SELECTED ABSTRACT

Ventriculoperitoneal shunt infections and re-infections in children: a multicentre retrospective study

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Abstract

Purpose

Ventriculoperitoneal shunt (VPS) is the most common treatment modality for hydrocephalus. However, VPS infection is a common and serious complication with high rates of mortality and morbidity. The objective of this study was to investigate causative agents and the management of VPS infections and to identify risk factors for re-infection in children.

Materials and methods

Retrospective, multicentre study on patients with VPS infection at paediatric and neurosurgery departments in four tertiary medical centres in Turkey between January 2011 and September 2014.

Results

A total of 290 patients with VPS infections were identified during the study period. The aetiology of hydrocephalus was congenital malformations in 190 patients (65.5%). The most common symptom of shunt infection was fever in 108 (37.2%) cases. At least one pathogen was identified in 148 VPS infections (51%). The most commonly isolated pathogen was coagulase-negative staphylococci, which grew in 63 cases (42.5%), followed by Pseudomonas aeruginosa in 22 cases (14.9%), Klebsiella pneumoniae in 15 cases (10.1%), and Staphylococcus aureus in 15 cases (10.1). The median duration of VPS infection was 2 months (range, 15 days to 60 months) after insertion of the shunt, with half (49.8%) occurring during the first month. VPS infection was treated by antibiotics and shunt removal in 211 cases (76.4%) and antibiotics alone without shunt removal in 65 patients (23.5%). Among the risk factors, CSF protein level greater than 100 mg/dL prior to VPS insertion was associated with a potential risk of re-infection (OR, 1.65; p =.01).

Conclusion

High protein levels (>100 mg/dL) before the re-insertion of a VPS may be a risk factor for VPS re-infection.

Commentary

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TVentricular peritoneal shunting is common neurosurgical procedure routinely performed for hydrocephalus in children and adults. The incidence of shunt infections is a serious complication. Any noninvasive methods available to identify those shunts that will get reinfected prior to re-insertion is a valuable tool. This review and meta-analysis has identified that identifying a high level of CSF protein is an indication that early re-infection is a risk factor. This may prompt change of practice to treat the infection for longer, use an external ventricular drain for a longer period of time and waiting till the levels are suitably low.

The most important factors to be considered in shunt surgery needs to be emphasised repeatedly, and principles of shunt insertion followed rigorously to minimise the risk of infection. This involves listing the procedure first on the list, minimising theatre staff and clear indication to reduce passage of personnel through theatre. The surgeon should be experienced in shunt surgery. Meticulous skin preparation and draping and glove change after preparation, skin incision and shunt handling. No touch technique and shunt priming with an antibiotic preparation unless antibiotic impregnated shunts are being used. A CSF sample should always be sent during ventricular catheterisation for a baseline value of cell counts and protein.

The clinical and cost-effectiveness of corticosteroid injection versus night splints for carpal tunnel syndrome (INSTINCTS trial): an open-label, parallel group, randomised controlled trial

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Published 20th October 2018 , Lancet 2018; 392: 1423–33

Background

Until now comparative effectiveness of steroid injection vs night splinting has not been compared in treating carpel tunnel syndrome

The Authors compared the two modalities of treatment in a primary care setting.

Methods

A randomised control trial was done involving 25 centres in UK primary heath care units from 17th April 2014 to 31st December 2016 with a total of 234 participants.118 had night splints and 116 had corticosteroid injection. Injection group had single injection of 20 mg methylprednisolone acetate (from 40 mg/mL) and the night splint group had a night-resting splint to be worn for 6 weeks.

The primary outcome was the overall score of the Boston Carpal Tunnel Questionnaire (BCTQ) at 6 weeks. Intention-to-treat analysis was used with multiple imputation for missing data, which was concealed to treatment group allocation.

Results

The BCTQ score was significantly better at 6 weeks in the corticosteroid injection group (mean 2·02 [SD 0·81]) than the night splint group (2·29 [0·75]; adjusted mean difference –0·32; 95% CI –0·48 to –0·16; p=0·0001). No adverse events were reported.

Conclusion

Based on above findings the author's concluded that "A single corticosteroid injection shows superior clinical effectiveness at 6 weeks compared with night-resting splints, making it the treatment of choice for rapid symptom response in mild or moderate carpal tunnel syndrome presenting in primary care."

Commentary

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Compared with compression neuropathies, such as tarsal tunnel, cubital tunnel, suprascapular syndromes and meralgia paresthetica, carpel tunnel syndrome is the commonest compression neuropathies encountered in clinical practice.

Mainly with modern life styles with computers and work related activities, predominant diabetes, osteoarthritis, and past injuries all seem to be risk factors for developing the disease. The disease is commonly diagnosed and managed by many professionals including, rheumatologists,

Neurologists, orthopaedic surgeons, general surgeons, physiotherapists, general practitioners, and neurosurgeons, hence there is difference in opinion on how this is best managed. The gold standard of managing advance disease remain surgical decompression of carpel tunnel, however there is less consensus on best managing early and moderate disease. Non-operative management include analgesics, local analgesic creams, physiotherapy, lifestyle modification, steroid injections and night splint.

Are steroid injections better than night splints in managing early disease?

Linda S Chesterton et al, through the above RCT (Randomised control trial) published in Lancet tried to answer the question. It appears according to her results the steroid injection appear to be better than night splint and patients have a better tolerance with the injection. Should this evidence change our clinical practice?

A comment published by Isam Atroshi on the above article in Lancet sums up this well (www.thelancet.com Vol 392 October 20, 2018 (1383-1384) as given below,

"This trial might justify a change in clinical practice in that patients with mild or moderate carpal tunnel syndrome can choose a single steroid injection in primary care instead of night splinting. A policy of initial treatment with steroid injection and considering surgery in case of inadequate improvement or recurrence of symptoms is reasonable and supported by evidence."

Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable.

Whitehead AL, Julious SA, Cooper CL, Campbell MJ. Stat Methods Med Res. 2015;25(3):1057–1073. doi:10.1177/0962280215588241

Keywords: Pilot trial; RCT; sample size; power; continuous outcome

Abstract

Sample size justification is an important consideration when planning a clinical trial, not only for the main trial but also for any preliminary pilot trial. When the outcome is a continuous variable, the sample size calculation requires an accurate estimate of the standard deviation of the outcome measure. A pilot trial can be used to get an estimate of the standard deviation, which could then be used to anticipate what may be observed in the main trial.

However, an important consideration is that pilot trials often estimate the standard deviation parameter imprecisely. This paper looks at how we can choose an external pilot trial sample size in order to minimise the sample size of the overall clinical trial programme, that is, the pilot and the main trial together. We produce a method of calculating the optimal solution to the required pilot trial sample size when the standardised effect size for the main trial is known. However, as it may not be possible to know the standardised effect size to be used prior to the pilot trial, approximate rules are also presented. For a main trial designed with 90% power and two-sided 5% significance, we recommend pilot trial sample sizes per treatment arm of 75, 25, 15 and 10 for standardised effect sizes that are extra small (0.1), small (0.2), medium (0.5) or large (0.8), respectively.

Commentary

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Pilot studies play an important role in estimating parameters necessary to calculate required sample sizes for research studies, especially in clinical trials. However, pilot studies, due to inherent small sample sizes, may produce imprecise estimates of these parameters. In this article the authors investigate existing methods that allows a researchers to adjust the sample size by adjusting for imprecise estimates and several rules of thumb commonly used. Furthermore, in many studies, pilot studies are considered as standalone studies conducted only to obtain estimates of parameters necessary for sample size calculations for main study which makes it difficult to minimize the overall number sample size needed for both pilot study and the main study. Therefore, the authors provide an interesting approach that considers the pilot study as part of the main study and a novel method to estimate the optimal pilot trial sample size that minimizes the overall sample size for a given main trial. However, application of these methods are demonstrated only for comparison of means and for known standardized effect size.

Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer (TAILORx trial)

Sparano JA, et al. New England Journal of Medicine. 2018;379(2):111-21.

Background

The recurrence score based on the 21-gene breast cancer assay (Oncotype DX) predicts chemotherapy benefit if it is high and a low risk of recurrence in the absence of chemotherapy if it is low; however, there is uncertainty about the benefit of chemotherapy for most patients, who have a midrange score (intermediate risk).

Methods

A prospective trial involving 10,273 women with hormone-receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative, axillary node–negative breast cancer was performed. Of the 9719 eligible patients with follow-up information, 6711 (69%) had a midrange recurrence score of 11 to 25 and were randomly assigned to receive either chemoendocrine therapy or endocrine therapy alone. The trial was designed to show noninferiority of endocrine therapy alone for invasive disease–free survival (defined as freedom from invasive disease recurrence, second primary cancer, or death).

Results

Endocrine therapy was noninferior to chemoendocrine therapy in the analysis of invasive disease–free survival (hazard ratio for invasive disease recurrence, second primary cancer, or death [endocrine vs. chemoendocrine therapy], 1.08; 95% confidence interval, 0.94 to 1.24; P=0.26). At 9 years, the two treatment groups had similar rates of invasive disease–free survival (83.3% in the endocrine-therapy group and 84.3% in the chemoendocrine-therapy group), freedom from disease recurrence at a distant site (94.5% and 95.0%) or at a distant or local–regional site (92.2% and 92.9%), and overall survival (93.9% and 93.8%). The chemotherapy benefit for invasive disease–free survival varied with the combination of recurrence score and age (P=0.004), with some benefit of chemotherapy found in women 50 years of age or younger with a recurrence score of 16 to 25.

Conclusions

Adjuvant endocrine therapy and chemoendocrine therapy had similar efficacy in women with hormone-receptor–positive, HER2-negative, axillary node–negative breast cancer who had a midrange 21-gene recurrence score, although some benefit of chemotherapy was found in some women 50 years of age or younger.

Commentary

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Findings from the this TAILORx trial has shown that for approximately 70% women with hormone receptor positive, HER2-negative, axillary lymph node–negative breast cancer, treatment with chemotherapy and hormone therapy after surgery is not more beneficial than treatment with hormone therapy alone.

These results give good-quality data to inform personalized treatment recommendations for women as it confirms that using Oncotype DX test to assess the risk of cancer recurrence can spare women unnecessary treatment if the test indicates that chemotherapy is not likely to provide benefit.

Based on evidence from earlier trials, women in the trial who had a score in the low-risk range (0–10) received hormone therapy only, and those who had a score in the high-risk range (26 and above) were treated with hormone therapy and chemotherapy. Women in the trial who had a score in the intermediate range (11–25) were randomly assigned to receive hormone therapy alone or hormone therapy with adjuvant chemotherapy.

The researchers found that invasive disease-free survival and overall survival were very similar in the two groups. They also confirmed that women with a score of 0–10 had very low recurrence rates with hormone therapy alone at nine years (3%). In addition, they found that women with a score of 26–100 had a distant recurrence rate of 13% despite receiving both chemotherapy and hormone therapy. This finding indicates the need to develop more effective therapies for women at high risk of recurrence. However, premenopausal women and those younger than 50 years old at the higher end of the intermediate-risk range (16–25), the results showed

there may be a small benefit from chemotherapy, and thus these women should be considered for chemotherapy.

Although Oncotype Dx test has been made available in Sri Lanka recently it comes at a significant cost to the patient. The cost of approximately Rs. 800,000/= it is way beyond the affordability of many Sri Lankan patients. However, chemotherapy also comes at a cost; both the cost of chemotherapy agents and major side effects which may require expensive therapy including ICU care for some patients. In addition, there are many new and cheaper alternative genomic profiling tests becoming available in the market (e.g. EndoPredict, Prosigna, Mammostrat, etc.). As these cheaper tests become more widespread certainly there is hope for 'average' Sri Lankan patients to get the benefit of genetic risk profiling and to receive personalized medicine.