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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Stroke Newsletter" which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

1. **Evaluation of association between lesion location and swallowing function characteristics in post stroke dysphagia patients**
2. **Clinical and radiological outcomes in patients commenced on early or late anticoagulation after ischaemic stroke or transient ischaemic attack**
3. **Investigation of the association between anticoagulation with Factor Xa inhibitors in the early phase after acute ischemic stroke or transient ischemic attack (TIA) with a lower risk of major bleeding events and Vitamin-K antagonists**
4. **Case report on low volume subdural hematoma and ipsilateral ischemic stroke presenting as capsular warning syndrome**

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Looking forward to your valuable feedback
Best Regards,
Medical Team, Micro Labs Ltd

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Evaluation of association between lesion location and swallowing function characteristics in post stroke dysphagia patients

Introduction

Post-stroke dysphagia (PSD) is a condition of impairment in swallowing, which is affecting 55% to 78% of patients who have had stroke.[1] Swallowing is a process which involves coordinating many muscle groups to transfer a bolus of food or liquid from the mouth to the stomach while protecting the airway and minimizing residue.[2] Researchers have found that lesion sites of patients who had stroke were associated with impaired swallowing function. Compared to the left cerebral hemisphere, the right cerebral hemisphere has a more targeted impact on swallowing function. Right hemisphere (RH) lesions were associated with pharyngeal phase impairment, while left hemisphere (LH) lesions were associated with oral phase dysfunction. Lesion sites associated with the clinical features of dysphagia was a direct method to verify their correlation with swallowing function. This makes it necessary to investigate the relationship between certain lesion sites and PSD characteristics.[1] The primary objective was to detect the difference of VFSS measurements between PSD with supratentorial lesion and those with infratentorial lesion while the secondary objective was to investigate differences of PSD with supratentorial left and right hemispheres lesions with infratentorial brainstem lesions.

Methods

This was a retrospective study that included 133 patients with stroke. Dysphagia was diagnosed using video-fluoroscopic swallowing study (VFSS). All patients were categorized into a brainstem stroke group and a supratentorial group (which included the LH and RH subgroups, which were further separated into cortical and subcortical subgroups) based on the site of the lesion. In order to investigate how various bolus volumes were affected by the lesion site, the VFSS values of 3 and 5 millilitres in each subgroup were compared. The upper esophageal

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sphincter opening (UESO), hyoid bone superior horizontal displacement, hyoid bone anterior horizontal displacement, pharyngeal transit duration (PTD), stage of transition duration, oral transit time, soft palate elevation duration, hyoid bone movement duration (HMD), UES opening duration, and laryngeal closure duration (LCD) were among the measures of VFSS. The Penetration Aspiration Scale (PAS) and the Functional Oral Intake Scale (FOIS) were used to evaluate general swallowing function.

Results

Out of 133 patients, 58 patients were included for final analysis. Out of which, 22 were diagnosed with supratentorial stroke lesions in the LH (10 cortical strokes, 12 subcortical strokes), 24 were diagnosed with lesions in the RH (12 cortical strokes, 12 subcortical strokes), and 12 were diagnosed with brainstem stroke. Significant differences were seen in the HMD ($p = 0.019$), PTD ($p = 0.048$), and LCD ($p = 0.013$) between the supratentorial and infratentorial (brainstem) groups in the 5 ml of diluted and thickened barium liquid data for the duration time. Between the L. cortical and the brainstem lesion group, significant difference in HMD ($p = 0.045$) was seen. There were notable differences between the L. subcortical and brainstem groups in the HMD ($p = 0.037$) and LCD ($p = 0.032$). Study found no group difference when taking the 3ml volume bolus. The upper oesophageal sphincter opening (UESO) for motion in the R. subcortical lesion site differed significantly between the 3 ml and 5 ml diluted barium liquid groups (Figure 1). A moderate association was found between PTD and the PAS scores in the 5 ml diluted barium liquid data ($r = 0.38$, $p = 0.0044$). Weak relationships were observed between the PAS scores and the HMD and LCD ($r = 0.32$, $p = 0.018$ and $r = 0.29$, $p = 0.039$, respectively). There were no observed relationships between the functional Oral Intake Scale (FOIS) scores and the VFSS characteristics.

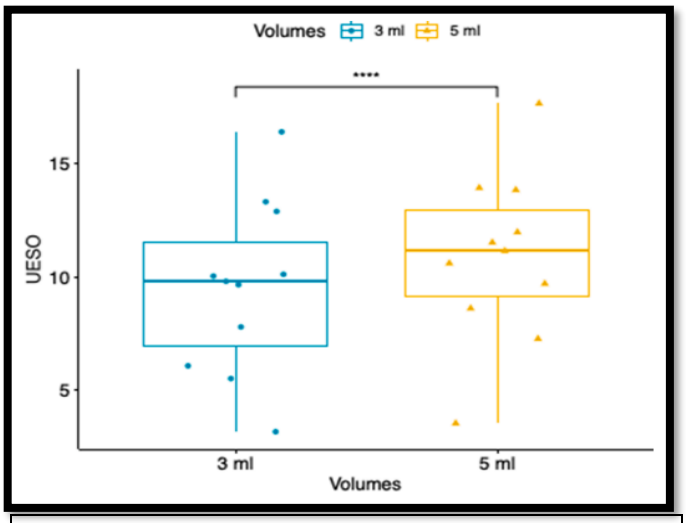

Figure 1. Effect of bolus volume on UESO between 3 and 5ml

Discussion

This study finding showed that there was no significant difference between the groups with a left cortical/subcortical lesion and a right cortical/subcortical lesion, suggesting that the effects

of LH and RH stroke on the oral and pharyngeal phases could be equivalent. When compared to the brainstem, the LH of the supratentorial parts—both the left cortical and left subcortical—was less impaired during the pharyngeal phase. Furthermore, only the RH subcortical lesion showed the impact of bolus volume, but not in the left and right cortical and the left subcortical and brainstem lesion groups. Therefore, the author speculated that, like RH, LH was involved in both the oral and pharyngeal phases. During the pharyngeal phase, the RH was predominant site. Furthermore, findings supported the hypothesis that impairments to the brainstem, bilateral cortex, and subcortical areas might impact sensory input and ultimately lead to swallowing problems.[1] Robbins et al. found that there were significant variations in the swallowing patterns of the LH and RH groups. Reduced coordination of the lingual musculature has been associated to oral dysfunction, and the RH group showed more severe pharyngeal stage dysfunction.[3]

Conclusion

This study highlighted the significant differences between supratentorial and infratentorial lesions, underscoring the critical role that lesion location plays in influencing swallowing function in PSD patients. Additionally, it suggested the effects of strokes to the left and right hemispheres (LH and RH) on the oral and pharyngeal phases were relatively similar, with the RH having a stronger effect on the latter.

The post-stroke dysphagia with brainstem lesion shows more sever dysfunction in the pharyngeal phases.

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Clinical and radiological outcomes in patients commenced on early or late anticoagulation after ischaemic stroke or transient ischaemic attack

Introduction

Initiating anticoagulants <4 days after stroke or transient ischaemic attack was associated with fewer ischaemic lesions.

Oral anticoagulation in patients with atrial fibrillation (AF) have a significantly lower risk of ischemic stroke and systemic embolism. Nevertheless, even while using oral anticoagulants, people with AF can experience an ischemic stroke.[1] The ideal period to start using anticoagulants following an acute ischemic stroke was not known. The incidence of stroke recurrence within 14 days was 2 times higher in individuals with ischemic stroke associated with AF and can reach 1.3% daily in these patients. Early anticoagulant initiation may increase hemorrhagic transformation, whereas delayed initiation may increase the risk of recurrent stroke. The aim of ATTUNE study (ATrial fibrillation in sTroke-Utility of Neuroimaging Evaluation) was to assess the frequency of silent ischemic lesions and haemorrhages on MRI at one month for patients who started anticoagulation early (<4 days, or 96 hours) vs late (≥ 4 days).

Methods

This was a multicenter, prospective observational cohort study which included patients with new or pre-existing diagnosis of non-valvular AF and clinical diagnosis of ischaemic stroke or TIA. Patients were divided into two groups, early (<4 days after symptom onset) and late commencement (≥4 days after symptom onset). Primary outcome included number of patients who started anticoagulation either late (≥4 days) or early (<4 days) and who had radiological evidence of recurrent ischemic lesions on MRI one month following an ischemic stroke or TIA. Secondary outcome included intracerebral haemorrhages on the 1-month follow-up MRI; and the relationship between the volume of the initial ischemic lesion, new ischemic lesions, and new haemorrhages on the follow-up MRI.

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Results

A total of 208 patients were analysed, of which 107 patients who received anticoagulation <4 days (early anticoagulation) and 101 who received anticoagulation ≥4 days (late anticoagulation) after the index event. Higher median initial ischaemic lesion volume was found in the late anticoagulation group, when compared with early group (11 mL vs 3.5 mL) respectively. Compared to the early group, patients in the late group had a decreased probability of being on therapeutic anticoagulation before admission (9% vs. 22%, respectively, p=0.02). On follow-up MRI, a total of 27 patients (13%) developed new ischemic lesions. Compared to 18/101 (17%) patients in the late group, 9 out of 107 (8%) patients in the early group experienced a new ischemic lesion (p=0.04). Upon excluding TIA patients, 8/100 (8%) patients in the early group and 17/96 (18%) patients in the late group experienced a new ischemic lesion (p=0.04). On follow-up MRI, a total of 55 patients (or 26%) experienced new haemorrhages. In the early group, 23 patients out of 107 (22%) experienced a fresh hemorrhage. In the late group, 32 patients out of 101 (32%) experienced a new hemorrhage. The patients were divided into four groups based on commencement of anticoagulation within a day, between 2 and 3 days, between 4 and 6 days, and 7 days or later. New ischemic lesions were predicted by increasing treatment delays (Figure 1).

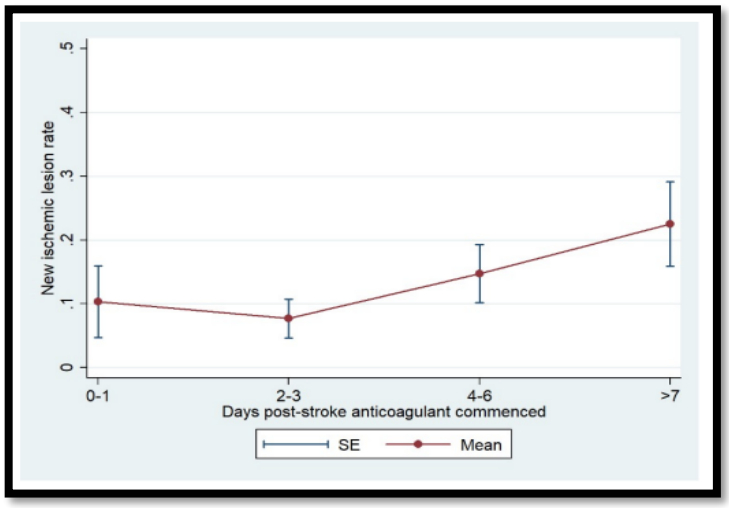

Figure 1. Time points showing commencement of anticoagulation and new ischaemic lesion rate

Discussion

Within this study group of patients with mild-to-moderate stroke severity, AF patients who started anticoagulation later than those who started it earlier saw a twofold increase in new radiological ischemic lesions after an ischemic episode (17% vs. 8%, p=0.04). When compared to late anticoagulation, early anticoagulation did not increase the number of new hemorrhages with ischemic lesion volumes of >5mL. In fact, the early initiation group observed lower haemorrhages and had smaller ischemic lesion volume (≤5 mL). This ATTUNE study was the first to demonstrate the association between commencing anticoagulation <4 days after an ischaemic event and fewer silent ischaemic lesions at 1 month.[2] The recently published TIMING study showed that early initiation (≤4 days) of anticoagulant medication was non-

inferior to later commencement (5–10days) for the primary composite endpoint of recurrent ischemic stroke, symptomatic ICH, and all-cause mortality at 90 days.[3]

Conclusion

In patients with AF, initiating anticoagulation <4 days following a stroke or TIA has been associated to fewer ischemic lesions at 1 month. These results indicated that early anticoagulation following mild-to-moderate acute ischemic stroke associated with AF may be tolerable, but more randomized controlled studies were needed to inform clinical practice.

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Investigation of the association between anticoagulation with Factor Xa inhibitors in the early phase after acute ischemic stroke or transient ischemic attack (TIA) with a lower risk of major bleeding events and Vitamin-K antagonists

Introduction

Oral anticoagulants (OACs), which include vitamin K antagonists (VKAs) and direct oral anticoagulants (DOACs) are widely used among people with atrial fibrillation, venous

Factor Xa inhibitors appear to be similarly effective in terms of bleeding events and ischemic endpoints compared to vitamin K antagonists.

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thrombosis, mechanical valve replacement, and autoimmune disorders such as antiphospholipid syndrome or vasculitis.[1] Patients with atrial fibrillation (AF) who have suffered an ischemic stroke or transient ischemic attack (TIA) were at greater risk of recurrent stroke. Consequently, oral anticoagulation should be started as early as possible. The PRODAST (Prospective Record of the Use of Dabigatran in Patients with Acute Stroke or TIA) study examined when oral anticoagulation should be started in relation to intracerebral hemorrhage and recurrent ischemic stroke in real-world setting.[2] This study aimed to investigate anticoagulation with factor Xa inhibitors (FXa), that was, apixaban, edoxaban, or rivaroxaban, with VKAs in AF patients with recent (within 1 week) TIA or ischemic stroke.

Methods

This was a multi-centre, non-interventional study which included 10,039 patients after recent (⩽7days) acute ischemic stroke or TIA with non-valvular AF. Patients were treated with FXa-inhibitor or a VKA, or other anti-thrombotic therapies, and followed until hospital discharge. The primary outcome was major bleeding episodes throughout the hospital stay. Secondary endpoints include recurrent strokes, recurrent ischemic strokes, TIA, systemic/pulmonary embolism, myocardial infarction, and death. In addition, study evaluated composite endpoint of stroke, systemic embolism, life-threatening bleeding, and death.

Results

The comparison of VKAs and FXa-inhibitors in terms of treatment outcomes was based on data collected from 6,924 patients during an average of 9 days in the hospital. Prior to or following their first ischemic stroke or transient ischemic attack, 5,874 individuals were treated with FXa inhibitors, while 1,050 patients received treatment with VKAs. During 33,297 treatment days with FXa-inhibitors, 49 major bleeding complications were observed (rate: 14.7 cases per 10,000 treatment days), and during 7,714 treatment days with VKAs, 16 cases were observed. (rate: 20.7 events per 10,000 treatment days). Recurrent stroke rates for patients treated with VKAs were 22.0 per 10,000 treatment days, whereas rates for patients treated with FXa-inhibitors were 18.9 per 10,000 therapy days. The combined endpoint was

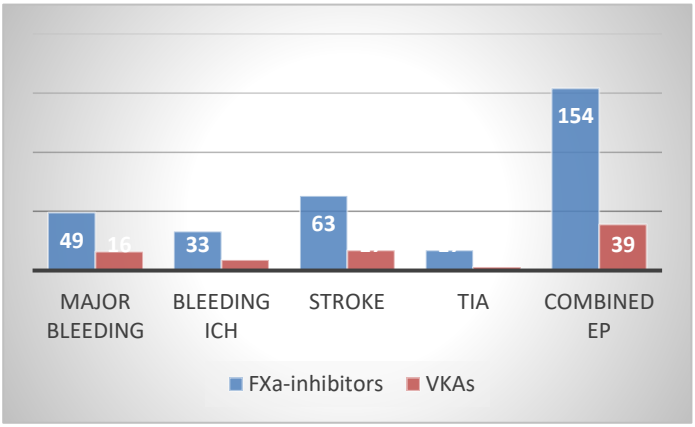

Figure 1. Representation of number and rate of endpoints observed in patients treated with FXa-inhibitors or VKAs.

observed in 46.3 per 10,000 treatment days for FXa-inhibitors and 50.6 per 10,000 treatment days in patients receiving VKAs (Figure 1). When Cox-regression event rates were directly compared to medication exposure modelling across time, it was shown that FXa-inhibitors had reduced hemorrhagic event risks for major bleeding (adjusted HR: 0.70). Treatment with FXa-inhibitors increased the risk of myocardial infarction more than therapy with VKAs (adjusted HR 2.52)

Discussion

Patients with AF with TIA or ischemic stroke had a very low overall risk of significant bleeding problems and ischemic events, including recurrent ischemic strokes. There were no discernible differences between starting oral anticoagulation with VKAs or FXa inhibitors in terms of ischemic endpoints. With a 46% decrease in risk, there was a tendency favouring FXa inhibitors in terms of major bleeding problems. In conclusion, this large registry study based on routine clinical practice indicated that FXa inhibitors seem to be as tolerable and effective as VKAs when it comes to bleeding episodes during the early stages of stroke recovery.[2] This results were similar to timing study, in which 888 patients who had suffered an ischemic stroke were randomly assigned to start anticoagulation with non-vitamin K dependent oral anticoagulants (NOACs) within 4 days compared to starting at 5–10 days. The results showed a significant tendency in favour of starting anticoagulation early.[3]

Conclusion

This extensive real-world investigation demonstrated that, in the early post-stroke phase of hospitalization, FXa inhibitors and VKAs appear to be similarly effective in terms of bleeding events and ischemic endpoints.

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Case report on low volume subdural hematoma and ipsilateral ischemic stroke presenting as capsular warning syndrome

Introduction

Capsular warning syndrome is characterized by recurrent transient ischemic attacks that typically present with motor or sensory symptoms following the first TIA episode.

Stroke is one of the leading cause of mortality and disability globally. About 101.5 million strokes occurred worldwide in 2019, with 77.2 million of those cases being acute ischemic strokes (AIS).[1] Simultaneous occurrence of both Subdural hematoma and ischemic stroke conditions in a single patient, although rare, poses a significant clinical complexity. A thorough neurological examination and neuroimaging techniques, such as magnetic resonance imaging (MRI) or computed tomography (CT), were necessary for the diagnosis of subdural hematomas in order to identify their size, location, and chronicity. Ischemic stroke arises from the occlusion of cerebral arteries which requires rapid and accurate diagnosis. Capsular warning syndrome (CWS) is a distinctive feature characterized by recurrent transient ischemic attacks (TIAs) that was accompanied by motor or sensory symptoms, indicating a substantial risk of imminent stroke, frequently in the first few days after the first TIA episode. This case report described the diagnostic and treatment complexities associated with these neurological condition.

Case presentation

A 83 years old male patient with the history of atrial fibrillation was undergoing apixaban anticoagulation therapy. Patient had a pre-existing condition of alcohol abuse and chronic folic acid deficiency. Patient has dyspnea and was diagnosed with suspected pulmonary embolism. However, computed tomography (CT) angiography of the thorax showed pulmonary embolism as the cause of the patient's dyspnea. After the patient experienced sudden left-sided hemiparesis, a non-contrast cranial CT scan was conducted, which indicated a low-volume

subdural hematoma localized to the right parietal hemisphere. Twist-drill craniostomy surgery was performed and a subdural drain was inserted parietally in the right hemisphere due to the size of the subdural hematoma and its neurological symptoms. Following monitoring, patient developed dysarthria and exacerbated left-sided hemiparesis. Subsequent CT scan revealed a decrease in the size of the subdural hematoma. An ischemic stroke co-existed with the hyperacute phase of the right corona radiata in the right anterior choroidal artery supply region, as demonstrated by a brain MRI scan. Diffusion-weighted imaging (DWI) revealed increased brightness and reduced apparent diffusion coefficient (ADC) values (Figure 1). Thorough examination of the nervous system showed that the distal M1 section of the left middle cerebral artery had mild stenosis. However, no antithrombotic therapy was started because of the recent operation and the absence of a significant intracranial artery blockage.

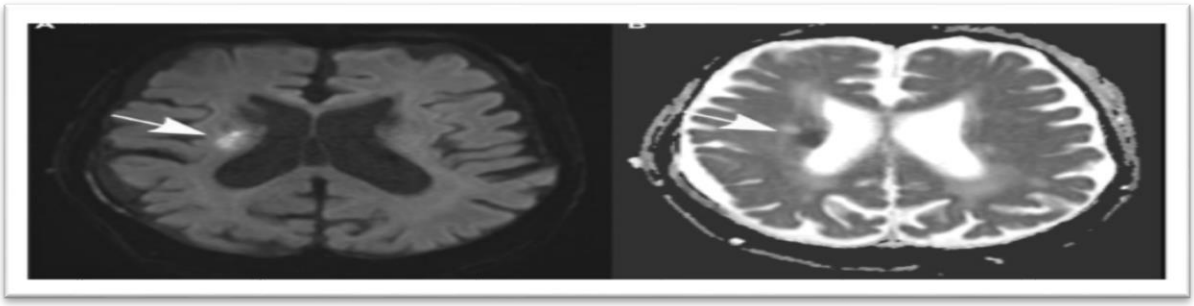

Figure 1. MRI images (A) showing an elevation in signal (B) decrease in right corona radiata

Discussion

This case emphasized how difficult to diagnose and treat ischemic stroke with small volume subdural hematoma concurrently, particularly if the stroke develops in the corona radiata and causes the variable symptoms described as capsular warning syndrome.[2] Around 71% of patients with CWS eventually develop permanent infarction while there was a lack of articles published about its prognosis, management and treatment outcomes. Research has shown that mean duration of repeated TIA episodes in CWS varies from 6 to 24 minutes and the internal capsule continued to be the most commonly implicated area of established infarct on MRI in 50%–70% of cases.[3]

Conclusion

This case report exhibited the challenges involved in treating individuals who have an ischemic stroke with a low-volume subdural hematoma. Also, it illustrated the difficult clinical issues involved in treating a patient on anticoagulant treatment with a small subdural hematoma and ipsilateral ischemic stroke.

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