

Evidence-based protection medicine therapy of brain injured patients

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ABSTRACT: OBJECTIVE Reviews the domestic and foreign protection medicine treatment brain to injure the patient foresightedness stochastic double blind clinical research, for soon develops the similar province scientific research to set up a topic to prepare.

METHODS Draws support specialized database: Cochrane in library homepage RCT database (E-mail: Injuries@ shtm. Ac. Uk), wanfang databases digitization periodical, Qinghuatongfang CHKD periodical entire library. In the comparison, the induction carries on the analysis with in the extract related content foundation.

RESULTS Collects overseas to has completed with the medicine treatment brain injure medicine treatment related system appraises 6; domestic related memoir 3, translation 3, special course 6. Domestic related memoir demonstration, The hydrochloride naloxone, the magnesium ion, the glycerol and fructose and so on injure the patient to the brain to be effective; But overseas has completed in more than 200 clinical multi- central stochastic double blind foresightedness research, The unusual medicine was confirmed injures the patient to the brain to have the affirmation the curative effect.

CONCLUSION Some many factors disturbance clinical research effect. Improves this kind of research the methodology is removes the disturbance factor the effective method. Must observe the principle below this kind of clinical research process: (1) Must be the stochastic double blind foresightedness clinical research; (2) The clinical treatment must standardize; (3) Collects the clinical material to have objective to be strict; (4) Is clear about the medicine effective treatment window; (5) Is clear about the medicine to organize the Chinese native medicine density and the security in sickness human brain; (6) GOS (Glasgow Outcome Scale) to take the curative effect judgment primary standard; (7) Wound latter 6 months achievement curative effect judgment time.

KEY WORDS: evidence-based medicine; brain injure; protection medicine treatment

循证护保性药物治疗颅脑损伤

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摘要: 目的 复习国内外保护性药物治疗颅脑损伤病人前瞻性随机双盲临床研究, 为即将开展同类型的省科研立项课题做准备。**资料与方法** 所借助的专业数据库: Cochrane 图书馆网页中的 RCT 数据库 (E-mail: injuries@ shtm. ac. uk)、万方数据库数字化期刊、清华同方 CHKD 期刊全文库。在比较、归纳和摘录有关内容的基础上进行分析。**结果** 搜集到国外已完成与药物治疗颅脑损伤药物治疗有关的系统评价 6 个; 国内有关研究报告 3 篇、译文 3 篇、专题讲座 6 篇。国内有关研究报告显示, 盐酸纳洛酮、镁离子、甘油果糖等对颅脑损伤病人有效; 而国外已完成的 200 多项临床多中心随机双盲前瞻性研究中, 少有药物被证实对颅脑损伤病人有肯定的疗效。**结论** 有诸多因素干扰临床研究效果。改进本类研究的方法学是排除干扰因素的有效方法。在本类临床研究过程中应当遵守以下原则: ①必须是随机双盲前瞻性临床研究; ②临床治疗必须规范化; ③收集临床资料必须客观严格; ④明确药物有效治疗窗; ⑤明确药物在病人脑组织中药物浓度和安全性; ⑥GOS(格拉斯哥预后评分 Glasgow Outcome Scale) 作为疗效判断基本标准; ⑦伤后 6 个月作为疗效判断时间。

关键词: 循证医学; 颅脑损伤; 保护性药物治疗

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Now our country, the brain injure disease incidence rate already surpassed 100/100,000 population. The heavy brain injure mortality rate and crippling rate stays at a high level. The total mortality rate maintains continuously at 30%~50% about. After wards the brain injure is causes the patient to cripple with the death important attribute. Some research indicated, after the wound occurs in the number day even number month, afterwards the brain injure still was carrying on. Therefore, after

prevented the wound afterwards the brain injure is the brain protection treatment goal. This article follows the card clinical direction through the review, By understands the domestic and foreign protection medicine treatment brain injure research the survey and the matters needing attention.

1 Material and method

1.1 literature selected standard (1) Brain injure clinical processing Chinese native medicine application aspect literature;

(2) Follows the card clinical guide; (3) Detailed introduction operation flow and principle request literature; Rejects the standard: (1) Has not introduced the medicine research the literature; (2) Pure economic analysis literature.

1.2 draws support database Cochrane in library homepage RCT database (E-mail: Injuries@shtm. Ac. Uk), wanfang databases digitization periodical, Qinghuatongfang CHKD periodical entire library.

1.3 methods In the comparison, the induction carries on the analysis with in the extract related content foundation.

2 Result

2.1 literature collection result collects overseas to has completed with the medicine treatment brain injure related system appraises 6, domestic related memoir 3, Translation 3, Special course 6.

2.2 domestic related memoirs

2.2.1 Hydrochloride naloxone in the domestic and foreign massive research proof brain wound cerebellum organization the meconium peptide content exceptionally changed in recent years has the possibility to participate in afterwards the brain wound being taken bad the process. The correlation research discovery experimental brain injures the animal and the acute brain injure in the patient cerebrospinal fluid β_2 neifeitai and qiangfeitai content obviously elevates, And concerns with the state of an injury with the prognosis. After the further research proof β_2 neifeitai and qiangfeitai possibly participated in the brain injure afterwards nerve function injure. The findings indicate^[1], After the hydrochloric naloxone can effectively block afterwards the brain harm which the acute brain injure self-source the meconium peptide content exceptionally elevates creates, After like can effectively maintain the brain wound the blood pressure and the brain pours into the pressure, the control cerebrospinal fluid pressure, reduces the hydro-cephalus, improvement brain metabolism and so on, Specially regarding stupor and breath suppression patient, The hydrochloric naloxone has the fast reversal consciousness barrier, relieves the breath suppression the function; The early application large dose hydrochloric naloxone can obviously reduce the acute brain to injure the patient mortality rate, the promotion cranial nerve function restores, the improvement forward quality of life condition, And has the quite reliable security.

2.2.2 Magnesium ions Brain organization magnesium ion participation cell many kinds of metabolism activity, mainly includes the cell sugar yeast solution, oxidized phosphorylation, in the cell breathes, DNA, RNA and protein synthesis and so on. After the heavy brain injure the magnesium ion drops may have a series of pathological reaction that, Causes the many kinds of enzyme activities to reduce, Line grain of in vivo massive Ca^{2+} gathers, Energy production barrier; Causes inside and outside the cell

Na^+ , the K^+ concentration gradient change, Causes the wound hydro-cephalus, Even loses to the Ca^{2+} adjustment ability, Causes in the cell the Ca^{2+} density excessively to be high, Creates the neuron afterwards the toxic injure. The findings indicate^[2], the early prompt supplement magnesium ion can promote the heavy brain to injure the patient nerve function restoration, Reduces crippling rate, Improves the forward quality of life, And has the quite reliable security.

2.2.3 Glycerol and fructose Brain injure has the blood rheology harm, the blood viscosity elevates, the performance after the erythrocyte sedimentation rate, the blood corpuscle specific volume, the whole blood compared to the viscosity, the whole blood returns to original state compared to the viscosity, the blood plasma compared to the viscosity, the red blood cell gathers the index wound comprehensively to elevate. The findings indicate^[3], after the glycerol and fructose can effectively improve the brain injure the blood rheology condition, to improves the microcycle, reduces afterwards the hydro-cephalus and reduces the cerebrospinal fluid pressure to have the vital clinical significance.

2.3 Overseas has completed with the medicine treatment brain injure related system review (SR)

2.3.1 calcium channel sretarder Acute brain injure is the main reason which the patient lethal and cripples. The partial scholars have used the calcium channel to oppress the anti-medicinal preparation to prevent the wound cerebellum vasospasm, Maintenance brain blood current capacity, Prevents afterwards the brain harm. Including four randomized controlled trials (RCT) the system review (SR) indicated that, The calcium channel oppresses the anti-medicinal preparation to injure patient's treatment function to the acute brain not to be inaccurate. Although in the intervention group nimmo is even not good responds the increase, Possible to prompt this medicine to be harmful to certain patients, But it under the arachnoidea the cavity bleeds patient's treatment after the brain flesh wound to be beneficial.

2.3.2 aminossteroids hormone Acute brain injure cell membrane lip in peroxideation, was considered causes one of brain afterwards harm mechanisms. The animal experimentation result indicated the amino steroid hormone can suppress the lip in peroxide the production, Possible to improve the brain flesh wound patient's prognosis. The SR result thought that, At present has not supported the conventional application aminosteroid hormone treatment acute brain injure the evidence.

2.3.3 Anti-epileptics brains injure early time epileptic paroxysm possibly causes afterwards the brain harm, this is because epilepsy may increase metabolism, makes the cerebrospinal fluid pressure to advance with the nerve hands over the nature excessive release the result. 10 RCT compiles the result to demon-

strate that, Preventive to reduces the acute brain injure future trouble early time epilepsy using the antiepileptic to manifest suddenly effectively, but at present does not have the evidence to indicate can reduce the later period epilepsy the occurrence and the reduced mortality rate and the improvement nerve function flaw symptom. At present uses in after appraising the brain injure the preventive application antiepileptic treatment true profit evidence is insufficient.

2.3.4 Barbitone kind of medicine cerebrospinal fluid pressure advances is one of heavy brain injure important illness complications, concerns with patient's high mortality rate. A Barbitone kind of medicine reduces the cerebrospinal fluid pressure through the suppression brain metabolism and the reduced brain blood current capacity. However, a Barbitone kind of medicine also reduces the blood pressure, therefore possibly pours into the pressure to the brain to produce not good affects. The SR result showed that, at present does not have the evidence to indicate the Barbitone therapy may enhance the heavy brain to injure patient's prognosis.

2.3.5 mannitol Mannitol to reverse the acute hydro-cephalus to have the remarkable function, but it continued in the treatment to the heavy brain injure the validity still to have the dispute. Some evidence demonstrated, Lengthens the mannitol medicine response time possibly to cause it to enter in the brain by the blood, and possibly causes the osmosis to reverse but increases the cerebrospinal fluid pressure. The SR result indicated that, the mannitol is possibly helpful in reduces the patient mortality.

2.3.6 nutritions Supports brain flesh wound increase organism metabolism responded, nutrition demand increase. Provides the enough nutrition support to be possible to improve patient's prognosis, But needs to give the nutrition support the best way (outside the entire intestines nutrition to support either stomach and intestines nutrition supports) and most at the right moment between(for example early time or later period) carries on the review and the review. And the lethality influence RCT findings demonstrated in view of the different nutrition support plan to brain flesh wound patient crippling rate that, the early time gives the nutrition support treatment possibly brings one kind of good development tendency to the patient survival and the disabled restoration (to bring into line with 6 RCT).

2.4 Overseas other literature situations

2.4.1 Sterilization medicines brain injure, blood brain barrier destruction, in the circumference blood single nucleus macrophage, the neutral granular cell and so on infiltrate to the brain essence, cell factor synthesis increase, the adherency member expresses excessively, lies between leads a series of inflammation injure. Therefore, after the anti-phlogosis is prevents the brain

injure one of after wards injure important countermeasures. Uses in the sterilization medicine which the brain protects studying maturely has one kind of synthesiscannaboid preparation dexaminol, entered II issue of security curative effect experiment^[4].

2.4.2 Nerves nutritions factor Nerve nutrition factor mainly includes the nerve growth factor, the brain source nerve nutrition factor, the nerve nutrition factor -3. They to the neuron growth, the differentiation, and the function maintain the vital role. Recently studied indicated, after brain injure self-source nerve nutrition factor expression increase, but stimulates in advance induces the nerve nutrition factor expression to be able to strengthen the neuron to staying power which injures once more, prompts the nutrition factor expression increase is the neuron resistance deficienting blood injure normal protection mechanism. Gives extraneous source nature brain source nerve nutrition factor and nerve growth factor can protect the central nervous system resistance deficienting blood injure^[5]. Its mechanism is possible and in the maintenance cell calcium stable state and the elimination free radical concerns.

2.4.3 Hemoglobins preparations Hemoglobins preparations is the gene recombination orchemistry decorates after the hemoglobin, can unify the carbon monoxide (CO), elevates the blood pressure, increases the heart, the brain and so on the important spot oxygen partial pressure^[6]. The early time using hemoglobins preparations can guarantee the wound brain injures the patient important internal organs oxygen for supplies with the blood, for further processes strives for the time. At present, had the very many hemoglobins preparation to enter II issue of or III issue of clinical test. Hands over the association aspirin double hemoglobin already through III issue of clinical security curative effect experiment^[7], and authorizes in Europe to put in the market. Another kind of synthesis preparation hyperpure polymerization ox blood red-paintedegg white liquor entered II issue of clinical test.

3 Discusses

3.1 Successes the experiences in order to can obtain the reliable high grade clinical research evidence, this kind of research adopts follows the card medicine system review the method quite to be appropriate, namely: Uses the big sample stochastic double blind control experiment the research technique; multi-central union experiment; carries on the system review to the multi-central similar research result. Most recent several years, you roentgen national multi-centers double blind clinical research groups organized by the gold to carry on "the Jin ERlun (hydrochloric naloxone) to treat the acute brain to injure the patient stochastic double blind multi-centers foresightedness clinical research" to carry out the similar research for us to make the demonstration,

its experience is worth profiting from.

3.2 Disturbances clinical research effect factor overseas has completed more than 200 clinical multi-central stochastic double blind foresightedness research, but the unusual medicine was confirmed injures the patient to the brain to have the affirmation the curative effect, the scattered clinical report often is compared by the large-scale review case of illness the research institute denial. These medicines majority all are study the certificate effective medicine through the brain injure animal experimentation, is why invalid to the clinical practice research? Analyzes its reason, cannot remove the research methodology aspect to have the problem. For example: 1) statistical method whether does have the flaw. Looked from the literature report, uses statistical method many and varied. At present compares conforms to this kind of research procedure is: Uses the SPSS710 statistical analysis software package to carry on the statistical data for the correlation data material the grouping to pair t separately to examine and to count the material chi -examinations, obtains the P value with the precise probability law. 2) the brain injure animal model and the clinical brain injure between patient's difference; 3) between clinical various centers medical treatment and nursing level difference; 4) the brain injures between patient's state of an injury, the age, the merge wound, the pathology type and the individual state of health difference; 5) various centers the conventional processing difference and nurse the standardized degree to the acute wound brain injure the difference; 6) between the clinical various centers experiments the design the difference and is short of. Like whether takes the high cerebrospinal fluid pressure the most important target; Each group of between patients are whether balanced; In the experiment grades by the Glasgow Coma Scale (GCS) chooses the patient whether at the same time also rests on CT; Whether determines the group the clinical remarkable difference. 7) Specimen is whether enough. In multi-central union research, quite part of central case of illness samples are short in 5, this is an influence test result primary factor. 8) The medicine primary gives the medicine time after the brain injure wound. The overwhelming majority medicine all requests in the wound latter 4hours even 1 hour to give the medicine, this is not easy in the practice to achieve. 9) Medicine in brain medicine generation of dynamics unknown. In high blood medicine in density situation, In the brain medicine density is how many, Medicine and acceptor union degree, the brain Chinese native medicine half-life and so on these medicine generation of dynamics situations decided formulates gives the medicine plan the success or failure. 10) Experiments starts the preparatory work is whether full. Like draws up the principle which the experiment stops, How guarantees the medicine securely and so on. Above these factors all possibly are disturb the medicine treatment brain

injure clinical research effect the factor. Moreover, the heavy brain injures patient's cranial nerve Yuan injure to repair, the regeneration with difficulty or to be unable to regenerate, enormously increased the heavy brain injure treatment difficulty.

3.3 research methodology improvement for improves this kind of research the methodology, Most recent several year American state-run nerve disease and the stroke research institute invite 34 international famous brains to injure the expert, researcher, the pharmacy expert discusses together, Below pointed out must observe the principle in the clinical research process: (1) Must be the stochastic double blind foresightedness multi- centers clinical research; (2) The clinical treatment must standardize (the note: May "Brain Injure Clinical Treat and cure Guide" at present in our country according to Chief Editor Jiang Ji-yao^[8] the standard clinical treatment); (3) Collects the clinical material to have objective to be strict; (4) Is clear about the medicine effective treatment window; (5) Is clear about the medicine to organize the Chinese native medicine density and the security in sickness human brain; (6) GOS (Glasgow Outcome Scale) to take the curative effect judgment primary standard; (7) Wound latter 6 months achievement curative effect judgment time. Moreover, the domestic similar research should participation internationally to center, on the one hand might let the domestic research results soon obtain the overseas colleague's acknowledgement, on the other hand also may raise the domestic research level.

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