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Reducing thumb extensor risk in laboratory rat gavage

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ABSTRACT

Gavage is a common technique for orally administering compounds to small laboratory animals using a syringe. It involves highly repetitive thumb extensor exertions for filling the syringe, a risk factor for DeQuervain's tenosynovitis. As an intervention, a series of bench tests were performed varying fluid viscosity, syringe size and needle size to determine the forces required for drawing fluid. Forces up to 28 N were observed for a viscosity of 0.29 Pa s. A guide is presented to minimize thumb forces for a particular combination of syringe (3 mL, 5 mL and 10 mL), fluid viscosity (0.001 Pa s, 0.065 Pa s, 0.21 and 0.29 Pa s), and needle length (52 mm, 78 mm and 100 mm) based on maximum acceptable exertion levels. In general, a small syringe and large needle size had a greater number of acceptable rat gavages per day due to the lower forces experienced as compared to all other syringe and needle combinations.

1. Introduction

Work-related musculoskeletal disorders among laboratory professionals are highly prevalent (Agrawal et al., 2014). It is well documented for example that pipette users often experience hand and shoulder ailments (Björksten et al., 1994), and are exposed to highly repetitive forces (Lu et al., 2008). Hand complaints among manual pipette users increase with longer exposures, larger volumes of materials that vary with pipette size (Lintula and Nevala, 2006), and greater plunger forces make the task more difficult to perform (David and Buckle, 1997). The physical demands of working with laboratory animals are also recognized as having potential risk for work related injuries (Kerst, 2003).

Rat gavage is a common laboratory technique for orally administering compounds. The procedure is performed using a syringe with a blunt plastic needle inserted into the esophagus of an animal and injecting the drug directly into the stomach. While many methods are available for oral administration in the laboratory, gavage is one of the most widely used procedures due to its efficiency, accuracy and simplicity (Waynforth and Flecknell, 1980). Similar to pipetting, gavage is performed repetitively by a technician, and while pipetting utilizes the thumb flexor mechanism, drawing materials into the gavage engages the thumb extensors. Although the practice may differ from one laboratory to another, a commercial laboratory technician may perform as many as 200 to 500 rat gavages per day.

The activity involved in drawing the syringe in rat gavage was observed for the current study in a commercial laboratory. The operator typically draws materials of various viscosities from a beaker while holding a syringe in one hand and pulling against the plunger by abducting and extending the thumb, often while deviating the wrist (Fig. 1). Repetitive and forceful thumb extensor exertions are risk factors for DeQuervain's syndrome, which can result in painful swelling of the sheath surrounding the extensor pollicis brevis and abductor pollicis longus (Harrington et al., 1998). The disorder is associated with repeated or sustained wrist bending in extreme posture (Le Manac'h et al., 2011). DeQuervain's syndrome has previously been reported among lab workers performing manual pipetting of high viscosity fluids (Asundi et al., 2005).

Based on a biomechanical analysis of tendon displacements in pipetting for estimating loads on the flexor pollicis longus tendon, Wu, et al. (2013) estimated it was within the range of those observed in other occupational activities, such as typing and nail gun operation. A study by Lintula and Nevala (2006) found that perceived strain on the wrist and thumb after pipetting was the least when the shortest pipette among three different sizes was used. Lin and Chen (2009) using EMG observed that use of a large syringe in pipetting increased thumb loading and muscle activity.

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We anticipate that similar extensor and abductor loading in relationship to syringe size might occur in rat gavage tasks. Given that median right hand female thumb abductor strength in comparison to thumb adductor strength is 12 N–58 N respectively (Rozmaryn et al., 2007), it is anticipated that even more stress and strain on the thumb may be associated with gavage activities that involve thumb abduction.

The current study considered factors that can reduce or eliminate risk in the gavage task for a large-scale commercial laboratory. The problem was addressed by establishing recommendations for gavage practice that can be performed using the minimum exertion necessary for different combinations of syringe diameter, fluid viscosity, and needle size. A laboratory bench study was performed for measuring the syringe drawing forces acting against the thumb while systematically varying syringe size, needle size and viscosity. These forces were then compared against the maximum acceptable abduction exertion for the thumb and used to control exposure in repetitive gavage tasks.

2. Methods

2.1. Forces due to pulling action of the thumb

The syringes and needles typically used for rat gavage are available in various sizes and the rate of filling a syringe is related to the flow rate of material while drawing, which is dependent on the rate of pulling and the material viscosity. The variables from Hagen-Poiseulli's equation are related to the pulling forces for a syringe plunger (Schaschke, 1998). The equation for fluid flow used to estimate the set of relevant factors involved in syringe pulling are described in Equation (1) as:

$$\Delta P = \frac{8\mu LQ}{\pi r^4} \tag{1}$$

where μ is the dynamic viscosity, L is the length of the pipe, Q is the volumetric flow rate, and r is the syringe radius. The equivalent factors considered are therefore the viscosity of the fluid, diameter of the plunger, diameter of the syringe needle, flow rate, and length of the gavage needle. A variation of each of the factors induces change in the required pulling force.

2.2. Design of experiment

The study included combinations of four levels of viscosity, three syringe sizes and three needle lengths, and a flow rate of 1 mL/s to characterize the pulling force. The test materials used in the laboratory for this study are known to have viscosity less than 0.3 Pa s. Hence, four liquid compounds with different viscosities ranging from 0.001 Pa s to 0.29 Pa s were used for testing. These four liquids were water (viscosity = 0.001 Pa s), extra light olive oil made by Pompeian Inc. (viscosity = 0.065 Pa s), motor oil SAE 10W-40 made by Mobil (viscosity = 0.21 Pa s), and motor oil SAE 15W-40 made by AMSOIL (viscosity = 0.29 Pa s).

It was observed that an air vacuum formed when the liquids with greater viscosities were withdrawn for large flow rates. The liquids would slowly reach the top of the plunger after a considerable delay time. In the lab, this would not be ideal, as the lab technicians would need to maintain constant force as liquid rises. Thus flow rates of 1 mL/s were chosen as the maximum rate.

The disposable syringes (Nipro Corporation) included small (3 mL), medium (5 mL) and large (10 mL) sizes. The animal feeding needles included small (Dispo Fuchigami, 52 mm length, 0.86 mm inner diameter, 1.46 mm outer diameter, 2.4 mm silicon tip), medium (Dispo Fuchigami, 78 mm length, 1.19 mm inner diameter, 1.79 mm outer diameter, 2.8 mm silicon tip) and large (Instech Solomon, 100 mm length, 1.2 mm inner diameter, 1.8 mm outer diameter, 2.8 mm silicon tip).

Lab technicians typically choose a syringe that is closest to the dosage needed. Those syringes are normally paired with one of three available needles with varying lengths depending on the size of the animal. Larger animals require the longest needle as the distance from the mouth to stomach is the longest. A total of 36 different combinations of flow rate, viscosity, syringes and needles were tested.

2.3. Force measurement

The syringe drawing force was measured using an MTS Criterion Model C43 materials testing machine (MTS Systems Corporation, Eden Prairie, MN, USA). The MTS machine was equipped with a force sensor for measuring changes in force as a function of time. The movements of the MTS machine were bidirectional: upwards and downwards. The configured experimental set up on the MTS machine is shown in Fig. 2.

In order to simulate the draw-up phase of the rat gavage, the syringe plunger was firmly anchored to the MTS machine fixture. The MTS screw action grip was then used to hold the other end of the syringe, which connects to the needle. It was essential that the grip was not located on the body of the syringe where the plunger rests, but rather located on the ring surrounding the thread that connects the syringe to the needle. Gripping the body of the syringe caused a significant increase to the syringe withdrawal force because the rubber piston had difficulty moving through the gripped portion. The tip of the threaded needle became submerged in the appropriate liquid contained by a weigh boat. Using this setup, the plunger of the syringe always moved upwards together with the MTS machine while the body of the syringe stayed in

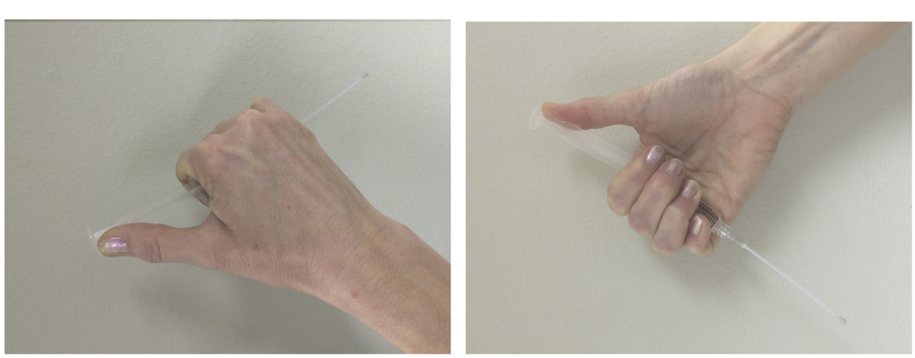

Fig. 1. Thumb position when drawing materials for gavage into a syringe.

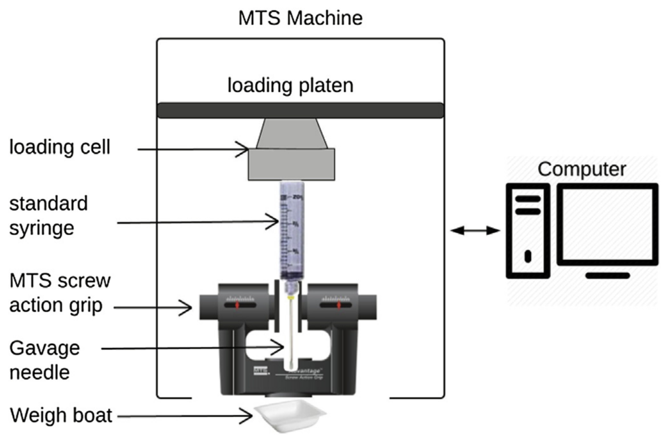

Fig. 2. Syringe plunger is firmly anchored to the MTS machine, while the MTS screw action grip is attached to the ring surrounding the thread that connects the syringe to the needle to anchor the syringe firmly.

place.

2.4. Maximum acceptable effort

Potvin (2012) developed an equation that predicts the maximum acceptable effort (MAE) for a repetitive task that takes into account the duty cycle (DC), where DC is:

$$Duty\ Cycle\ (DC) = \frac{work\ time}{work\ time + rest\ time} \tag{2}$$

The DC is then used to calculate the MAE with the following equation:

$$MAE = 1 - \left[DC - \frac{1}{28800}\right]^{0.24} \tag{3}$$

Maximum acceptable force (MAF) can be estimated based on strength as:

$$MAF = MAE \times Maximum\ Voluntary\ Strength \tag{4}$$

Work time is when the technician's thumb is abducted while drawing materials into the gavage syringe, and *rest time* is when the technician is not using the thumb abductor muscles. The *DC* term in relation to the gavage task is the ratio of time when the thumb is abducted, to the total time spent doing the gavage task in a work day. The *MAF* is therefore the maximum force that can be exerted using the thumb abductors, when repeated over the work time and rest time for a given *DC*. It was assumed that no other thumb abduction/extension tasks are performed.

Thumb abduction strength used for analysis was 6.57 Nm (SD = 2.49 Nm) torque for males less than 60 years, and 3.02 Nm (SD = 1.12 Nm) torque for females less than 60 years (Boatright et al., 1997). The associated thumb force was estimated based on the mean digit 1 thumb length of 12.34 cm for males and 11.05 cm for females (Greiner, 1991). Based on these values, the 25 percentile female thumb strength was 20.49 N and the 5 percentile male thumb strength was 20.06 N. A nominal force of 20 N was therefore used for thumb strength.

Based on a rate of rat gavages performed per day and the maximum flow rate of 1 mL/s to fill a given syringe, the DC was calculated using Equation (2). The MAE was then calculated using Equation (3), and the MAF was based on exertion strength of 20 N and Equation (4).

3. Results and discussion

The forces required to draw water (viscosity = 0.001 Pa), olive oil (viscosity = 0.065 Pa s), low viscosity motor oil (viscosity = 0.21 Pa s), and high viscosity motor oil (viscosity = 0.29 Pa s), for a flow rate of 1 mL/s with different syringe and needle combinations are given in Table 1. These forces ranged from 3.5 to 28 N. Force increased when the syringe size increased and the needle size decreased.

Based on calculations using the forces in Table 1, the maximum number of rats per day were calculated in order to not exceed the MAE. These are plotted for combinations of syringe and needle sizes for water (Fig. 3), olive oil (Fig. 4), motor oil1 (Fig. 5) and motor oil2 (Fig. 6).

As seen in Figs. 3–6, by using a smaller syringe and larger needle size, a technician could potentially perform more rat gavages per day, due to the lower forces experienced (Table 1) as compared to all other syringe and needle combinations. Based on the viscosity of a particular compound, the appropriate set of curves (Figs. 3–6) are selected. The daily number of rat gavages, based on the maximum acceptable load, is determined by the intersection of dose in mL, and the syringe and needle size used.

For example, if a 5 mL dose is needed for a compound having 0.29 Pa s viscosity (e.g. high viscosity motor oil) using a medium syringe and large needle (SmNl), Fig. 6 indicates that 20 doses per day would be acceptable, whereas if a small syringe was used (SsNl), 300 doses would be acceptable. Similarly, if the same dose and compound (e.g. 5 mL dose of a 0.29 Pa s viscosity compound) were administered using a medium syringe and a small needle (SsNs) were changed to a large needle (SsNl), the acceptable daily number of doses would increase from 80 doses to 300 doses (Fig. 6).

For combinations of syringe and needle sizes (SlNs, SlNm and SlNl) at viscosities of 0.21 Pa s and 0.29 Pa s, and combinations of syringe and needle sizes (SlNs and SlNm) at viscosity of 0.065 Pa s, forces greater than the maximum acceptable force of 20 N were observed, hence not recommended for rat gavage. The greater the viscosity of a liquid compound, the greater the intermolecular forces that exist among the molecules. This greater interaction among the molecules tends to exhibit greater adhesion with the syringe. Greater adhesion of liquids to the syringe walls increases resistance to the plunger's movement. This increased friction induced by greater intermolecular forces tends to result in a greater minimum force than is required to pull the syringe. Hence, it is expected that there is a positive correlation between the force exerted against the plunger and the viscosity of the liquid compound contained in the syringe.

As expected, the rat gavage rate decreased as a function of dose volume. However, as observed from Figs. 3–6, higher viscosities using medium or large syringe sizes irrespective of needle size, yielded a much smaller rat gavage rate for any practical implementation.

Pitcher and McCannel (2011) characterized the fluidic parameter of a syringe-based portable vitrectomy device named the Intrector® and compared these data to other commercially available vitrectomy systems. Their study investigated the pulling force on a syringe plunger with constant force that could be comfortably sustained for 10–20 min on eight test subjects including male and female with different physical capability. The study indicates operator mean sustainable comfortable pull force was approximately 10 N. The fluidics of the Intrector® have been investigated using water and egg white, with results showing slightly lower generated vacuum than traditional console systems (120–135 mm Hg vs 250–600 mm Hg) and equivalent aspiration flow rates (0.39 mL/min vs 0.29–0.9 6 mL/min). However, these values only serve as a reference since there is a significant difference between a

Table 1
Force (N) needed to draw water, olive oil, low viscosity motor oil and high viscosity motor oil at flow rate of 1 mL/s with different syringe and needle combinations.

Needle size	Materials											
	Water			Olive oil			Low viscosity motor oil			High viscosity motor oil		
	Syringe size											
	SM	MD	LG	SM	MD	LG	SM	MD	LG	SM	MD	LG
SM	5.0	8.2	17.8	10.9	16.4	21.18	13.3	16.67	27.7	13.2	16.5	28.0
MD	4.3	7.1	15.4	10.2	15.6	19.34	10.8	15.93	23.6	11.3	16.0	22.6
LG	3.5	7.0	13.5	8.94	14.7	18.13	9.9	15.33	24.0	10.2	14.9	22.0

SM – small, MD – medium, LG – large.

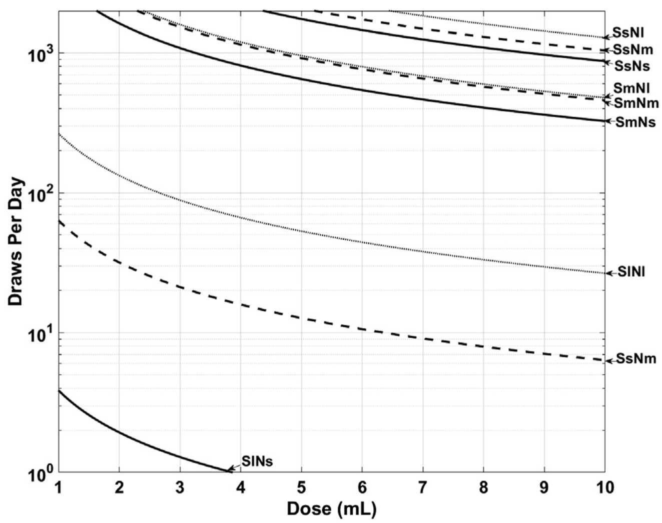

Fig. 3. Family of curves for the rats treated per day as function of volume of water (viscosity = 0.001 Pa s) with different syringe and needle combinations. SsNs, SmNs, SlNs = Syringe small, medium, large respectively for needle small. SsNm, SmNm, SlNm = Syringe small, medium, large respectively for needle medium. SsNl, SmNl, SlNl = Syringe small, medium, large respectively for needle large. The curves are identified by the needle size.

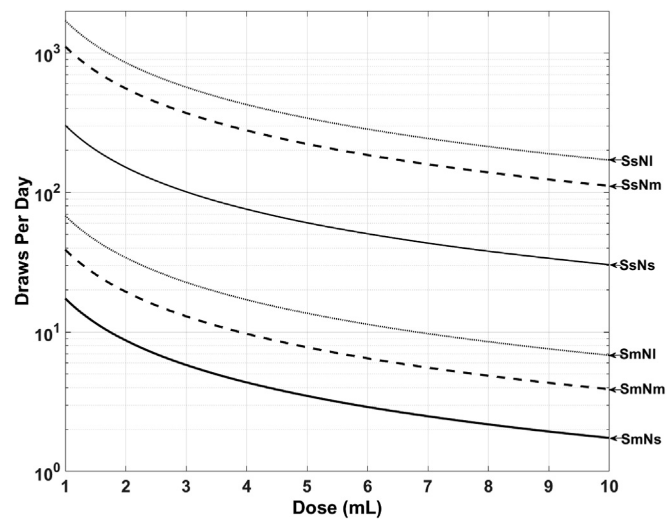

Fig. 5. Family of curves for the rats treated per day as function of volume of low viscosity motor oil (viscosity = 0.21 Pa s) with different syringe and needle combinations. The curves due to SlNs, SlNm and SlNl were not plotted as they exceeded the maximum acceptable force of 20 N. SsNs, SmNs, SlNs = Syringe small, medium, large respectively for needle small. SsNm, SmNm, SlNm = Syringe small, medium, large respectively for needle medium. SsNl, SmNl, SlNl = Syringe small, medium, large respectively for needle large. The curves are identified by the needle size.

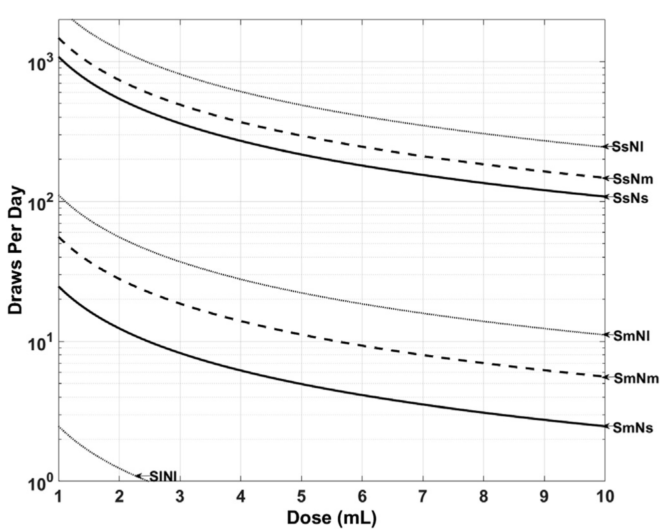

Fig. 4. Family of curves for the rats treated per day as function of volume of olive oil (viscosity = 0.065 Pa s) with different syringe and needle combinations. The curves for SlNs, SlNm were not plotted as they exceeded the maximum acceptable force of 20 N. SsNs, SmNs, SlNs = Syringe small, medium, large respectively for needle small. SsNm, SmNm, SlNm = Syringe small, medium, large respectively for needle medium. SsNl, SmNl, SlNl = Syringe small, medium, large respectively for needle large. The curves are identified by the needle size.

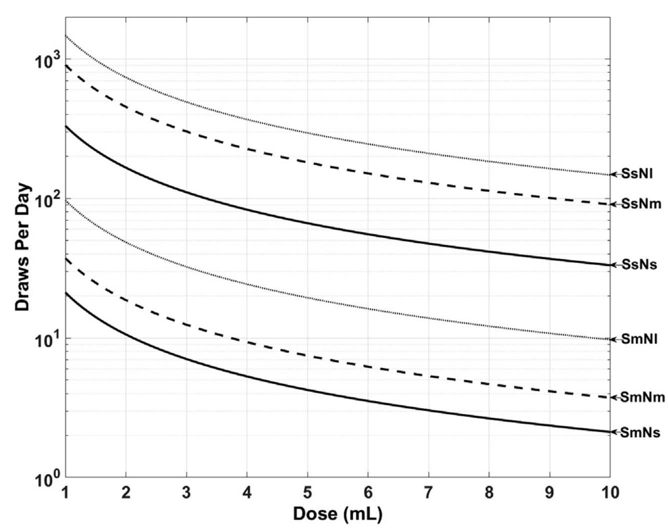

Fig. 6. Family of curves for the rats treated per day as function of volume of high viscosity motor oil (viscosity = 0.29 Pa s) with different syringe and needle combinations. The curves due to SlNs, SlNm and SlNl were not plotted as they exceeded the maximum acceptable force of 20 N. SsNs, SmNs, SlNs = Syringe small, medium, large respectively for needle small. SsNm, SmNm, SlNm = Syringe small, medium, large respectively for needle medium. SsNl, SmNl, SlNl = Syringe small, medium, large respectively for needle large. The curves are identified by the needle size.

vitrectomy device, which is specifically designed to remove vitreous humor (gel) from the eye, and a conventional syringe. Also, the fluids used do not cover a wide variety of viscosity typically used in gavage.

Cilurzo et al. (2011) provided a standardized scoring system for choosing the optimal needles. They tried four solutions when distinct viscosities and needles of different lengths were used. The force was measured using a texture analyzer as the crosshead pushed the plunger at a rate of 1 mm/s. While the current study shares similarities in methods, the objectives were different and the flow rate was held constant throughout the study. In addition, testing dealt with the measurement of pushing forces instead of pulling forces and using gavage needles.

While increasing the needle size leads to decreasing the force of the draw, it may not be practical for certain laboratory rat gavage scenarios due to the animal welfare component. The specific implementation should utilize the least invasive mechanism to deliver the dose to the animal, in this case the smallest needle. Additionally for dose accuracy, the smallest gauge syringe should be used.

These recommendations are limited to the syringe filling activities that utilize the thumb abductor muscles. The other activities typically performed by gavage technicians do not use these muscles and therefore are considered rest time. If the worker also performs other activities involving similar exertions, these daily rate recommendations would be reduced.

4. Conclusions

We examined the forces needed to draw water, olive oil, low viscosity motor oil and high viscosity motor oil at flow rate of 1 mL/s with different syringe and needle combinations. We used these forces as MAF, and the maximum voluntary strength of 20 N corresponding to the 25 percentile female thumb strength and the 5 percentile male thumb strength, in Equation (4) to calculate MAE. Using the calculated MAE and Equations (2) and (3), we developed a family of curves which will provide the lab technician the acceptable rat gavage rate for the various dosages of different viscosities, needle size and syringe type. In general, when using a small syringe and large needle size, a technician could potentially perform more rat gavages per day, due to the lower forces experienced as compared to all other syringe and needle combinations, providing the needle is suitable for the animal's size.

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