Xiao procedure: problems with ethics, methodology, and results from the double-blind trial of Tuite et al.


There are major factual, scientific, and ethical problems in this article, and in the accompanying editorials. I will begin by clarifying the facts of my involvement in “the first in history” double-blind clinical trial for a major surgery in disabled children.

First, regarding my involvement in the trial, Dr. Tuite’s team traveled to China in 2009 and personally examined more than a dozen children with myelomeningocele (MM) and lipomyelomeningocele (LMM) who were cured by the Xiao procedure 2 to 3 years ago. These children voided voluntarily and emptied their bladders almost completely without incontinence. Dr. Tuite and colleagues then invited me to All Children’s Hospital to help them to begin the Xiao procedure 2 days before my keynote speech at the First World Congress on Spina Bifida Research and Care, March 15–18, 2009, in Orlando, Florida. They scheduled 2 cases in 2 operating rooms (ORs) at the same time. I observed and helped in identifying the correct nerve roots; then they stopped the operations and I was informed for the first time that they were conducting a double-blind study. I immediately expressed my strong objection, based on 2 reasons. The first reason I objected was that the Xiao procedure had been proven to be very effective by many centers involving thousands of cases and many formal publications,4–6,12 including in the US (Beaumont Hospital, New York University Medical Center, and Louisiana State University; Patwardhan R, Mata J: Case report on Xiao procedure for a 6 year old SCI girl to gain bladder control, presented at the International Symposium on Neural Regeneration, Detroit, Michigan, 2009–2012). I believe it is unnecessary and unethical to perform a double-blind trial using major surgery in children, especially these disabled children. My second objection was that it is impossible scientifically and technically to perform a double-blind trial for a very complicated major surgery in children with spina bifida whose history, anatomy, neural defects, bladder situation, and voiding management may be quite different from each other. The major technical dilemma was that children who had undergone the Xiao procedure had to stop clean intermittent catheterization (CIC) and anticholinergic medications 3 months postoperatively to allow regenerated axons working with the bladder and urethra to coordinate voiding, while children who did not undergo the Xiao procedure were to continue using CIC and anticholinergics as the guidelines indicated to protect the upper urinary system. How could you manage this dilemma in a double-blind trial for 3 years?

Despite my strong objections, Dr. Tuite’s team decided to proceed with the double-blind trial. I immediately and permanently withdrew my involvement in the trial on the very first day. Thus, unlike the description in the article, I did not personally assist with the first 7 cases, but only 2 cases on the first day. With sorrow, I had to tell the investigators that I found the donor ventral root (T-12) was cut incorrectly and closely from the cord in 1 of the 2 cases; the root had to be reattached to the cord by microanastomosis, and then its distal end was anastomosed to the S-3 root as in the Xiao procedure. If this kind of accident occurs, the patient should be excluded from any type of trial, because the root re-attached to the cord may not work at all and could jeopardize the rest of the Xiao procedure. Yet, I found the child was still listed as Case 5 (detethering [DT] + Xiao procedure [X]) in the article.

Second, the trial and the article showed major defects and errors in terms of methodology and statistics. A randomized, double-blind study requires the strictest methodology and the most objective quantity and quality control. Whereas in the randomized, double-blind trial by Tuite et al., in addition to using another result (variable surgery) as a control, and a very small sample size that cannot meet the statistical power requirements, each subject’s preoperative lower urinary tract condition, abnormal anatomy, neural defects, and prior surgical history were different from those of the other patients. In addition, each of the 4 neurosurgeons who performed the procedure had
different levels and experience in surgical skills. But the most significant defect of the trial was that postoperative care was different among the enrolled children regarding anticholinergics and CIC. The authors tried to cover up the defect by twice stating in the article that “CIC and the use of BAMs [bladder-active medications] were terminated 2 weeks prior to preoperative evaluations, and most patients were able to refrain from both of these modalities for the entire 3-year follow-up.” This statement completely invalidated the scientific and methodological grounds of this so-called double-blind study: postoperative care must be strictly the same in all patients, i.e., either all should use CIC and the same dosage of BAMs, or all should not use CIC and BAMs. How many patients was “most”: 11, 15, 18? The authors did not report these critical and most important data. But nevertheless, it was fundamentally wrong to paralyze the bladders of some patients using BAMs while not paralyzing those of other patients during postoperative follow-ups in a double-blind trial, and then collect and analyze their data together.

Third, I do not believe it was true that “CIC and the use of BAMs were terminated 2 weeks prior to preoperative evaluations, and most patients were able to refrain from both of these modalities for the entire 3-year follow-up.” Given my experience during the first US pilot study of the Xiao procedure at Beaumont Hospital, I know how hard and difficult it was to try to convince the team of Peters et al. and the local primary care doctors to stop anticholinergics and CIC for children with spina bifida who underwent the Xiao procedure. These investigators refused to follow my methods for 2 years before agreeing reluctantly, and then got the expected good results in 1 month. I would also like to cite a passage from a paper published by researchers in Denmark regarding use of anticholinergics in the Xiao procedure, to show how urologists deal with anticholinergics seriously in the US and Europe: “Although these criteria were first published after the current study began, most of them were met in our series except the upper limit of bladder capacity and the cessation of anticholinergic medication. In regard to the latter we deemed that the medication was essential for patient well-being throughout the 18-month study period.”

This seemed to be a similar situation with the patients in the trial of Tuite et al.: they were scattered over different states under the care of their local primary care doctors who would not dare to not use anticholinergics and CIC for 3 years. So I would suggest the authors and/or the editor of the Journal of Neurosurgery: Pediatrics collect data from these children’s local doctors and provide the real facts regarding the postoperative usage of CIC and anticholinergics over the 3 years of the study. In fact, I did ask Dr. Tuite about this information last year during the only email contact I had with him since my withdrawal, but he did not provide details in his response.

Fourth, the article is not the end of this trial. I am confident I can reverse the results to some degree. My suggestions are as follows.

Because the study is no longer double-blind, please let the 10 children who underwent the Xiao procedure wear a diaper, stop anticholinergics, and let them try to void by pushing, leaking, or any other means for 2 months, and then see what happens. Giving the neurosurgeons a 50% learning curve deduction, there should still be at least 3 or 4 children who will be able to void voluntarily without incontinence and CIC. All kids with spina bifida do not need to scratch to pee after undergoing the Xiao procedure. For the 3000 kids who had the Xiao procedure performed, none needed bladder augmentation.

In China, my hospital has an open policy regarding Xiao procedure patients, which is: “If the patient cannot void voluntarily within 1 year (for a child) or 18 months (for an adult) post Xiao procedure, Prof. Xiao will redo the procedure himself for you for free, no matter who did the original Xiao procedure or where it was performed.” Now, I would like to extend this policy internationally. I will redo the Xiao procedure for free for all children in the trial of Tuite et al. who did not attain success, including those who served as controls. I am confident that 80% of the kids will regain bladder and bowel control and voluntarily void within a year, or at least as well as in the trial results of Peters et al. The results could be better than 80%, but I have to be cautious in my predictions because these patients underwent intradural neurosurgery on the same location at least 2 times.

I also have to respond in this letter to part of Dr. Andrew Jea’s editorial, which was aimed at my hospital and the Xiao procedure directly. I built a hospital 5 years ago with 300 beds, and 30 beds have been dedicated to helping patients with spinal cord injury and spina bifida undergo the Xiao procedure in connection with 3 major charity organizations for disabled children in China. All patients who undergo the Xiao procedure only pay $8000 US or less for all costs, and many poor people do not pay anything. My hospital and I have not “capitalized on medical tourism, where despairing foreigners, including Americans, would pay out of pocket to have this procedure performed” as stated in the editorial by Jea.

Lastly, I appreciate Dr. John R. W. Kestle’s comments. They are objective and helpful comments from an experienced surgeon. I welcome Dr. Kestle, and any other interested neurosurgeons, to team up with urologists and visit China, to scrub in with me for the Xiao procedure for 10 cases, and to follow up as many of these kids cured of spina bifida as you wish. Before the Xiao procedure, all patients with spina bifida were unable to experience any meaningful improvement in their bladder function or their urinary system; it would only get worse and worse until the patient died. The Xiao procedure is now as effective, safe, reliable, and simple as a hernia repair for restoring bladder function and voluntary voiding for the great majority of kids with spina bifida, as long as the crossover anastomosis is satisfactory. Most fortunately, there are already a dozen successful cases of the Xiao procedure in the “polarizing” soil of the US, which preserves hope for millions of desperate kids with spina bifida and their parents.

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References