TOURO COLLEGE & UNIVERSITY SYSTEM

The Science Journal of the Lander College of Arts and Sciences

Volume 5
Number 1 *Fall 2011*

2011

Is Thrombolytic Therapy Safe When Used to Treat Elderly Patients?

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Abstract

Recently, research has been conducted to determine if thrombolytic therapy works to dissolve clots and if it is a safe treatment option. The specific purpose of this study is to determine if thrombolytic therapy is safe for use in the elderly. This study was conducted by reviewing the relevant literature that has been published from the time that research began to test the usefulness of thrombolytic therapy. Numerous journals were examined to ensure impartiality and emerge with an unbiased conclusion. The journals were discovered using PubMed article finder, using Google as a search engine, and by scrutinizing relevant references found within articles citing previous studies. It was discovered during the course of the study that thrombolytic therapy has been proven to be a useful treatment. The main danger of the therapy comes not from the drug itself but from the possibility of causing an intracranial hemorrhage due to reperfusion to the ischemic tissue. Thrombolytic therapy should not be withheld from the elderly based solely upon age; rather, each patient's full history should be considered, and the decision should be based on the patient's blood pressure, glucose level, age, and history of recent surgery or trauma. The issue of microbleeds has been examined, and there is no conclusive evidence to suggest that they cause or do not cause intracranial hemorrhage in patients treated with thrombolytic agents.

Discussion

There are two types of strokes: embolic and hemorrhagic. Hemorrhagic strokes are caused by ruptured blood vessels in the brain. Embolic strokes are caused by a blood clot that forms in the brain and prevents blood from reaching the neurons or from a blood clot that forms in the extremities and subsequently travels to the brain with the same deleterious effect. The axiom doctors refer to when treating embolus strokes is, "Time lost is brain lost." The longer the brain fails to receive fresh, oxygenated blood the more damage there is likely to be. In a typical middle cerebral artery ischemic stroke, two million nerve cells are lost each minute reperfusion has not been achieved (Saver et al. 2010). One of the newest, most innovative, and controversial treatments for both strokes and heart attacks is thrombolytic therapy. This therapy involves using drugs that break down clots to restore blood flow. These drugs have been proven to be effective in treating both strokes and heart attacks. However, there is an inherent risk in using thrombolytic therapy. Drugs commonly used for clot lysis are not specific to brain clots; they break apart all clots formed anywhere around the body. The irony of thrombolytic therapy is that, while attempting to curtail damage caused by a stroke, it may end up causing an intracranial hemorrhage.

In general, any therapeutic approach must conform to the sequence of events of a stroke: after interruption of the blood supply, while some tissue probably suffers irreparable damage within minutes, a variable amount remains deactivated but in a viable state for several hours. Restoration of the blood supply, therefore, may save the ischemic tissue and improve the patient's overall outcome. Although research suggests that the blocked artery will open by itself sometime between twenty-four hours and a week, information on this is scanty at best; many factors including composition, age, and location (e.g. middle cerebral vs. superior cerebellar) contribute to overall recovery. There is clear evidence, however, that spontaneous lysis of a thrombus does occur. Current research is aimed at studying if the spontaneous process can be accelerated in time to restore the useful brain function without unacceptable risk (Wardlaw and Warlow 1992).

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Research on thrombolytic therapy has increased in response to strokes being the third most common cause of death in the developed world. In addition, strokes leave many people disabled and dependent on family and social or health services. Stroke has defied the considerable efforts of medical science to find an effective treatment (Wardlaw and Warlow 1992). Considerable interest in the use of thrombolytics also stems from the fact that they have been proven to work in patients suffering acute myocardial infarctions. The general thought is that if thrombolytic agents have been proven useful in heart attacks, they should also be a viable alternative to stroke treatment (Hommel et al. 1996).

To fully appreciate the benefits and risks of thrombolytic therapy, it is necessary to first understand the biochemistry and molecular biology of thrombolytic drugs. The assumed

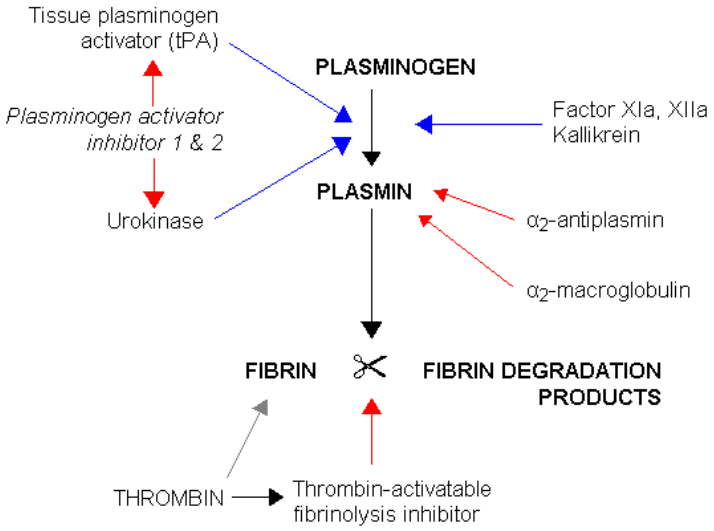

Figure 1: Schematic representation of the fibrinolytic system
Source: Kunamneni et al. 2007

culprit of strokes is fibrinogen; the goal of the clot-busting drug is to dissolve the fibrin clot, a process known as fibrinolysis. Plasminogen is an inactive proteolytic enzyme, which upon activation becomes plasmin. Plasmin is able to hydrolyze many types of coagulation proteins, most notably fibrinogen. Plasminogen is activated by plasminogen activators released from endothelial cells, normally. Plasminogen activators include streptokinase (SK), urokinase (UK), and tissue plasminogen activator (TPA). In the case of an acute heart attack or stroke, these activators can be given to the patient. In cellular biology, where one finds activators, one also finds inhibitors. All the different plasminogen activators are inhibited by plasminogen activator inhibitor-1 (PAI-1). Plasmin, which breaks down fibrin to fibrin degradation product (FDP), is inhibited by numerous inhibitors including alpha-2-antiplasmin (Figure 1) (Kunamneni et al. 2007).

A thorough understanding of the biochemical mechanisms of thrombolytic drugs is important in understanding how they work. If the activators are being used as a cure for heart attacks and strokes, then perhaps, in the event of an intracranial hemorrhage, use can be made

of the inhibitors to prevent fibrinogen breakdown and induce clotting. Perhaps these inhibitors can even be used to assist in treating hemophiliacs[1].

If clot-busting drugs carry such a high risk of intracranial hemorrhage, why would doctors use these drugs as opposed to another safer method? The answer is that no other medications seem to work. Antiplatelet agents such as aspirin and anticoagulant agents such as heparin reduce platelet aggregation and thrombin formation; however, they have no effect on fibrinogen and blood viscosity. In fact, in two different studies, aspirin and heparin were given to patients having acute strokes, and they both showed very little effect. Thrombolytic agents, on the other hand, fill all three functions in one therapy: they lower the viscosity of the blood by fibrinogen reduction, potentially allowing blood flow back into the blocked region of the brain; they act as anticoagulants, and they may act as antiplatelet agents (Lowe 1998).

Antiplatelet agents, anticoagulant agents, and thrombolytic agents pose nearly the same risk of interfering with hemostatic plug formation (the forming of a clot to maintain hemostasis). It can be inferred that the risks of intracranial hemorrhage are not necessarily reduced using alternative drugs. Indeed, based on trial evidence, alternative drugs do lower the chances of recovery. Aspirin was tested as a preventive drug against strokes, and it was noted during the 4.6-year long trial that, not only did aspirin not prevent stroke (in men with a mean age of 57), it also increased the risk of intracranial hemorrhage. Although some studies found aspirin to be helpful to middle aged women predispositioned to certain types of stroke, women who took it in excess (> 15 tablets/week) had a higher rate of hemorrhage (Cornett et al. 2008. In a later study, patients treated with thrombolytic therapy also received both a platelet aggregation inhibitor (aspirin) and an anticoagulant (heparin), and neither the heparin nor the aspirin were associated with intracranial hemorrhage. It can be suggested that the seeming disassociation between aspirin, heparin, and intracranial hemorrhage was because the aspirin and heparin were given several hours after the thrombolytics were administered. In fact, if signs of intracranial hemorrhage became apparent, the heparin and aspirin would not have been given (Simoons and Maggioni 1993).

This information would seem to suggest that there is a connection between fibrinogen levels, blood viscosity, and instance of stroke. A study proving the connection appears in the New England Journal of Medicine as early as 1984. The study shows that fibrinogen is as important a predictor of stroke as high blood pressure; consequently, patients with both high blood pressure and high fibrinogen levels have the highest risk of stroke (reviewed in Lowe 1998). Another study, appearing in 1996, shows that fibrinogen levels predict atrial fibrillation and congestive heart failure, which are both risk factors for strokes. This study, though, shows that high fibrinogen is a secondary cause of stroke, not a direct cause. A study comparing incidence of stroke and fibrinogen levels in Americans vs. Japanese shows that Japanese have a lower level of fibrinogen and, correspondingly, a lower incidence of stroke (reviewed in Lowe 1998). In another early study, showing a more direct relationship, the fibrate drug clofibrate (used to lower cholesterol levels in blood) lowered the plasma fibrinogen and blood viscosity, resulting in a significant increase in the cerebral blood flow (reviewed in Lowe 1998).

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[1] In the event of an intracranial bleed it would seem to be too late to try using deactivators; however, this knowledge could present a possible entry point into looking for a treatment.

Once scientists realized the potential for thrombolytic therapy, they had to ask themselves: Is this treatment option really going to work? And, even if this potential treatment does work, is it safe? In 1992, research was conducted to assess whether or not thrombolytic therapy is effective. The results of 10 different trials were combined and examined, and it was noted that there was a reduction in the risk of death and deterioration to stroke patients treated with thrombolytic therapy. This provides some evidence that thrombolysis is beneficial in acute ischemic stroke. The study concludes that although this was not enough evidence to recommend widespread usage of the thrombolytic drugs, there was enough improvement in patient outcome to encourage larger randomized trials (Wardlaw and Warlow 1992).

The main problem with this retrospective study is that the administration of thrombolytic drugs, which should have begun within 24 hours from the time of symptom onset, ranges anywhere from 24 hours up to five days later (the median being 72 hours). Additionally, the severity of the stroke was not taken into account.

Hommel et al. (1996) record the results of a trial done to determine if thrombolytic therapy is indeed safe. The trial included 154 patients in a placebo group and 156 patients in a streptokinase group. Six months after treatment, 124 patients from the streptokinase group and 126 patients from the placebo group had either died or were severely disabled. At ten days after treatment, more patients who received the thrombolytics had died than placebo patients. Researchers noted that most of the deaths came about because of cerebral hemorrhage. Hommel et al. conclude, "Treatment with streptokinase resulted in an increase in mortality. The routine use of streptokinase cannot be recommended in acute ischemic stroke." However, they did note at the end of the article that those patients who had been treated with the thrombolytic agent and survived the treatment without subsequent disability had significant improvement in their level of function. Fewer patients in the streptokinase group were disabled as compared to the placebo group. Hommel et al. cautiously speculate that one possible explanation of this can be that thrombolytic agents do actually work to improve function.

It is important to note that when trial participants were treated with these drugs, the doctors did not know about the various contraindications. The criteria for exclusion during this trial were previous hemorrhagic stroke, recent surgery or trauma, pregnancy, or other illness known to compromise the prognosis. Nowadays researchers know more about the contraindications, e.g., hypertension, diabetes, gender, use of oral anticoagulants, and, possibly, age. Furthermore, only 25% of the patients treated with the thrombolytic agents received the therapy within 3.75 hours of symptom onset. The median delay from symptom onset was 4.6 hours. Presently, the drug companies are trying to have the FDA approve the drugs to be given after 4.5 hours; less than 25% of patients in this trial received the drug in that time slot.

In May 2009, the American Heart Association guidelines for the administration of recombinant tissue-Plasminogen Activator (rt-PA) following acute stroke were revised to expand the window of treatment from 3 hours to 4.5 hours to provide more patients with an opportunity to receive benefit from this therapy. Eligibility criteria for treatment in the 3 to 4.5 hours after acute stroke are similar to those for treatment at earlier time periods; however, there are additional exclusion criteria: patients older than 80 years, patients taking oral anticoagulants, and patients with a history of stroke and diabetes. Patients falling into any of these categories are excluded (Saver et al. 2010).

In 2004, a research group pooled together all the data of six randomized placebo-controlled trials of intravenous rt-PA to study whether or not thrombolytics are helpful after 3 hours of symptom onset. They retrospectively analyzed 2775 patients from more than 18 countries, thus ensuring a large sample population and randomization in the test subjects. The problem was that every research group that did a trial used their own eligibilty criteria, and they grouped the patients differently based on time of treatment. The group did, however, feel it safe to confirm on the basis of the collective data that rapid treatment is associated with better outcomes at 3 months. The group also stated that the possible benefit of rt-PA treatment may extend beyond 3 hours, but it definitely does not extend to 6 hours, because, as time goes on with the stroke untreated, progressive disappearance of the ischemic penumbra (ischemic but still viable cerebral tissue) occurs. Accordingly, patients who have potentially viable ischemic brain tissue at later time might have substantial treatment benefits (Hacke et al. 2004).

During the course of the research, the team noticed a striking phenomena. Patients with more severe strokes arrived at the hospital earlier than those with less severe strokes, thereby receiving rt-PA earlier. The mortality and disability rates are high for those patients in early treatment intervals due to the severity of the stroke, but, at the same time, the effect of the rt-PA is greatest in those treated early despite the greater stroke severity (Hacke et al. 2004) . This proves the effectiveness of rt-PA when given early.

One of the big concerns that doctors have is the presence of microbleeds. A microbleed is a tiny focal collection of blood breakdown products adjacent to histologically abnormal small vessels, resulting from blood leakage through the fragile vessel wall (Figure 2). The actual size of a microbleed is likely to be less than a millimeter. It is suggested that microbleeds result from small vessel damage. Recent research suggests that there may be a genetic component as well (Werring 2007).

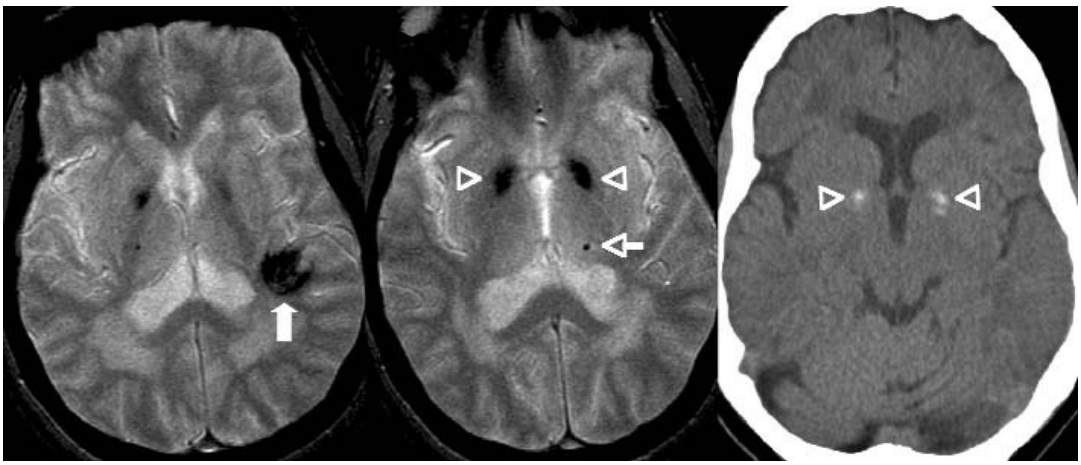

Figure 2: Cerebral microbleeds: A microbleed can be seen in the middle picture located near the right thalamus and marked with an arrow. Source: Werring 2007

One of researchers' concerns regarding microbleeds is whether there is a connection between cerebral microbleeds and treatment with a thrombolytic agent during an ischemic stroke. The basis for this well placed assumption is that cerebral microbleeds are found in 54% to 71% of all primary intracerebral hemorrhage occurrences (Werring 2007). Ho Sung Kim et al. (2006) retrospectively evaluated 279 patients and selected 65 patients (37 men, 28 women, mean age being 67 years old) who fit their extremely selective criteria. The criteria

included: symptom onset within 6 hours of receiving the drug, no previous history of intracranial hemorrhage, thrombolytic treatment immediately after the initial MRI, and another MRI 1-3 days after the thrombolytic treatment. They found that, after being treated with thrombolytic agents, 25 patients of those 65 had microbleeds. Of the 40 patients who did not have microbleeds, 9 had signs of hemorrhage. Of the 25 patients that did have microbleeds, 8 had signs of hemorrhage. From this research it seems clear that there is no correlation between presence of microbleed and subsequent intracranial hemorrhage as a result of treatment with a thrombolytic agent.

A limitation of this experiment is that the test group used is very small. They began with 279 patients which is already small, and the test numbers were further reduced due to the very selective criteria. Further research with more test subjects involved is needed to reach a firm conclusion. The author also mentions that the maximum number of microbleeds any patient had was 10, and, in future studies, he would like to see what happens to patients with more than 10 microbleeds.

Another study comparing location of microbleed and symptomatic hematoma (collection of blood outside blood vessels) concluded that there is a correlation between the two; however, they were not sure how to interpret the correlation (Roob et al. 2000).They note that there was some tendency toward a regional association between microbleed location and the site of a symptomatic hematoma, but they could not discern the specific patterns of microbleed distribution. Kim's study, which mentions that presence of a microbleed is not a contraindication to thrombolysis, seems to contradict Roob's study, which notes a correlation between the two.

Also interesting is that in Roob et al.'s study, which was also done retrospectively, the population consisted of 109 patients who had an intracranial hemorrhage (as opposed to 65), which is still very small for a study, and 54% of those patients had microbleeds. However, the patients in this study had up to 90 lesions, which is a great deal more than anyone else in Kim et al.'s study, but the average number of microbleeds was still 14, which is not that much more than Kim et al.'s study. In Roob et al.'s study, the researchers grouped the individual with 90 microbleeds in the same group as the patient with one microbleed. What would be interesting is if there was research conducted which would compare number of microbleeds to incidence of intercranial hemorrhage, because there is limited data to suggest that microbleed number may actually be a predictor of future bleeding risk after intracranial hemorrhage. In fact, microbleeds are associated with larger volume of intracranial hemorrhage (Werring 2007).

One of the primary concerns of both doctors and researchers is: is thrombolytic therapy safe for use on the elderly? The problem that researchers had is that most of the information about hemorrhage as a result of thrombolytic therapy comes from clinical trials, and elderly individuals are either scarcely selected due to the highly selective criteria of the trials, or not included in the trial at all. The reason for this is that elderly patients often have a poor prognosis for recovery, high mortality rate, high health care costs, and in the case of a heart attack the doctor can always treat the patient with angioplasty. Therefore, information about how the elderly would respond to thrombolytic agents is scarce (Brass et al. 2000). Pundik et al. (2008) set out to determine three things: the rate of intracranial hemorrhage associated with thrombolytic therapy for elderly patients suffering an acute heart attack, whether there are any independent predictive factors for intracranial hemorrhage, and a way of estimating the risk of an intracranial hemorrhage.

Stroke is more common in the elderly, and the morbidity and mortality after a stroke are higher with increasing age. The incidence of stroke doubles with each consecutive decade above the age of 55, and the mortality for patients over 85 years old is tripled compared with a younger group. In addition, the rates of a favorable outcome after a stroke are significantly lower in older patients. Because stroke rates are so high in the elderly, researchers and clinicians need to find a viable treatment, and thrombolytic therapy seems to be the most promising. The problem is that, unlike higher admission blood pressure, treatment delay, and hyperglycemia, which have all been proven to be risk factors of intracranial hemorrhage, advanced age is not a clear indicator (Pundik et al. 2008).

A research team analyzed the charts of 218,663 patients who were eligible and treated 31,732 of them with thrombolytic therapy. The mean patient age was 73 years old. Out of 31,732 patients, 455 (1.43%) of the patients ended up with intracranial hemorrhage, and 72% of the patients that had intracranial hemorrhage died within 6 months compared to 18% of the patients who did not receive the therapy and died within 6 months (Brass et al. 2000).

The goal then was to figure out what some of the risk factors for intracranial bleeding are, because if some of the risk factors can be identified, the individual patient's risk of hemorrhaging can be assessed. Studies previous to the 1993 study by Simoons and Maggioni suggested that age, hypertension, overdose of drugs based on body weight, being female, previous central nervous disease, and the use of oral anticoagulants are all associated with increased risk of hemorrhage. It has been suggested that the reason the elderly are at greater risk is not because of age per se; it is actually because elderly patients tend to have more contraindications to thrombolytic therapy. They found that patients over the age of 75 were more likely to have a history of hypertension, diabetes, congestive heart failure, previous bypass, and stroke among others (DeGeare and Grines 2000). Poor outcomes after ischemic stroke in the elderly could also be caused by other factors that are associated with aging. It has been shown in animal and clinical studies that effects of ischemia and reperfusion on brains are hastened in aged organisms (Pundik et al. 2008).

Researchers theorized that the reason elderly patients with congestive heart failure do not respond well to thrombolytics is because poor cardiac pump function results in decreased perfusion, making it difficult for the thrombolytic agents to penetrate the occlusive thrombus. This theory is hard to accept because, if the thrombolytic agent is not able to penetrate the thrombus because the heart is not pumping strong enough, it stands to reason that the thrombolytic agent would not be able to cause a hemorrhage either. If the elderly patients would simply not respond to the drug at all then they would have a valid point, but it does not seem to follow that the thrombolytic agent cannot get to the thrombus but can get to the brain.

As stated above, one of the primary predictors of intracranial hemorrhage is hypertension. However, research suggests that the bleeding risk depends not only on the state of the intracranial blood vessels but also predominantly on the blood pressure at the time of the thrombolytic therapy. This is based on an observation that patients with intracranial stroke often have higher blood pressure than those patients experiencing other types of strokes. Consequently, before beginning any course of thrombolytic treatment, the patient's blood pressure should be assessed and, if necessary, corrected (Simoons and Maggioni 1993).

In 2002, Tanne et al. reported that intravenous rt-PA is an effective therapy for acute ischemic stroke, but they wanted to identify baseline factors that are associated with thrombolysis related intracranial hemorrhage. During their retrospective investigation of 1,205 patients treated with rt-PA within 3 hours of symptom onset, of which 72 patients (6%)

developed intracranial hemorrhage, they determined that the main contraindications were diabetes melitus, past cardiac disease, increasing stroke severity, advancing age, use of an antiplatelet agent before treatment, and elevated pretreatment blood pressure. They determined that advanced age is a risk factor because they noted a particularly low rate of intracranial hemorrhage in patients under 60 years old (Tanne et al. 2002).

In 2004, research was done by Simon et al. to assess whether or not thrombolytic agents are safe for the elderly. As part of an ongoing monitoring process, a database was created that records all the details of patients treated for strokes with rt-PA since 1996. The database gives researchers access to many important details such as demographic data, blood pressure and glucose level at time of admission, severity of the stroke, and age of the patient. Of the hundreds of patients that received rt-PA during those years, 62 patients were over 80 years of age. Six out of those 62 patients experienced a severe intracranial hemorrhage, only slightly higher than the 6.4% of patients under 80 years of age who experienced severe intracranial hemorrhage. Thus, while it is true that patients over the age of 80 suffer from higher mortality and morbidity rates than younger patients, the elderly should not be denied the chance to benefit from thrombolytic therapy based on age alone (Simon et al. 2004).

In 2006, a systematic review performed by Engelter, Bonati, and Lyrer analyzed data taken from many websites such as PubMed, MEDLINE, and Science Citation Index and found many instances where elderly stroke victims were treated with thrombolytic agents. They found that stroke patients over 80 years old that receive rt-PA do have a substantially higher mortality rate than patients under 80. Additionally, older patients, even if they do recover, will not have as favorable a recovery (based on various neurological tests such as the Rankin scale). However, they also found that the risk of Intracranial hemorrhage was similar in both groups. They believe that age is a predictor of how well an elderly patient will recover after a stroke , but, because the likelihood of intracranial hemorrhage did not favor one age group, they conclude that rt-PA is a viable treatment option for the elderly, because the potential bleeding risks are unlikely to outweigh the potential benefit of treatment.

In 2008, researchers collected data from the Brain Attack Database at University Hospitals in Cleveland, Ohio. The database contained all cases of acute stroke dating back to 1993. The researchers had 488 cases where the patients suffered an acute stroke and were subsequently treated with a thrombolytic agent. Of the 488 patients, 404 were under age 80 (mean age 62 years old with a range of 20-79) and 78 patients where above age 80 (mean age 83 with a range of 80-99). The rate of intracranial hemorrhage in the elderly was 12.82%, but that figure was then adjusted. The reason is that most of the elderly patients who subsequently hemorrhaged did so as a result of treatment with intra-arterial therapy (not intra-venual therapy). The rate of hemorrhage in the younger group was 10%. Based on this research evidence, thrombolytic therapy should not be ruled out as a treament for an elderly patient simply because of advanced age, although method of treatment should be considered (Pundik et al. 2008).

There are some interesting trends in the demographic characteristics that deserve mentioning. In the younger group (age under 80), 43% of the patients treated for stroke were women, and in the older group, 55% of the patients were women. Pundik et al. (2008) suggest that the reason for this is because there is a prevalence of acute ischemic stroke in older women. Also interesting to note is that 61% of the younger patients exhibited hypertension compared to 80% that exhibited hypertension in the elderly group. Another significant trend is that in the younger group, 22% of the patients had a history of smoking compared to 8% of the older group that has a history of smoking.

The problem with their conclusion is that they suggest that thrombolytic therapy is safe for patients above 80 with no maximum age. Perhaps it would be helpful if in the future, the research team would, instead of using ranges of 20-79 and 80-99, break the ranges down into 5 year intervals. By ranging the patients in groups of 80-85, 85-90, and so on, the researchers can perhaps establish a maximum age for thrombolytic therapy.

Doctors believe in thrombolytic therapy as a treatment for acute stroke, and they want this therapy to work. The problem is that a great danger is associated with the therapy. What if doctors could lower the risk of intracranial hemorrhage? Researchers compared how patients treated in a CCSU – a Critical Care Stroke Unit recovered as compared to those patients treated in an ASU – Acute Stroke Unit. They found that patients treated in Acute Stroke Units received more treatments with rt-PA, had a shorter length of stay in the hospital, and had a lower 90-day mortality and disability rate. The researchers suggest that the reason for the better outcome is because in the Acute Stroke Unit, patients receive care quicker, and they are monitored very closely for fever, hypertension, hypotension, cardiac arythmias, and glucose levels. It is suggested that the continued monitoring and specialized nursing of the Acute Stroke Unit permitted the early detection, control, and treatment of factors related to hemorrhage (Roquer et al. 2008).

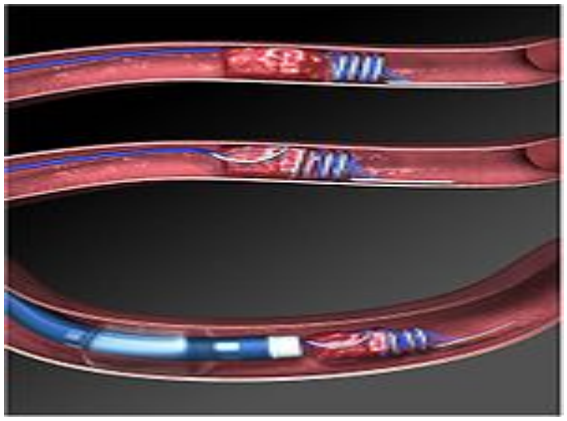

Figure 3: Mechanical Thrombectomy. Source: wikipedia.com

Perhaps the biggest problem with t-PA is that the FDA states that after 3 hours it is not safe for a physician to administer this potentially life saving or life ending drug. Is there an alternative treatment to t-PA for after 3 hours? In 2005, research was conducted to see if a blood vessel occlussion could be removed by mechanical means. This would be accomplished by inserting a catheter into the femoral artery, directing it into the cerebral circulation, and deploying a corkscrew-like device to ensnare the clot which is then withdrawn from the body. (Patients who were candidates for treatment with t-PA were excluded from this trial.) The Mechanical Embolus Removal trial was attempted as long as 8 hours after the onset of symptoms. The overall mortality was 44% of the patients, which is very high although not unexpected, as 8 hours is a long time after symptom onset. However, in 48% of the patients, recanalization was achieved, which means that the treatment has potential but just needs some fine tuning to be made safe and more effective (Cornett et al. 2008).

Another treatment method that is being looked into is angioplasty and stenting. The theory is that if angioplasty has been proven effective in preventing heart attacks, it should also be effective in preventing strokes. Early trials suggest that this could be a viable treatment option for patients who can not receive thrombolytics, but more research is needed (Saver et al. 2010).

Conclusion

Thrombolytic agents restore cerebral blood flow in some patients with acute ischemic stroke and may lead to improvement or resolution of neurologic deficits. Unfortunately, thrombolytics can also cause symptomatic intracranial hemorrhage. Therefore, if a patient is a

candidate for thrombolytic therapy, inclusion and exclusion criteria must be reviewed thoroughly. The exclusion criteria focus largely on identifying the risk of hemorrhagic complications associated with thrombolytic use (Saver et al. 2010). Based on research done within the last 5-10 years, it would seem that if a patient comes into a hospital having a stroke (assuming it is a stroke severe enough to warrant treatment with a thrombolytic agent) and the patient is in otherwise good health, i.e., no prior history of heart disease, not a diabetic, not hypertensive, and no history of bleeding disorders, and it is within 3 hours of symptom onset (perhaps 4.5 hours of symptom onset), then it would seem to be safe to administer the drug. If any of these contraindications are present the doctor needs to weigh the possible risk of hemorrhage vs the severity of the stroke. Interestingly enough, based on the recent research, clinicians should be more concerned about treating an obese 40 year old with a history of high blood pressure than an 85 year old who is in otherwise perfect health.

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