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# Survey on medication administration to patients receiving parenteral nutrition

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# Abstract

**Background**: Multiple medications are often administered simultaneously during parenteral nutrition, typically using a three-way stopcock. Therefore, care must be taken regarding infection control during catheter handling and changes in drug compositions within the catheter. Consequently, flushing is performed before and after drug administration via the side port to flush the inside of the three-way stopcock and the catheter lumen. However, detailed management methods for flushing procedures are not specified in guidelines, and it is presumed that many facilities leave this to individual discretion.

**Objective**: A questionnaire survey was conducted on the actual practice of administering parenteral nutrition. This research was performed with the aim of contributing to the appropriate use of drugs and infection control in the future and also assisting in the formulation of guidelines.

**Methods**: A request for survey cooperation was sent to hospitals belonging to the Osaka Prefecture and Nara Prefecture Societies of Hospital Pharmacists. A questionnaire survey was conducted using Google Forms from September 2024 to January 2025, targeting 75 hospitals that responded positively to participate. Approval was obtained from the Ethics Committee of the Faculty of Pharmacy, Osaka Otani University (BE-0096-24).

**Results**: Responses were obtained from 63 facilities (84%). The sterile preparation of Total Parenteral Nutrition (TPN) solutions was performed in 41 facilities (65%), with pharmacists being involved in infection prevention and control and pharmaceutical management. However, this was only the case for Peripheral Parenteral Nutrition (PPN) solutions in 9 facilities (14%). Furthermore, as many as 20% of facilities administered lipid emulsions at inappropriate infusion rates. The present results also revealed the lack of standardization regarding the volume or method of administration for the flush before and after drug administration.

**Discussion:** Many facilities perform the aseptic preparation of TPN solutions; however, pharmacists are not involved in the aseptic preparation of PPN solutions. Furthermore, there are currently no established guidelines for medication management involving devices such as three-way stopcocks, and pharmacists are unable to intervene. Further pharmacist involvement is necessary to ensure the appropriate administration of parenteral nutrition solutions.


# Introduction

Parenteral nutrition is an essential nutritional therapy for patients unable to utilize the digestive tract to obtain nutrients. Total parenteral nutrition (TPN) and peripheral parenteral nutrition (PPN) are selected based on the duration of oral intake inability and involve the use of lipid emulsions alongside carbohydrates and proteins. Lipid emulsions are considered to be important not only as an energy source, but also for supplying essential fatty acids. Their administration is highly significant for maintaining or improving the nutritional status during disease treatment. However, due to their nutrient richness, lipid emulsions are reportedly [1-4] prone to microbial proliferation, necessitating appropriate

infection control. Furthermore, during parenteral nutrition administration, therapeutics for disease treatment are often administered concurrently with the parenteral nutrition solution. This necessitates careful attention to potential changes in drug compatibility within the infusion catheter and three-way stopcock. However, detailed management protocols for three-way stopcocks and catheters are not typically stipulated in guidelines, and it is presumed that many institutions leave this to individual discretion. When administering multiple medications simultaneously or changing medications, flushing – namely, flushing the inside of the three-way stopcock or the line - is performed before and after medication administration. Furthermore, flushing methods and flush volumes markedly vary between facilities. In addition, if a pharmacist is stationed in the ward or ICU, they may perform management methods; however, in many cases, this is left to the nurses on site. Although we previously reported [5, 6)] that flushing was effective not only for preventing compatibility issues, but also for infection control, it is presumed that administration methods and volumes markedly vary between institutions, and the current situation remains unclear. Therefore, we conducted this survey to investigate actual practices surrounding the administration of parenteral nutritional solutions, with the aim of contributing not only to infection control, but also to the appropriate use of therapeutics and development of guidelines in the future.

# Methods

### 1. Survey Method

A request for survey cooperation was sent to hospital pharmacists belonging to the Osaka Hospital Pharmacist Association and the Nara Hospital Pharmacist Association. A questionnaire survey was conducted using Google Forms from September 2024 to January 2025, targeting 75 hospitals that consented to the survey.

### 2. Survey Items

We investigated the actual status of parenteral nutrition administration, focusing on aseptic preparation and the administration methods of infusions and flushing (Table 1).

### 3. Ethical Considerations

This study was conducted in compliance with “Ethical Guidelines for Medical and Biological Research Involving Human Subjects” and was approved by the Ethics Committee of the Faculty of Pharmacy, Osaka Ohtani University (Approval Number: BE-0096-24).

The survey was conducted anonymously, with sufficient care being taken to ensure that neither the facilities nor individuals were identifiable.

# Results

## 1. Respondent Information

The number of cooperating institutions was 75. The scales of the institutions were as follows: large hospitals (500 beds or more) 11 (14.7%), medium-sized hospitals (100–499 beds) 55 (73.3%), small hospitals (20–99 beds) 7 (9.3%), and clinics 2 (2.7%). Sixty-three facilities responded to the survey (response rate: 84%), with all respondents being pharmacists. Most respondents were in their 40s and 50s, and consequently, most had more than 20 years of experience (Figures 1 and 2).

## 2. Sterile Preparation Practices

Forty-one facilities (65%) reported performing aseptic preparation for TPN solutions, while four planned to implement it in the future (Figure 3). Regarding the frequency of TPN solution preparation, 17 facilities (41%) reported preparing ‘all prescriptions on all days (including weekends and holidays)’, followed by 10 facilities (24%) preparing ‘recurring prescriptions on all days (including weekends and holidays)’. Sterile preparation is performed for most prescriptions on weekdays (Table 2). In all 41 facilities performing sterile preparation, pharmacists are responsible for preparation. In 9 facilities (22%), nurses also perform preparation alongside pharmacists. Four facilities planning future implementation indicated that preparation would be performed solely by pharmacists.

Regarding PPN solutions, 9 facilities (14%) reported performing aseptic preparation, while three planned to implement it in the future (Figure 4). Six facilities responded that they aseptically prepare most of the solutions, such as ‘recurring prescriptions on all days (including weekends and holidays)’ or ‘all prescriptions on weekdays and Saturdays’, while the other three facilities responded that they prepare solutions in accordance with the facility’s arrangements, such as only prescriptions that fall under pre-agreed rules (Table 3). The sterile preparation of PPN solutions is performed by pharmacists at all nine facilities. At four facilities (44%), this task is conducted by both pharmacists and nurses.

## 3. Lipid emulsions

Lipid emulsions were used in 56 facilities (89%), with 45 (80%) using 20% formulations (100 mL) (Table 4). Regarding the timing of lipid emulsion administration to patients receiving TPN, the most common response was ‘administered upon recommendation from NST or pharmacists’ (33 facilities, 58.9%), while 4 (7.1%) responded ‘never administering’ (Table 5-a). Regarding their administration to patients receiving PPN, the most common response was ‘administered upon recommendation from NST or pharmacists’ (38 facilities, 67.9%), while only 2 (3.6%) reported ‘never administering’ (Table 5-b). Regarding the administration time for lipid emulsions, in response to the question ‘When administering 100 mL of a 20% lipid emulsion to a patient weighing 50 kg, how long does it take to administer it?’, the most common response was ‘4 hours or more’ (33 facilities, 58.9%). However, 12 facilities (21.4%) indicated ‘approximately 2 hours’, ‘approximately 1 hour’, or ‘unknown’ (Figure 5).

## 4. Flush administration

Regarding flushing, in response to the question ‘Are there any hospital regulations regarding ‘flush’ administration?’, 31 facilities (49.2%) answered ‘Yes’ and 32 (50.8%) answered ‘No’. Regarding the question ‘When administering lipid emulsions or other medications via the side port of the infusion line, do you flush the line before and after administration? When is that?’, 25 facilities (39.7%) responded that they flush not only for lipid emulsions, but also for other medications administered via the side port. Subsequently, 16 facilities (25.4%) responded that they flush only when administering lipid emulsions (Table 6). Regarding medications other than lipid emulsions, many required attention to incompatibility, such as omeprazole (10 cases) and antibiotics (8 cases). Concerning flushing volumes, 35 facilities (73%) had predefined administration volumes, while 13 (27%) had no set volume or were unsure. The most common flush volume administered was ‘10 mL’(Table 7). Regarding administration methods, ‘Slow infusion rate (injection at a constant rate)’ was used in 31 facilities (89%), representing the majority; however, 4 (11%) adopted ‘Pulsing method (administered in several divided doses)’.

# Discussion

Parenteral nutrition is an indispensable therapeutic modality for both nutritional and pharmacological therapies when enteral nutrition is unavailable or insufficient. Lipid emulsions are considered to be important not only as an energy source, but also for supplying essential fatty acids, and are highly significant for maintaining and improving the nutritional status. Guidelines[7)] state that lipid emulsions may be administered concurrently with amino acid preparations, and when administered simultaneously, this is often conducted using a three-way stopcock. However, management methods are not specified in guidelines, and it is presumed to be left to individual discretion. Therefore, a survey was conducted on the actual practice of administering parenteral nutrition solutions, with the aim of ensuring the appropriate use of parenteral nutrition solutions and related equipment and establishing guidelines.

Forty-one facilities prepare TPN solutions under aseptic conditions, and include 4 facilities planning to implement this practice in the future, for a total of 45 facilities (71.4%). Conversely, the number of facilities implementing or planning to implement aseptic preparation for PPN solutions is only approximately 20%, indicating a low implementation rate. TPN solution preparation is widely performed as aseptic preparation across many facilities due to the billing of ‘aseptic preparation fees’. Aseptic preparation also covers all days, including weekends and public holidays, in most facilities. However, no facility conducts PPN solution preparation under aseptic conditions for all prescriptions on all days. Instead, they only prepare solutions according to predetermined protocols (such as routine prescriptions or specific medications).

PPN solutions are less nutritious than TPN solutions; however, since they are administered via peripheral veins, they are often prepared with an isotonic osmolarity and a pH generally around 6.7 [8)]. When microorganisms contaminate these solutions, they provide an environment that is conducive to microbial growth. Therefore, there are concerns that PPN solutions may become a source of infection. To control infection, it is necessary for pharmacists to perform aseptic preparation not only for TPN solutions, but also for PPN solutions. Furthermore, lipid emulsions used during parenteral nutrition are

considered to be important not only as an energy source, but also for supplying essential fatty acids. Guidelines recommend their administration from the start of infusion, regardless of whether the TPN or PPN treatment is conducted. This survey revealed that lipid emulsions are adopted and used in approximately 90% of facilities, although their usage methods vary. It also showed that pharmacists and NST are frequently involved in the administration of lipid emulsions. Lipid emulsions are considered to be useful not only for preventing essential fatty acid deficiency, but also for preventing complications, such as liver dysfunction and fatty liver disease caused by an excessive carbohydrate intake [9], necessitating careful attention to their administration methods. Guidelines [7] specify an administration rate of 0.1 g/kg/hr for lipid emulsions. However, this survey revealed that approximately 20% of facilities administered a 20% lipid emulsion formulation (100 mL) to a patient weighing 50 kg over 1 or 2 hours. Since increasing the administration rate of lipid emulsions may lead to complications, such as reduced fat utilization efficiency and elevated serum triglyceride levels [10, 11], pharmacist interventions are essential to ensure appropriate pharmacotherapy. Furthermore, lipid emulsions frequently exhibit compatibility issues with other agents, limiting the drugs that may be concurrently administered. Although guidelines state that lipid emulsions may be administered concomitantly with amino acid preparations, it is important to consider that various drugs are often administered concurrently, particularly via peripheral venous access, and that these drugs may mix within the line. The present results confirmed that many facilities administer a flush volume before and after the administration of a lipid emulsion, although the dosage markedly varies from 5 to 10 or 20 mL. Approximately 50% of the facilities responded that they have no internal regulations concerning flush volumes, and it also become apparent that pharmacists had insufficient understanding of the administration of a flush volume. Regarding the administration method for flushing, most facilities implement the method of ‘Slow infusion rate (injection at a constant rate)’. However, it has been demonstrated that ‘pulsing methods’ administered intermittently result in fewer microbial residues inside the three-way stopcock than constant rate administration [6]. Since this survey found that only approximately 10% of facilities implemented this method, there is a need to promote the use of pulsing methods in more facilities. Pharmacists confirm and dispense injectable medications based on the prescription; however, this alone is insufficient for identifying key aspects of route management, including the route of administration, the presence or absence of flushing, the flush volume, and the administration method.

Pharmacists may intervene in drug therapy leading to injection administration by aseptically preparing all injectable medications, including PPN solutions. Furthermore, by recognizing that the absence of detailed guidelines on flush volumes and administration methods is a factor contributing to the variability in volumes and administration methods used, it is imperative to establish guidelines on matters related to injectable administration, such as the flush volume, administration methods, and handling of three-way stopcocks. This survey revealed that pharmacists, as part of their duties, prepare TPN solutions in many facilities and are further involved in nutritional therapy. However, it also showed that they were not yet able to intervene in the preparation of PPN solutions or in the administration of injectable medications, including injections and flushing. To practice appropriate drug therapy, pharmacists - as the healthcare professionals possessing the most pharmaceutical knowledge - need to

become more involved in the management of injectable medications. By undertaking the aseptic preparation of PPN solutions, alongside TPN solutions, pharmacists may engage in the management of injectable medications more broadly. This will enable their involvement in previously challenging aspects of injectable management, such as route management and performing flushing, thereby contributing to the implementation of appropriate drug therapy.

## Conclusion

When administering parenteral nutrition, in addition to establishing guidelines, further pharmacist involvement is essential.

## Declarations

# Conflict of Interest

There are no conflicts of interest to disclose concerning this paper.

# Funding

Not applicable.

# Author Contribution

S.O. wrote the original draft of the manuscript. N.C. and Y.Y. contributed to analysis the data. M.M. contributed to the design of the questionnaire survey and proofread the entire manuscript. All authors gave final approval for the submission of the manuscript.

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## References

1. Deitel M, Kaminsky VM, Fuksa M. Growth of common bacteria and Candida albicans in 10% soybean oil emulsion. Can J Surg. 1975;18:531–5.
2. Jarvis WR, Highsmith AK. Bacterial growth and endotoxin production in lipid emulsion. J Clin Microbiol. 1984;199:17–20.

3. Mershon J, Nogami W, Williams JM, Yoder C, Eitzen HE. Lemons JA. Bacterial/fungal growth in a combined parenteral nutrition solution. JPEN J Parenter Enter Nutr. 1986;10:498–502.
4. Kuwahara T, Kaneda S, Shimono K, Inoue Y. Effects of lipid emulsion and multivitamins on the growth of microorganisms in peripheral parenteral nutrition solutions. Int J Med Sci. 2013;10:1079–84.
5. Omotani S, Hatsuda Y, Katsui Y, Asao A, Toujou H, Ihara K, Tani K, Myotoku M. Microbial growth and importance of flushing inside closed-type infusion devices during administration of lipid emulsion in vitro setting. Int J Med Sci. 2021;18:3106–11.
6. Omotani S, Umemura M, Miki M, Taniguchi Y, Masui S, Niki S, Hatsuda Y. Myo otoku M. Efficacy of pulsative flushing on Candida albicans growth inside three-way stopcocks. Clin Nutr Open Sci. 2025;59:45–55.
7. Japanese Society for Parenteral. and Enteral Nutrition, editor, Parenteral and Enteral Nutrition Guidelines, 3rd Edition, Shoryusha, Tokyo, pp.35–41, 2013.
8. Shiraishi T, Nakagawa Y. Evaluation of infusion fluids on the outgrowth of several bacterial strains related to hospital-acquired infection. Japanese J Infect Prev Control. 2007;22:165–9.
9. Iriyama K. Current status and issues in the administration of fat emulsions during central venous nutrition. Nutrition: Evaluation Treat. 2009;26:324–7.
10. Iriyama K, Tonouchi H, Azuma T, et al. Capacity of high-density lipoprotein for donating apolipoproteins to fat particles in hypertriglyceridemia induced by fat infusion. Nutrition. 1991;7:355–7.
11. Iriyama K, Tsuchibashi T, Miki C, et al. Elimination rate of fat emulsion particles from plasma in Japanese subjects as determined by a triglyceride clamp technique. Nutrition. 1996;12:79–82.

## Tables

Tables 1 to 7 are available in the Supplementary Files section.

## Figures

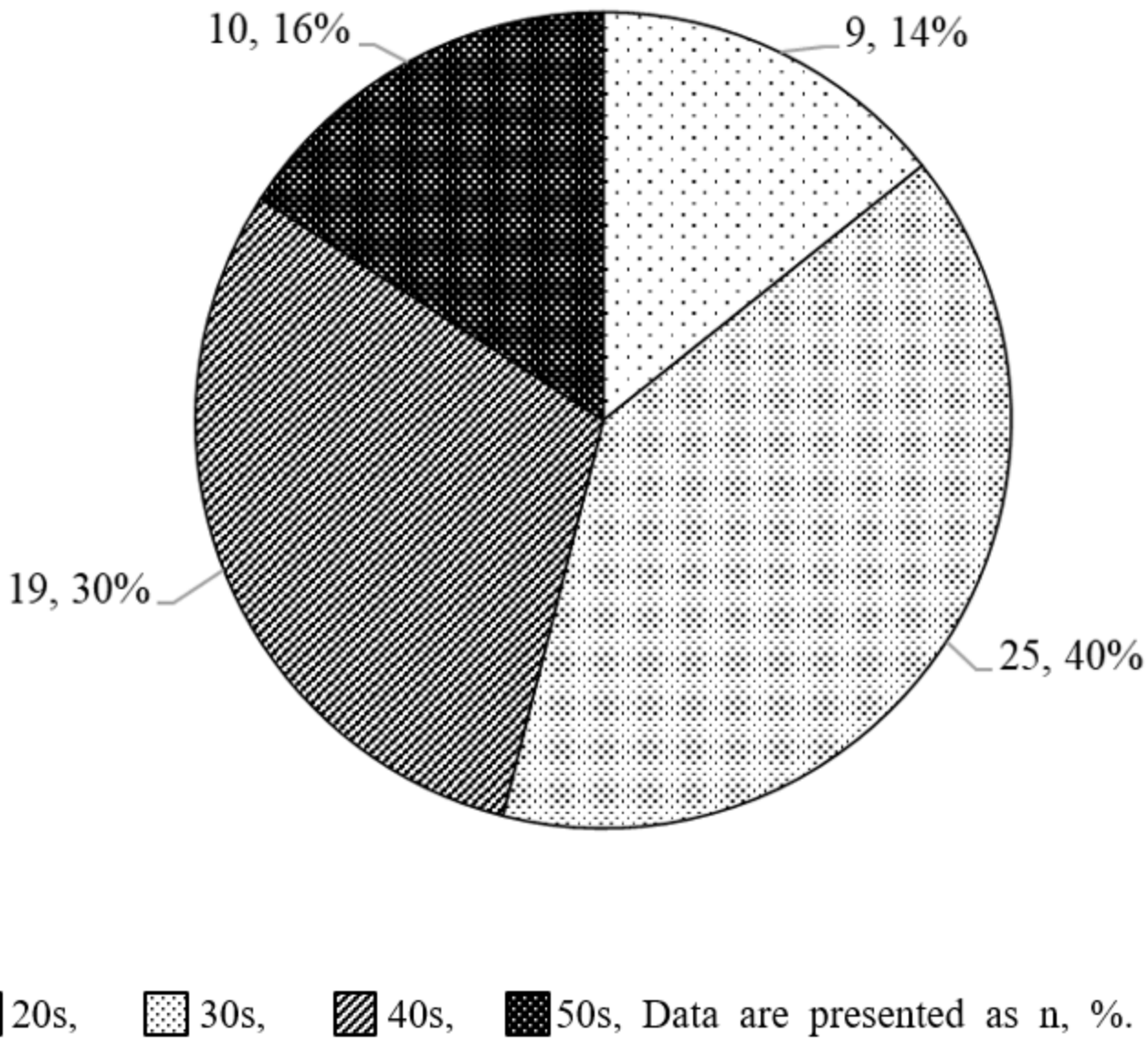



**Figure 1**

Age group of respondents

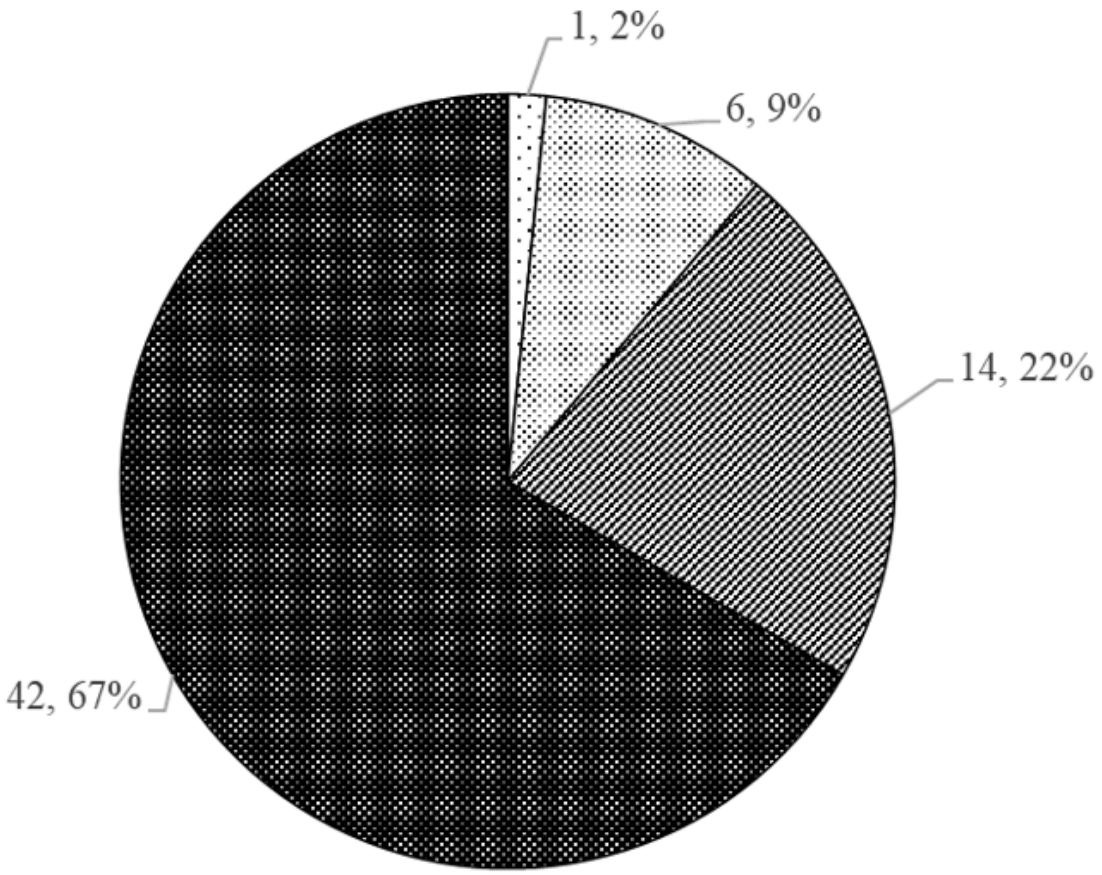
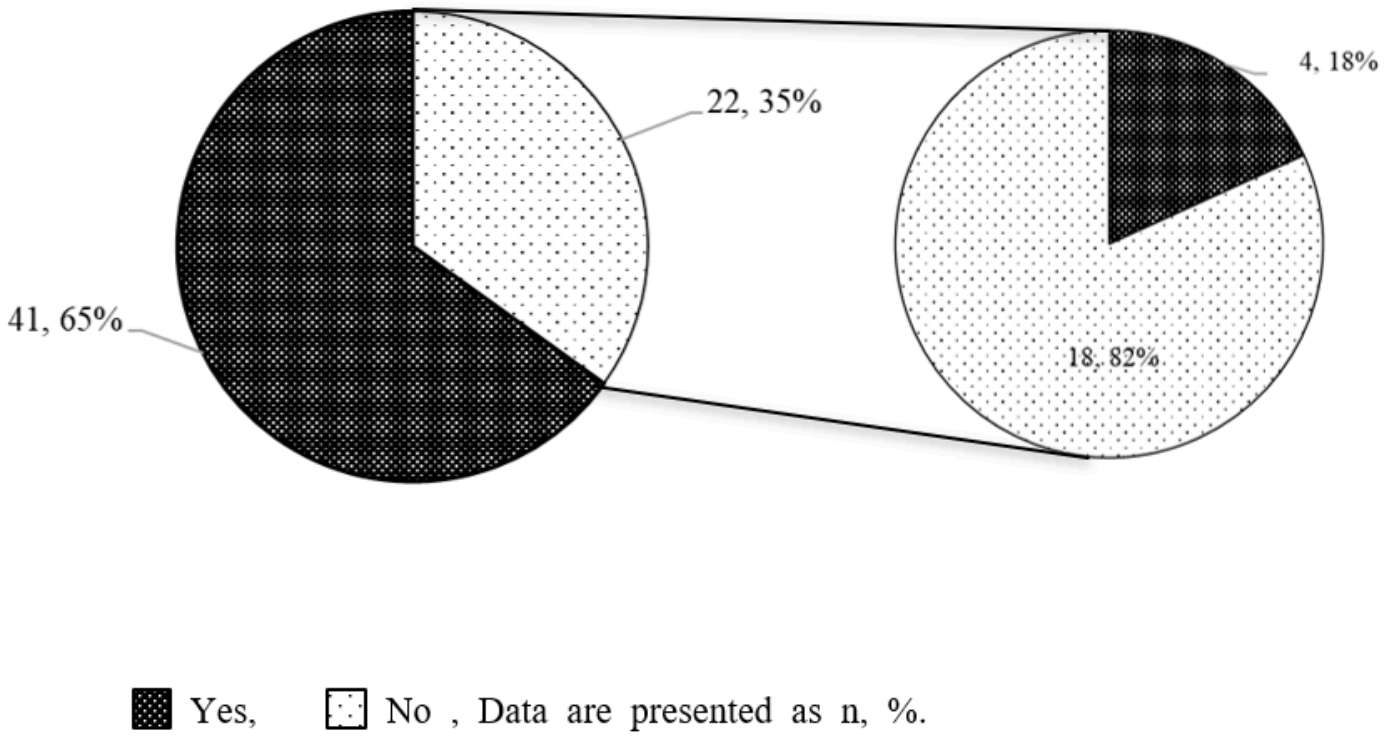


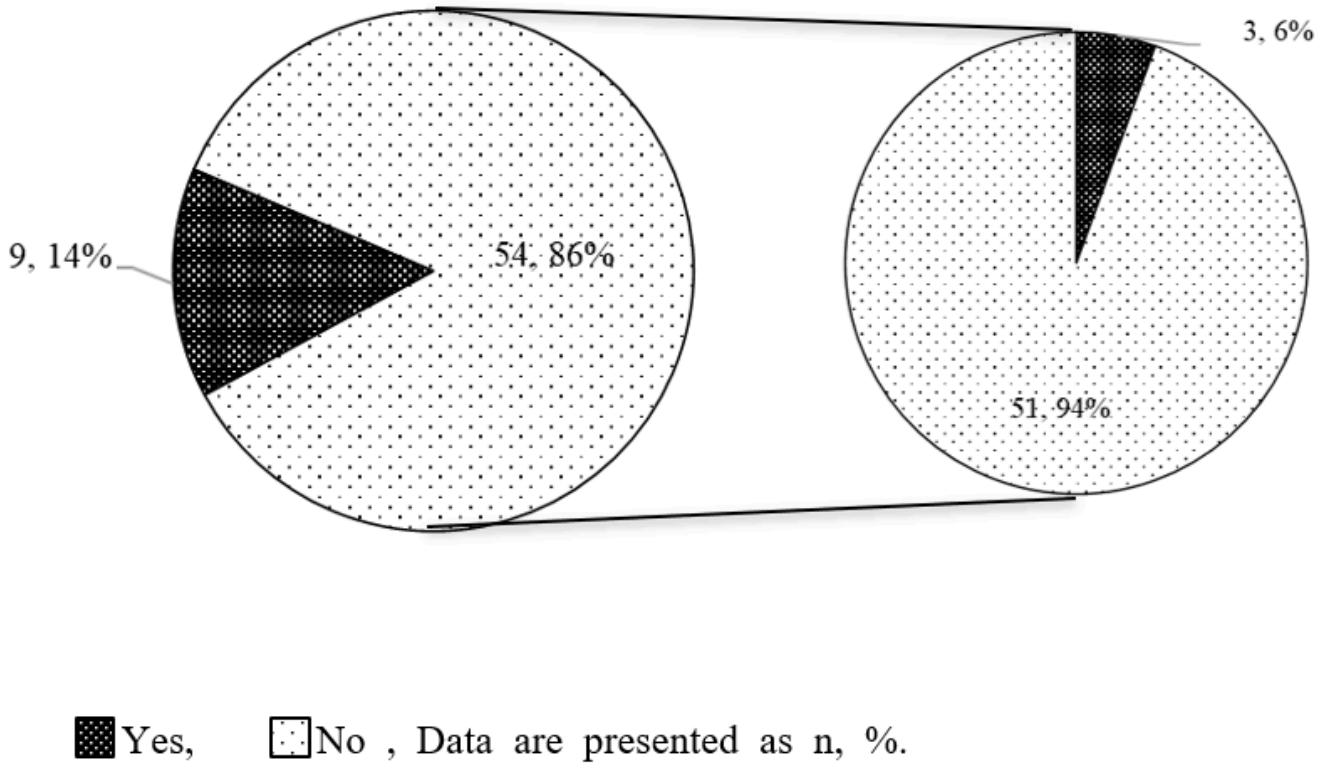

**Figure 2**

Respondent years of experience




## Figure 3

Implementation status of TPN solution preparation under sterile conditions




## Figure 4

Implementation status of PPN solution preparation under sterile conditions

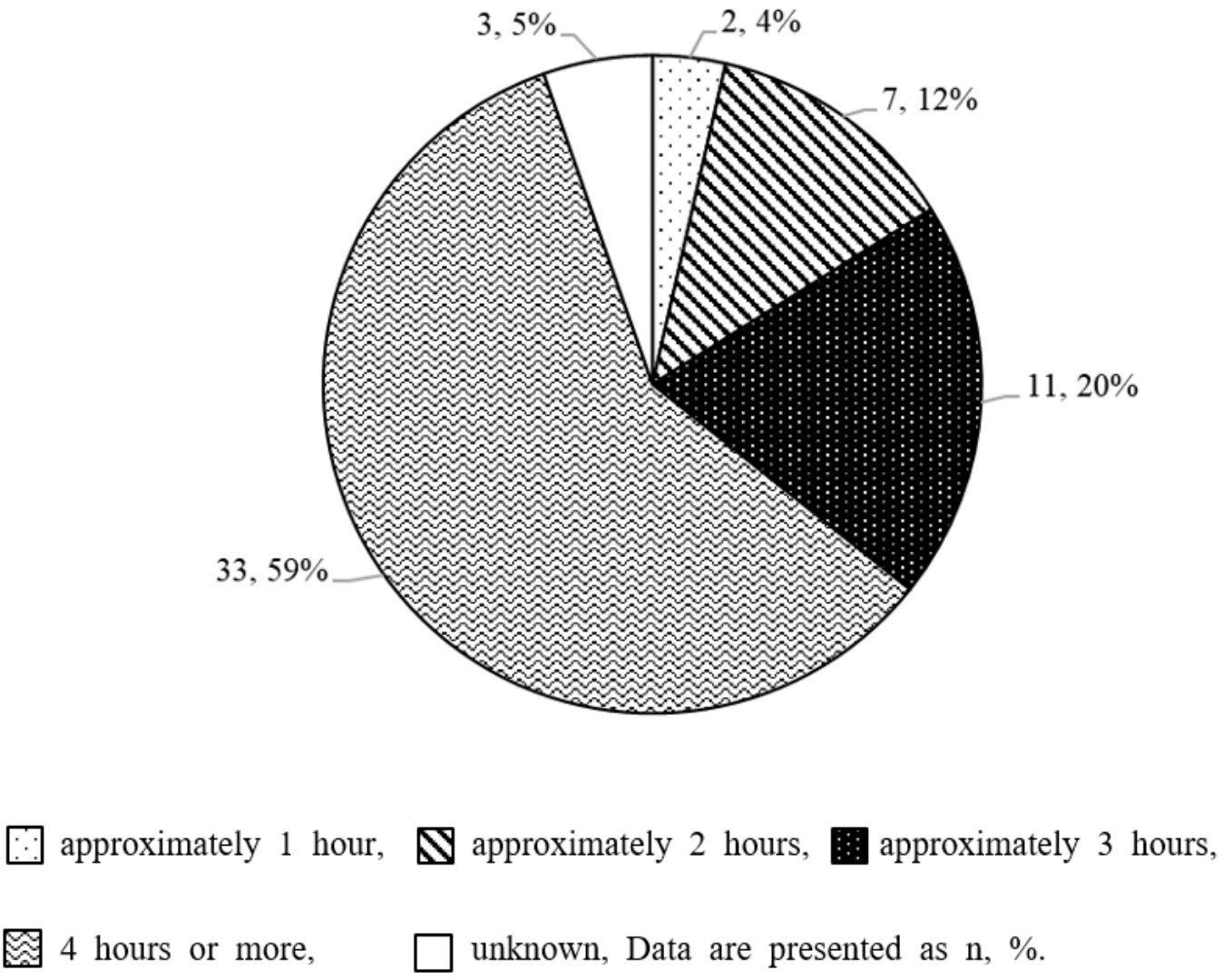



**Figure 5**

Administration rate of lipid emulsions

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.xlsx
- Table2.xlsx
- Table3.xlsx
- Table4.xlsx
- Table5.xlsx
- Table6.xlsx
- Table7.xlsx