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The Use Of Nanochitosan For Local Prophylaxis Of Postoperative Infections In Hip Arthroplasty: An Experimental Study

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Abstract: This experimental study evaluates the effectiveness of nanochitosan as a local prophylactic agent against postoperative infections following hip arthroplasty. The investigation included assessment of inflammatory and immunological biomarkers such as C-reactive protein (CRP), procalcitonin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), ferritin, and white blood cell counts in animal models. Results demonstrate that nanochitosan significantly reduces markers of systemic inflammation and infection compared to traditional prophylactic methods. The findings suggest that nanochitosan coatings on implants may provide a promising strategy for preventing periprosthetic joint infections, thereby improving postoperative outcomes and reducing complications.

Keywords: Nanochitosan, hip arthroplasty, postoperative infection, local prophylaxis, inflammation markers, periprosthetic joint infection, implant coating, experimental study.

1. Introduction: Infection-related complications following hip arthroplasty continue to represent a significant challenge and remain among the primary drivers of unsatisfactory outcomes in surgical treatment. The persistent risk of infection, manifesting as periprosthetic joint infection (PJI), can lead to prolonged morbidity, revision surgery, and diminished quality of life for patients [1-3]. Addressing this critical issue necessitates a multifaceted approach, with a particular focus on the development of targeted preventative strategies. The exploration of localized prophylactic methods, employing cutting-edge biomaterials and antibiotics, is opening up promising new avenues for the prevention of infection and improvement of patient outcomes [4]. Traditional systemic antibiotic prophylaxis, while still utilized, has limitations including potential for antibiotic resistance development and inadequate local concentrations at the implant site. Therefore, localized delivery systems offer a more precise and potentially more effective means of combating bacterial colonization. A particularly compelling and increasingly researched direction within this field involves the utilization of nanostructured forms of chitosan incorporated into implant coatings [5, 6]. Chitosan, a naturally derived polysaccharide with inherent antimicrobial properties and excellent biocompatibility, lends itself well to modification and incorporation into various coating formulations. Nanostructuring chitosan enhances its surface area and allows for controlled release of both the chitosan itself and any incorporated antibiotics, creating a sustained antimicrobial effect directly at the implant-bone interface [7-9]. This approach aims to proactively inhibit bacterial adhesion and biofilm formation, thereby minimizing the risk of PJI and contributing to the long-term success of hip arthroplasty procedures. Further research is focused on optimizing chitosan nanoparticle size, antibiotic loading, and coating techniques to maximize efficacy and minimize potential adverse effects.

2. Methods

This experimental study was conducted on 36 rabbits (n = 6 per group), with an average body weight of 2,22 ± 0,06 kg.

The animals were randomly assigned to the following six groups:

Intact group – no surgical intervention (baseline control);

Control group – hip joint arthroplasty without infection prophylaxis;

Group A1 – systemic antibiotic prophylaxis with vancomycin;

Group B1 – local coating of the implant with an antiseptic (chlorhexidine);

Group B2 – antiseptic combined with a biopolymer (chitosan);

Group B3 – antiseptic combined with nanochitosan and vancomycin.

All animals, except those in the intact group, underwent surgical modeling of hip joint arthroplasty with the implantation of a sterile titanium endoprosthesis, following a standardized surgical protocol. In groups B1 through B3, the implants were pre-coated with the respective compositions before implantation.

Evaluation of prophylactic efficacy against purulent complications.

Blood samples were collected at 1, 12, 24, and 72 hours postoperatively to assess systemic inflammatory response. The following biomarkers were measured:

- ✓ C-reactive protein (CRP)
- ✓ Procalcitonin
- ✓ Interleukin-6 (IL-6)
- ✓ Tumor necrosis factor-alpha (TNF-α)
- ✓ Ferritin
- ✓ Complete blood count with differential

Biochemical and immunological parameters were analyzed using enzyme-linked immunosorbent assay (ELISA) and automated hematology analyzers.

Research Aim: To evaluate the effectiveness of various approaches to preventing purulent complications in joint arthroplasty, with a focus on the use of nanochitosan coatings.

3. Results

Following the surgical procedure, the level of C-reactive protein (CRP), a key indicator of inflammation, demonstrated a statistically significant decrease across all investigated groups when compared to the baseline control levels at each measured time point. Remarkably, even just one-hour post-intervention, a reduction in CRP was observed in group A1, amounting to 1,26 times the initial level. This early decrease suggests a rapid commencement of suppression of the inflammatory response. However, groups B1, B2, and B3 exhibited a more pronounced reduction, with respective decreases

of 1,47, 2-10, and a substantial 5,87 times the initial CRP levels. This favorable trend persisted at the three-hour mark, where CRP levels remained reduced by 1,34 times in group A1, while group B3 achieved the most significant reduction, reaching 5.49 times the initial level. Subsequently, at the twelve-hour assessment, CRP levels in groups B2 and B3 continued to remain significantly lower than the control values - specifically, 2,22 and 4,42 times lower, respectively. In contrast, groups A1 and B1 showed reductions of 1,15 and 1,63 times, respectively. A consistent pattern was also observed at the twenty-four-hour mark, with group B3 demonstrating a reduction in CRP of 4,26 times, and values at the seventy-two-hour mark remaining within a range of reduction from 1.10 times in group A1 to 4,50 times in group B3. Consequently, the observed reduction in CRP levels reflects a meaningful suppression of inflammation, with the most pronounced effect noted in group B3 (Figure 1).

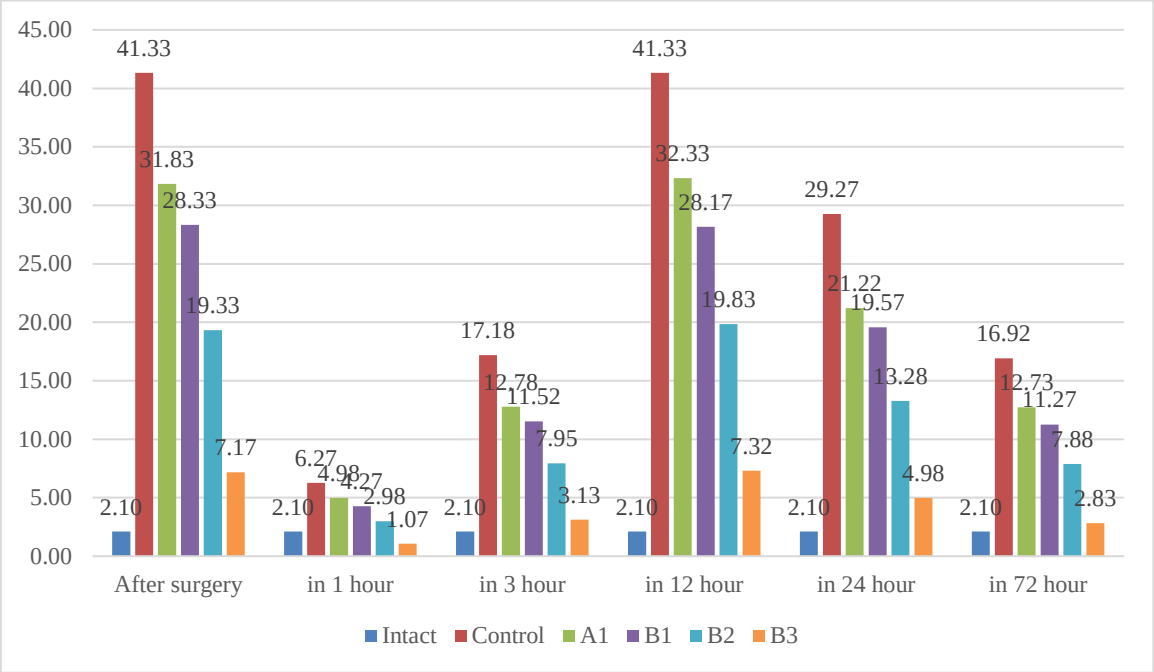

Figure 1. Changes in C-reactive protein (CRP) levels after surgery in study groups

A parallel and similarly encouraging dynamic was observed with procalcitonin, a recognized marker of both systemic inflammation and infection. Just one hour after the operation, the procalcitonin level in group A1 was reduced by 1,33 times. Notably, group B3 exhibited a more dramatic decrease, reaching an impressive 10,8 times the initial level, which strongly indicates a potent anti-inflammatory effect. At the three-hour point, procalcitonin remained significantly below the baseline control level, with the most substantial reduction observed in group B3, amounting to 8,58 times the initial value. The trend towards continued reduction persisted through the twelve-hour and twenty-four-hour assessments. Specifically, at the twenty-four-hour mark, group B3 achieved a remarkable reduction of 24,6 times, while group B2 demonstrated a reduction of 15,37 times, further highlighting the prolonged and substantial anti-inflammatory effect. By the seventy-two-hour assessment, procalcitonin remained significantly lowered in groups B2 and B3, signifying a stabilization of the patient's condition and effective control of the inflammatory process (Figure 2).

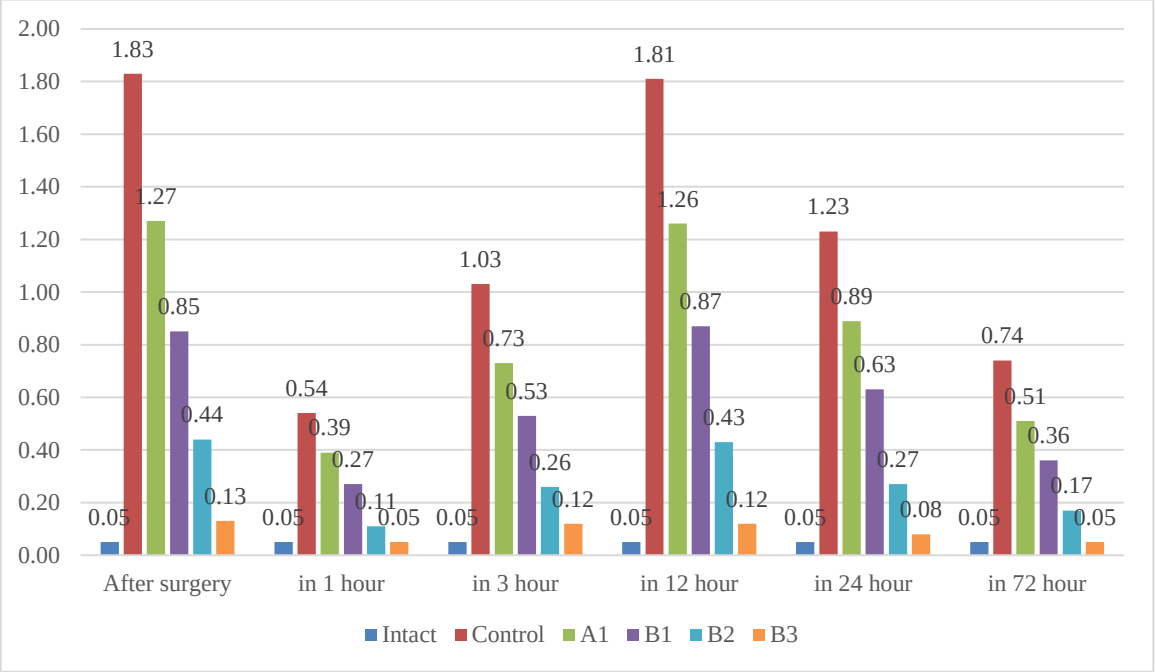

Figure 2. Changes in procalcitonin levels after surgery in study groups

The level of interleukin-6 (IL-6), a pivotal pro-inflammatory cytokine known to play a significant role in the body's inflammatory response, also demonstrated a consistent and substantial reduction across all investigated groups. Notably, as early as one hour following the surgical procedure, IL-6 levels were observed to be reduced by a factor of 1,31 in group A1 and a remarkable 4,36 times in group B3 compared to baseline control levels. This initial decrease proved to be remarkably stable as measurements were taken at three and twelve hours' post-operation. In group B3, the reduction reached an impressive near six-fold decrease by the twelve-hour mark, clearly reflecting a powerful dampening of the inflammatory cascade. Consistent with these findings, similar trends were also observed at twenty-four and seventy-two hours' post-surgery, providing strong evidence for the sustained impact of the intervention on mitigating IL-6 production and its associated inflammatory effects. This prolonged effect suggests a fundamental shift in the body's inflammatory response, rather than a transient reaction (Figure 3).

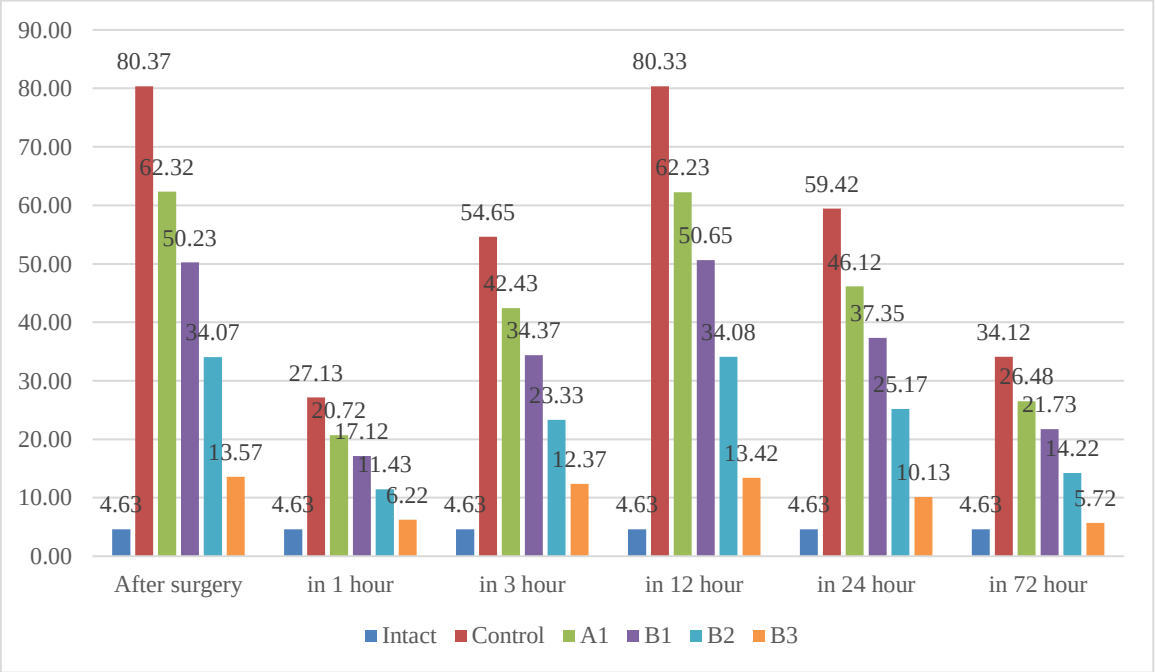

Figure 3. Change in IL-6 levels after surgery in study groups

Measurements of TNF-α (Tumor Necrosis Factor alpha), another crucial pro-inflammatory mediator and a key player in systemic inflammation, also showed a marked decrease in all groups studied. Even within the first hour after the operation, TNF-α levels were reduced by a factor of 1,26 in group A1 and a more significant 3,31 times in group B3 relative to the pre-operative baseline. This reduction remained consistent and stable as assessments were made at the three-hour and twelve-hour time points. Furthermore, by the twenty-four-hour mark, the decrease in group B3 had intensified to an impressive nine-fold reduction. While a slight, albeit minor, increase was observed at the seventy-two-hour assessment, TNF-α levels remained significantly below the initial control values, indicating a well-managed and controlled inflammatory process, rather than uncontrolled or escalating inflammation (Figure 4).

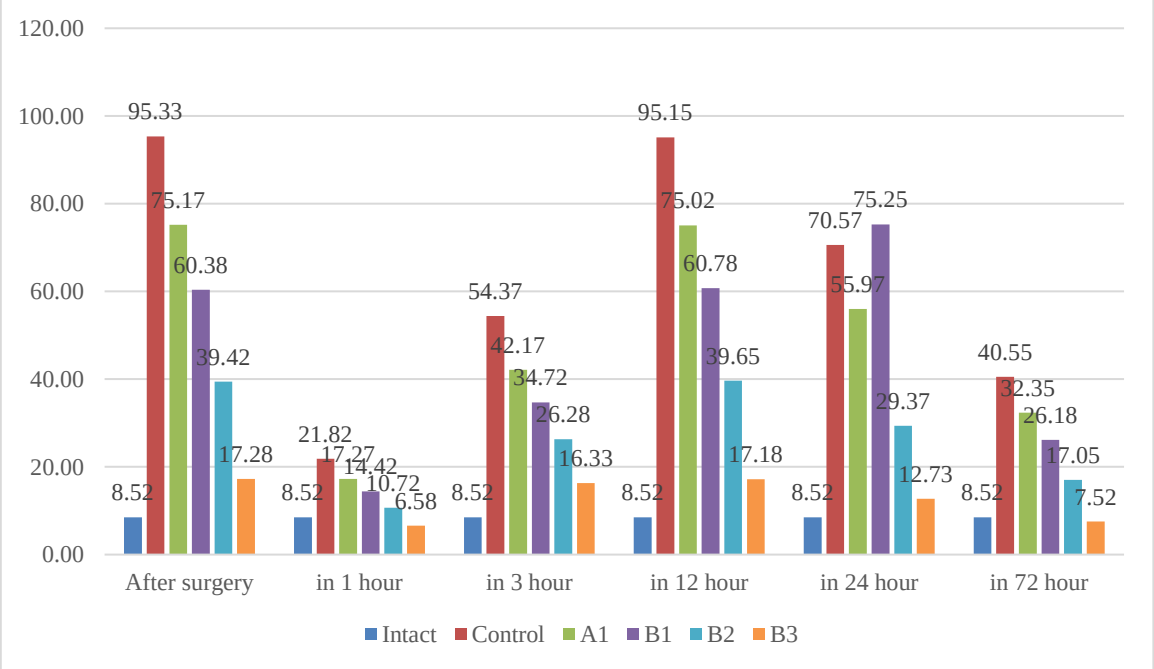

Figure 4. Change in TNF-α levels after surgery in study groups

Turning to cellular indicators, the levels of leukocytes, or white blood cells, which are a primary component of the immune system and often elevated during inflammation, showed a substantial decrease in all groups following the surgical intervention when compared to pre-operative control values. The most pronounced reduction was observed as early as one-hour post-operation - by a factor of 1,85 in group A1 and a striking 4,07 times in group B3. Over time, leukocyte levels remained below the baseline control values, although the degree of reduction gradually lessened, a phenomenon that may reflect the body's immune system adapting to the altered conditions and initiating a recovery phase. At seventy-two hours' post-operation, leukocytes were reduced by a factor of 1,76 in group A1 and 2,19 times in group B3, demonstrating a continued, albeit less dramatic, impact on the cellular inflammatory response (Figure 5).

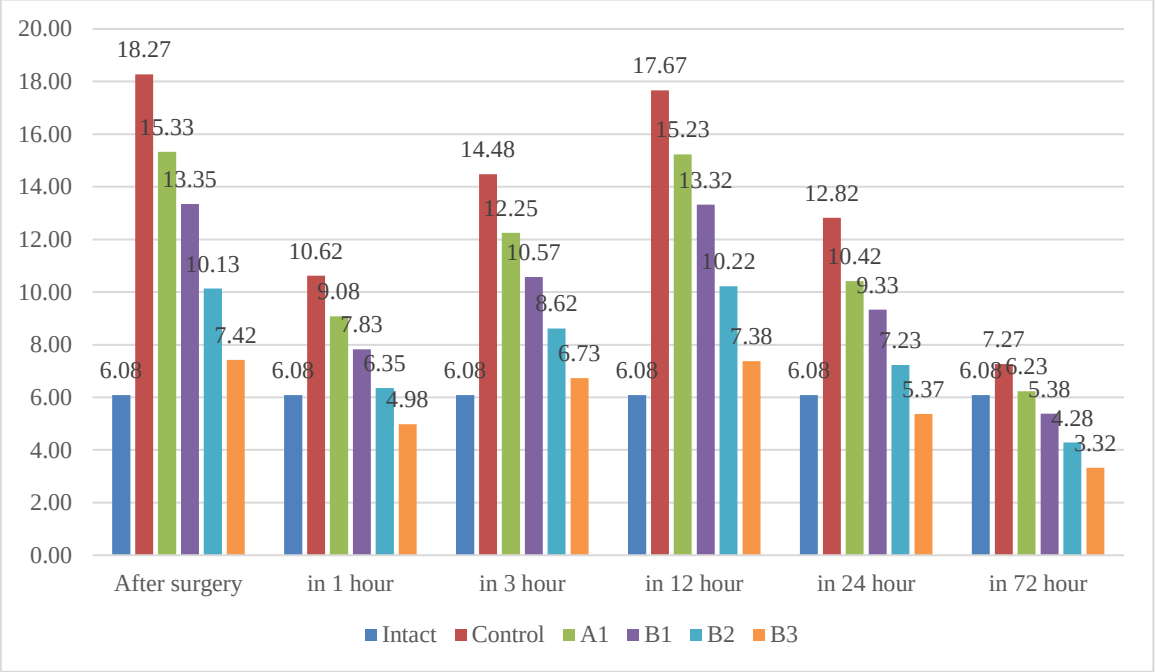

Figure 5. Changes in leukocyte levels after surgery in study groups

The proportion of neutrophils, which are key cells involved in the acute inflammatory response and are often the first responders to tissue injury, also exhibited a decrease in all groups. One hour after the operation, their numbers were reduced by an average of 1,31 times in group A1 and 1,73 times in group B3. This reduction persisted throughout the entire observation period, although it became less pronounced at the later time points, suggesting a gradual restoration of the immune status and a return towards normal neutrophil levels. This pattern indicates a controlled and regulated resolution of the acute inflammatory phase (Figure 6).

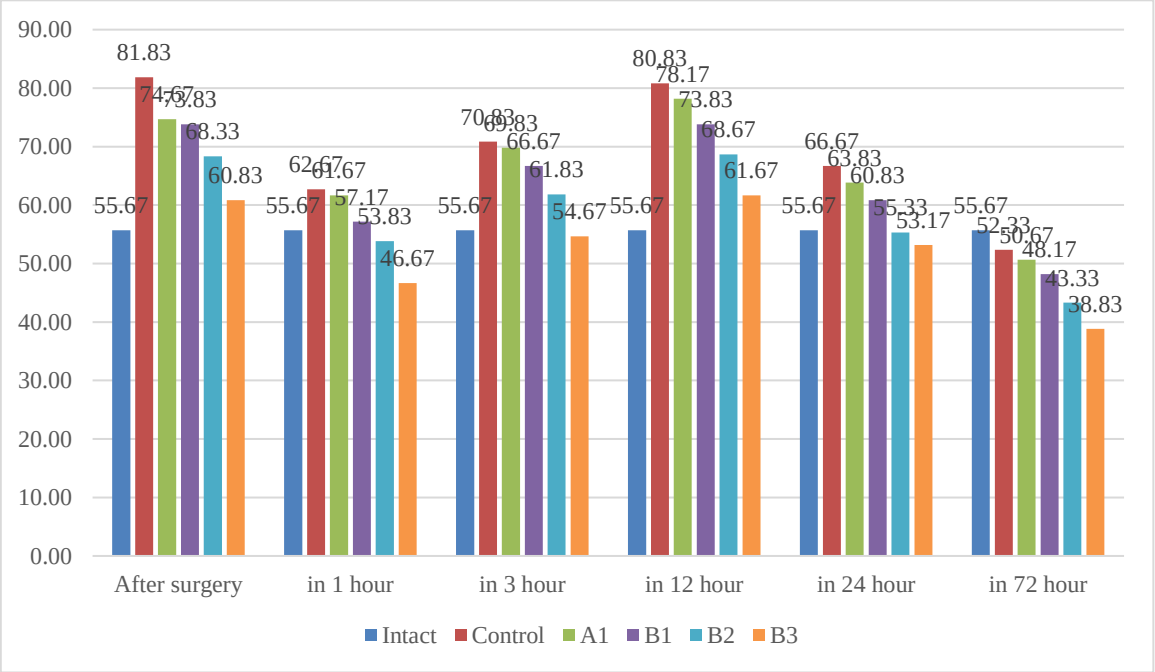

Figure 6. Changes in neutrophil levels after surgery in study groups

Ferritin, a crucial biomarker reflecting both the body's iron stores and the degree of systemic inflammation, exhibited a notable decrease across all study groups. However, the reduction was most pronounced in Group B3, where ferritin levels diminished by approximately 3,7 times within just one hour following the surgical procedure. This rapid decline suggests a particularly swift impact on the inflammatory cascade.

In contrast, Group A1 experienced a comparatively less significant reduction, with ferritin levels decreasing by roughly 1,8 times during the same timeframe. This difference in response highlights the varying efficacy of the different treatment approaches (Figure 7).

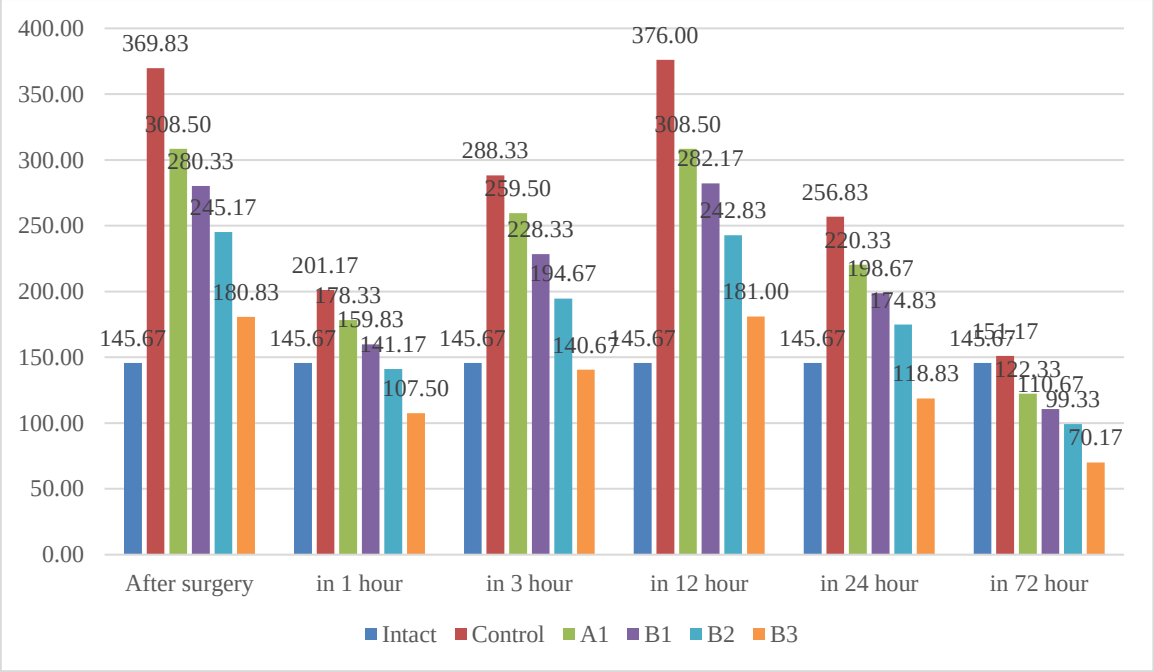

Figure 7. Change in ferritin levels after surgery in study groups

Following the initial hour, ferritin levels remained consistently and stably reduced within all groups for the subsequent 72 hours. This sustained reduction, particularly evident in Group B3, strongly supports and confirms the durability and persistence of the observed anti-inflammatory effect. The continued suppression of ferritin, a protein involved in iron metabolism and a key indicator of inflammation, suggests that the therapeutic intervention in Group B3 effectively modulates the body's inflammatory response over an extended period. For example, elevated ferritin levels are often seen in conditions like rheumatoid arthritis and chronic inflammatory diseases, and a reduction indicates a lessening of that underlying inflammatory burden (Figure 7).

4. Conclusions

In conclusion, Group B3 consistently demonstrated the highest level of efficacy across all key indicators of inflammation, encompassing a range of biomarkers including C-reactive protein (CRP), white blood cell counts (leukocytes), and, as detailed above, ferritin. The treatment method employed within this group appears to provide the most rapid and sustained suppression of the inflammatory response, as evidenced by the substantial and prolonged reduction in these critical biomarkers. Group B2 exhibited a moderate effect, while Groups A1 and B1 showed a less pronounced, but still discernible, improvement. These findings collectively reinforce the promise and rationale for utilizing the therapy applied in Group B3 to optimize the postoperative management and care of patients. The observed benefits suggest a potential for improved patient outcomes, reduced recovery times, and a decreased risk of complications associated with the inflammatory response following surgery. Further research and clinical trials are warranted to fully explore and validate these encouraging results.

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