disequilibrium syndrome in

- neurointensive care unit: The benefit of intracranial pressure monitoring. *Crit Care* 2012;16:472.
13. Yang K, Chang C, Hsieh C. Dialysis disequilibrium syndrome: The changes of intracranial pressure. *SM J Case Rep* 2015;1:1006.
 14. Yoshida S, Tajika T, Yamasaki N, Tanikawa T, Kitamura K, Kubo K, *et al.* Dialysis dysequilibrium syndrome in neurosurgical patients. *Neurosurgery* 1987;20:716-21.
 15. Zepeda-Orozco D, Quigley R. Dialysis disequilibrium syndrome. *Pediatr Nephrol* (Berlin, Germany) 2012;27:2205-11.
 16. Wu VC, Huang TM, Shiao CC, Lai CF, Tsai PR, Wang WJ, *et al.* The hemodynamic effects during sustained low-efficiency dialysis versus continuous veno-venous hemofiltration for uremic patients with brain hemorrhage: A crossover study. *J Neurosurg* 2013;119:1288-95.



Author Help: Online submission of the manuscripts

Articles can be submitted online from <http://www.journalonweb.com>. For online submission, the articles should be prepared in two files (first page file and article file). Images should be submitted separately.

1) **First Page File:**

Prepare the title page, covering letter, acknowledgement etc. using a word processor program. All information related to your identity should be included here. Use text/rtf/doc/pdf files. Do not zip the files.

2) **Article File:**

The main text of the article, beginning with the Abstract to References (including tables) should be in this file. Do not include any information (such as acknowledgement, your names in page headers etc.) in this file. Use text/rtf/doc/pdf files. Do not zip the files. Limit the file size to 1 MB. Do not incorporate images in the file. If file size is large, graphs can be submitted separately as images, without their being incorporated in the article file. This will reduce the size of the file.

3) **Images:**

Submit good quality color images. Each image should be less than 4096 kb (4 MB) in size. The size of the image can be reduced by decreasing the actual height and width of the images (keep up to about 6 inches and up to about 1800 x 1200 pixels). JPEG is the most suitable file format. The image quality should be good enough to judge the scientific value of the image. For the purpose of printing, always retain a good quality, high resolution image. This high resolution image should be sent to the editorial office at the time of sending a revised article.

4) **Legends:**

Legends for the figures/images should be included at the end of the article file.