Safety Study of 20% Mannitol Infusion via Midline Catheter in Neurocritical Care Patients: Postprint

Authors: Qu Yuanyuan, Sun Yan, Zhu Liying, Li Honglei, Lin Baoqian, Zhang Zhe, Zang Xiaoying, Zang Xiaoying

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Abstract

Background: 20% mannitol is a hyperosmotic dehydrating diuretic used to reduce cerebral edema and intracranial pressure, commonly prescribed for neurocritical care patients. The solution is acidic and hyperosmotic. Midline catheters are widely used in clinical practice due to their low cost, simple operation, and fewer complications, serving as an economical and safe intravenous access for neurocritical patients. However, controversy persists regarding the types of solutions that can be safely infused through midline catheters.

Objective: To investigate the safety of administering 20% mannitol via midline catheters in neurocritical care patients.

Methods: A retrospective analysis was conducted on 262 neurocritical care patients who used midline catheters in the Neurological Intensive Care Unit (ICU) of Tianjin Medical University General Hospital from January 2019 to December 2022. General patient data were collected including gender, age, diagnosis, use of other irritant drugs, white blood cell count, platelet count, albumin, D-dimer, prothrombin time (PT), activated partial thromboplastin time (APTT), etc. Patients were divided into a mannitol group (n=89) and a non-mannitol group (n=173) based on whether they received mannitol infusion. Catheter dwell time and complication rates were compared between the two groups. Using the occurrence of catheter-related complications as the dependent variable, variables that might affect complication occurrence were included as independent variables in a binary logistic regression analysis.

Results: The catheter dwell time in the mannitol group was 16.50 (10.00, 26.00) days, and in the non-mannitol group was 17.00 (9.00, 26.00) days. There was no statistically significant difference in catheter dwell time between the two groups

(P>0.05). Regarding complication rates, the incidence of catheter-related complications in the mannitol group was 11.24% (10/89), including 5 cases of oozing (5.62%), 2 cases of leakage (2.25%), 2 cases of phlebitis (2.25%), 1 case of thrombosis (1.12%), and 1 case of catheter occlusion (1.12%). One case experienced both oozing and leakage simultaneously. The incidence of catheter-related complications in the non-mannitol group was 12.14% (21/173), including 7 cases of oozing (4.05%), 4 cases of leakage (2.31%), 3 cases of phlebitis (1.73%), 2 cases of thrombosis (1.16%), 2 cases of fibrin sheath (1.16%), 4 cases of catheter occlusion (2.31%), and 1 case of catheter dislodgement (0.58%). One case experienced both phlebitis and leakage, and another case experienced both leakage and thrombosis simultaneously. There was no statistically significant difference in complication rates between the two groups (P>0.05). Binary logistic regression analysis showed that catheter dwell time (OR=1.022, 95%CI=1.004~1.041) and PT (OR=0.833, 95%CI=0.702~0.990) were influencing factors for catheter-related complications (P<0.05).

Conclusion: Administering 20% mannitol via midline catheters in neurocritical care patients is safe, with no significant differences in catheter dwell time or complication rates between the mannitol and non-mannitol groups. This approach warrants clinical promotion and application.

Full Text

Study on the Safety of Midline Catheters for Infusion of 20% Mannitol in Neurocritical Care Patients

Qu Yuanyuan[1], Sun Yan[1], Zhu Liying[1], Li Honglei[1], Lin Baoqian[1], Zhang Zhe[1], Zang Xiaoying[2]*

[1]Department of Neurology, Tianjin Medical University General Hospital, Tianjin 300052, China
[2]School of Nursing, Tianjin Medical University, Tianjin 300203, China

Corresponding author: Zang Xiaoying, Professor/Doctoral supervisor; E-mail: xiaoyingzang@163.com

Abstract

Background: 20% mannitol is a hypertonic dehydrating diuretic used to relieve brain edema and reduce intracranial pressure, representing one of the most commonly administered medications in neurocritical care patients. The solution has acidic and hypertonic properties. Midline catheters have gained widespread clinical application due to their low cost, simple operation, and low complication rates, serving as an economical and safe infusion pathway for neurocritical care patients. However, controversy remains regarding the types of solutions that can be safely infused through midline catheters.

Objective: To investigate the safety of infusing 20% mannitol through midline catheters in neurocritical care patients.

Methods: A retrospective analysis was conducted on 262 neurocritical care patients who received midline catheters in the Neurology Intensive Care Unit (ICU) of Tianjin Medical University General Hospital between January 2019 and December 2022. General patient data were collected, including gender, age, diagnosis, use of other irritant drugs, white blood cell count, platelet count, albumin, D-dimer, prothrombin time (PT), and activated partial thromboplastin time (APTT). Patients were divided into a mannitol group (n=89) and a non-mannitol group (n=173) based on whether they received mannitol infusion. Catheter indwelling time and complication rates were compared between the two groups. Binary logistic regression analysis was performed with catheter-related complications as the dependent variable and potential influencing factors as independent variables.

Results: The median catheter indwelling time was 16.50 (10.00, 26.00) days in the mannitol group and 17.00 (9.00, 26.00) days in the non-mannitol group, with no statistically significant difference (P>0.05). The incidence of catheter-related complications in the mannitol group was 11.24% (10/89), including 5 cases of bleeding (5.62%), 2 cases of exudate (2.25%), 2 cases of phlebitis (2.25%), 1 case of thrombosis (1.12%), and 1 case of catheter occlusion (1.12%), with one patient experiencing both bleeding and exudate simultaneously. In the non-mannitol group, the complication rate was 12.14% (21/173), comprising 7 cases of bleeding (4.05%), 4 cases of exudate (2.31%), 3 cases of phlebitis (1.73%), 2 cases of thrombosis (1.16%), 2 cases of fibrin sheath (1.16%), 4 cases of catheter occlusion (2.31%), and 1 case of catheter dislodgement (0.58%), with one patient developing both phlebitis and exudate, and another experiencing both exudate and thrombosis. No significant difference in complication rates was observed between the two groups (P>0.05). Binary logistic regression analysis identified catheter indwelling time (OR=1.022, 95%CI=1.004~1.041) and PT (OR=0.833, 95%CI=0.702~0.990) as influencing factors for catheter-related complications (P<0.05).

Conclusion: Infusing 20% mannitol through midline catheters in neurocritical care patients is safe, with no significant differences in catheter indwelling time or complication rates compared to non-mannitol infusions. This practice is worthy of clinical application and promotion.

Keywords: Critical care; Neurocritical care; Midline catheter; 20% Mannitol; Catheter indwelling time; Complication; Retrospective analysis

Introduction

Neurocritical care patients refer to individuals with stroke, encephalitis or meningitis, traumatic brain injury, spinal neuromuscular diseases, brain-derived mul-

tiple organ dysfunction, and those requiring specialized treatments, all accompanied by increased intracranial pressure, coma, mental disorders, status epilepticus, or respiratory pump failure. These patients are characterized by acute onset, severe conditions, large infusion volumes, and numerous irritant medications. Normal human blood pH ranges from 7.35 to 7.45, with plasma osmotic pressure between 280 and 310 mOsm/L. Infusion of solutions with osmotic pressure exceeding 600 mOsm/L through peripheral veins can cause chemical phlebitis within 24 hours.

20% mannitol, a hypertonic dehydrating diuretic for reducing cerebral edema and intracranial pressure, is a commonly used medication in neurocritical care patients, with a pH of 5.0~7.0 and osmotic pressure of 1,098 mOsm/L, classifying it as an acidic, hypertonic drug. Due to its hypertonic nature, peripheral venous infusion increases the risk of phlebitis to 20.0%~41.7%, making the selection of an appropriate venous access route critically important. While Peripherally Inserted Central Catheter (PICC) lines are not widely used in neurocritical care patients due to higher costs and the requirement for chest radiography to confirm catheter position, midline catheters (also known as Midlines), measuring 20~30 cm in length and inserted from the antecubital fossa region into the basilic, cephalic, or brachial veins with the tip located in the axillary vein thoracic segment or subclavian vein, have been validated as an economical and safe infusion pathway for neurocritical care patients due to their low cost, simple operation, and low complication rates. Multiple studies have demonstrated that compared to central venous catheters, midline catheters have lower complication rates and reduced economic costs, while offering lower complication rates and avoiding the pain of repeated punctures associated with peripheral venous catheters. Some research has even identified modified midline catheters as the most suitable infusion method for critically ill stroke patients.

However, controversy persists regarding the appropriate applications of midline catheters. The Infusion Nurses Society (INS) Standards of Practice states that midline catheters should not be used for continuous infusion of vesicants, parenteral nutrition (PN), or fluids with extreme pH and osmotic pressure values. Conversely, the Expert Consensus on Clinical Application of Midline Venous Catheters indicates that hypertonic and corrosive drugs may be infused intermittently or for short durations (with caution due to undetected extravasation risk). Therefore, investigating the safety of infusing 20% mannitol through midline catheters holds significant importance for guiding clinical practice. This retrospective analysis of neurocritical care patients with midline catheters examines differences in catheter indwelling time and complication rates between mannitol and non-mannitol groups, with binary logistic regression analysis of potential complication factors to further explore safe midline catheter use and guide nursing practice.

Methods

1.1 Study Subjects A retrospective analysis was conducted on neurocritical care patients hospitalized in the Neurology Intensive Care Unit (ICU) of Tianjin Medical University General Hospital between January 2019 and December 2022, who provided informed consent and underwent midline catheter placement. Inclusion criteria were: age $\geq$ 18 years, confirmed neurological disease, and meeting midline catheter placement standards without contraindications. Exclusion criteria included catheter tip position in the superior vena cava as shown by post-placement X-ray. The 262 patients were divided into a mannitol group (n=89) and non-mannitol group (n=173) based on 20% mannitol usage. This study was approved by the Ethics Committee of Tianjin Medical University General Hospital (approval number: IRB2024-YX-266-01), and all patients provided informed consent.

1.2 Materials and Procedures **1.2.1 Materials:** Shubeikang midline venous catheters (4 Fr, 30 cm length, 10 mL/min flow rate), disposable central venous catheter disinfection kits, bedside ultrasound machines, and treatment carts.

1.2.2 Catheterization and Maintenance: Placement was performed by qualified nurses. Patients were positioned supine with the arm abducted 90° to fully expose the limb for puncture, with the healthy side preferred in hemiplegic patients. Bedside vascular ultrasound was used to identify the puncture vein, and the insertion length was measured from the puncture site along the venous path to the ipsilateral midclavicular line. The puncture site was disinfected using 75% alcohol swabs in a spiral motion for three rounds, covering 20 cm above and below and extending to the arm margins and lateral elbow, followed by three rounds of disinfection with 0.5% iodophor swabs or 2% chlorhexidine gluconate swabs using the same method. Sterile packages were opened, sterile gowns and gloves were donned, and aseptic non-touch technique (ANTT) was employed during puncture. The catheter was pre-flushed with normal saline, and the modified Seldinger technique (MST) was used under ultrasound guidance to advance the catheter to the measured length. After connecting a positive pressure connector, the catheter was secured in a U-shape or L-shape with a transparent dressing. Dressing changes were performed 24 hours post-placement and weekly thereafter, with immediate replacement for contaminated, wet, or lifted dressings. Nurses received standardized training, and both groups received identical catheterization and maintenance procedures from the same nursing team.

1.3 Data Collection **1.3.1 Patient Basic Data:** Included gender, age, diagnosis, use of other irritant drugs, white blood cell count, platelet count, albumin, D-dimer, prothrombin time (PT), and activated partial thromboplastin time (APTT).

1.3.2 Catheterization-Related Data: Included puncture limb, puncture site, vein selection, catheter tip position, and catheter indwelling time (calcu-

lated as days from catheter insertion to removal).

1.3.3 Catheter-Related Complication Rates: Included bleeding, exudate, phlebitis, thrombosis, fibrin sheath, catheter occlusion, and catheter dislodgement. Complication definitions were: (1) Bleeding: blood oozing from the puncture site after 48 hours; (2) Exudate: light yellow or clear fluid leakage from the puncture site; (3) Phlebitis: assessed using the "Phlebitis Scale" from the Expert Consensus; (4) Thrombosis: symptomatic thrombosis characterized by redness, swelling, and pain in the ipsilateral upper limb, shoulder, or neck, with limb swelling, increased skin temperature, or color changes such as erythema; (5) Fibrin sheath: "mechanical valve" phenomenon where fluid could be infused but difficult to withdraw, with ultrasound showing thickened catheter walls; (6) Catheter occlusion: partial or complete blockage indicated by inability to withdraw blood return, slow blood return, slow infusion rate, inability to flush or infuse, frequent pump occlusion alarms, or infusion site leakage, swelling, or exudate; (7) Catheter dislodgement: catheter external displacement exceeding 3 cm. Daily assessments were performed and recorded by responsible nurses, with suspected complications evaluated by two intravenous therapy specialist nurses blinded to mannitol group assignment, and a third evaluator consulted for discrepancies.

1.4 Statistical Methods Data were analyzed using SPSS 20.0 software. Normally distributed continuous variables were expressed as mean ± standard deviation ($\bar{x}\pm s$) and compared using independent samples t-tests. Non-normally distributed continuous variables were expressed as median (P25, P75) and compared using Mann-Whitney U tests. Categorical variables were expressed as frequencies and percentages and compared using ^{2} tests. Binary logistic regression analysis was performed with catheter-related complications as the dependent variable and potential influencing factors as independent variables. Statistical significance was set at $P<0.05$.

Results

2.1 Comparison of Basic Patient Data Among the 262 patients (138 male, 124 female) aged 16-92 years, diagnoses included cerebral infarction (152 cases, 58.02%), intracranial infection (34 cases, 12.98%), epilepsy (19 cases, 7.25%), myasthenia gravis (13 cases, 4.96%), Guillain-Barré syndrome (13 cases, 4.96%), and other conditions (31 cases, 11.83%). The mannitol group comprised 89 patients (53 male, 36 female) with a median age of 64 (17, 92) years, while the non-mannitol group included 173 patients (85 male, 88 female) with a median age of 67 (16, 92) years. As shown in , significant differences between groups were observed in disease diagnosis, use of other irritant drugs, and albumin levels ($P<0.05$), while no significant differences were found in gender, age, white blood cell count, platelet count, D-dimer, PT, or APTT ($P>0.05$).

2.2 Comparison of Catheterization-Related Data Both groups predominantly used right upper limb placement, puncture site 10 cm above the elbow, basilic vein selection, and catheter tip positioning in the axillary vein thoracic segment or subclavian vein. No significant differences were observed between groups in catheter indwelling time, puncture site, or vein selection (P>0.05). However, significant differences were found in puncture limb and catheter tip position (P<0.05), as shown in .

2.3 Comparison of Catheter-Related Complications The overall complication rate was 11.24% (10/89) in the mannitol group, comprising 5 cases of bleeding (5.62%), 2 cases of exudate (2.25%), 2 cases of phlebitis (2.25%), 1 case of thrombosis (1.12%), and 1 case of catheter occlusion (1.12%), with one patient experiencing both bleeding and exudate. The non-mannitol group had a complication rate of 12.14% (21/173), including 7 cases of bleeding (4.05%), 4 cases of exudate (2.31%), 3 cases of phlebitis (1.73%), 2 cases of thrombosis (1.16%), 2 cases of fibrin sheath (1.16%), 4 cases of catheter occlusion (2.31%), and 1 case of catheter dislodgement (0.58%), with one patient developing both phlebitis and exudate, and another experiencing both exudate and thrombosis. No significant differences were observed between groups in overall complication rates or individual complications (P>0.05), as detailed in .

2.4 Comparison of Clinical Data Between Complication and Non-Complication Groups Patients were divided into complication (n=31) and non-complication (n=231) groups. The complication group included 13 males and 18 females with a mean age of $58.9 \pm 21.0 years, while the non-complication group comprised 125 males and 106 females with a mean age of 62.4±$17.6 years. As shown in , no significant differences were observed between groups in gender, age, diagnosis, puncture limb, puncture site, vein selection, catheter tip position, or catheter indwelling time (P>0.05).

2.5 Binary Logistic Regression Analysis of Factors Influencing Catheter-Related Complications Binary logistic regression analysis was performed with catheter-related complications as the dependent variable (no=0, yes=1) and age, catheter indwelling time, serum albumin, PT, platelet count, D-dimer, gender, puncture limb, catheter tip position, and 20% mannitol infusion as independent variables (assignments shown in). The results indicated that catheter indwelling time (OR=1.022, 95%CI=1.004~1.041) and PT (OR=0.833, 95%CI=0.702~0.990) were influencing factors for catheter-related complications in neurocritical care patients (P<0.05), as presented in .

Discussion

3.1 Infusion of 20% Mannitol Through Midline Catheters Does Not Affect Catheter Indwelling Time Comparison between groups revealed no

statistically significant difference in catheter indwelling time between patients receiving 20% mannitol and those who did not. Although disease diagnoses differed between groups in this study, these differences did not affect complication rates. Research has demonstrated that modified midline catheters offer distinct advantages for hypertonic drug infusion, with indwelling times generally meeting patient needs. Italian nursing researcher FABIO et al. recommended midline catheters as optimal for patients requiring 10-30 days of infusion at the same site. In this study, catheter tips were positioned in the axillary vein thoracic segment or subclavian vein level, where blood flow rates of 350-900 mL/min represent a substantial increase from the 150-350 mL/min in the initial axillary segment, thereby expanding the drug compatibility range of midline catheters. Results also indicated that shorter coagulation times correlate with increased bleeding at puncture sites, necessitating enhanced observation and timely management to prevent catheter-related infections. Xue et al. similarly demonstrated that improved puncture and maintenance techniques for midline catheters can reduce complication rates.

3.2 Infusion of 20% Mannitol Through Midline Catheters Does Not Increase Catheter-Related Complication Rates Comparative analysis and regression modeling revealed no statistically significant difference in catheter-related complication rates between mannitol and non-mannitol groups. The Infusion Therapy Standards of Practice guidelines indicate that solutions with pH<5.0 or pH>9.0, high osmotic pressure, vesicants, or irritant drugs can cause extravasation. Current debate continues regarding the suitability of midline catheters for corrosive, hypertonic drugs. The INS Standards state that midline catheters should not be used for continuous vesicant infusion, PN, or fluids with extreme pH and osmotic pressure values, while some research suggests midline catheters are unsuitable for continuous corrosive drug therapy, parenteral nutrition, or fluids with osmotic pressure >900 mOsm/L. However, the Expert Consensus on Clinical Application of Midline Venous Catheters permits intermittent or short-term infusion of hypertonic and corrosive drugs (with caution regarding undetected extravasation risk). Increasing evidence supports the safety of modified midline catheters for irritant drug infusion. Studies have shown that positioning midline catheter tips in the axillary vein thoracic segment for parenteral nutrition infusion does not adversely affect vascular morphology, blood flow velocity, or volume, consistent with our findings. Other researchers analyzing factors influencing mannitol infusion complications through midline catheters identified tip positioning at the subclavian vein opening as a protective factor. Therefore, while 20% mannitol infusion through midline catheters does not increase complication rates, thorough pre-placement assessment is recommended, with catheter tip positioning at the subclavian vein level when infusing irritant drugs such as mannitol.

3.3 Increased Catheter-Related Complication Rates Associated with Longer Indwelling Times and Shorter Coagulation Times Controversy

persists regarding optimal midline catheter indwelling time. The Expert Consensus recommends 1-4 weeks, while some studies report indwelling times up to 49 days. The INS Standards caution against catheter removal based solely on dwell time, as optimal duration remains undetermined. Research demonstrates that enhanced catheter assessment and maintenance can prolong indwelling time. However, our findings indicate that extended indwelling time increases complication rates, consistent with Jin et al. Daily catheter assessment is therefore essential, with prompt removal of unused catheters, daily functional evaluation, and diligent maintenance. Once complications occur, timely interventions should be implemented. Additionally, patients with shorter coagulation times exhibit higher bleeding rates at puncture sites, requiring intensified observation and management during catheter dwell periods.

This retrospective analysis of neurocritical care patients demonstrates that infusing 20% mannitol through midline catheters is safe, with no significant differences in indwelling time or complication rates compared to non-mannitol infusions, warranting clinical promotion and application. However, this study has limitations. First, as a retrospective study, baseline differences in disease diagnosis existed between groups, and factors such as mannitol dosage, treatment duration, and vascular risk factors like hypertension and diabetes were not analyzed, potentially introducing bias. Second, the sample size was relatively small. Future large-sample, multicenter, high-quality randomized controlled trials are needed for validation.

Author Contributions

Qu Yuanyuan: Conceptualization, study design, implementation, and manuscript writing. Li Honglei and Lin Baoqian: Data collection and collation. Zhu Liying: Statistical analysis, table preparation, and presentation. Sun Yan and Zhang Zhe: Manuscript revision. Zang Xiaoying: Quality control, review, overall responsibility, and supervision.

Conflict of Interest: The authors declare no conflict of interest.

ORCID IDs:
Qu Yuanyuan: https://orcid.org/0009-0004-7604-4701
Zang Xiaoying: https://orcid.org/0000-0001-6953-1721

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Note: Figure translations are in progress. See original paper for figures.