



Skin Complications of Orthopedic Procedures and Devices

Zahra AZIZIAN¹, *Parvin MANSOURI², Zeinab HESAMI¹, Adel EBRAHIMPOUR³, Bahamin ATTAR³, Reza CHALANGARI^{2,4}

1. Dept. of Dermatology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

2. Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran

3. Dept. of Orthopaedic, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4. Kassir Dermatology, Dallas, Texas, USA

*Corresponding Author: Email: mansouripr@yahoo.com

(Received 15 Jul 2017; accepted 12 Nov 2017)

Abstract

Background: Knowledge of skin complications and contributing factors in orthopedic patients is important for design and development of preventive approaches. Therefore, this study was designed to assess skin complications in orthopedic patients.

Methods: In this case-series study, 126 orthopedic patients referred to Rasoul-e-Akram and Bahman hospitals from 2012 to 2016 with skin complications were analyzed. The adverse effects were assessed with respect to type and contributing factors. Fisher's exact test, Chi-square, and independent sample t-test were performed to assess the associations between skin complications and other variables.

Results: Skin complications in orthopedic patients included infections in 33 (26.1%) cases and hypersensitivity reactions in 88 (40%) cases. In total, 66 (55%) cases of fracture and 35 (29.2%) cases of cellulitis were detected, while the remaining cases involved complications such as disc herniation, nerve involvement, and osteoarthritis-related arthroplasty. Severe reactions presenting as toxic epidermal necrolysis were observed in 3 patients, 2 of whom died eventually. Age and gender were not related to the type of skin complications ($P>0.05$).

Conclusion: Complications due to orthopedic treatments were not common. However, since the disease may become fatal on certain occasions, patients should receive more attention from physicians and nurses.

Keywords: Skin complication, Orthopedic procedures, Orthopedic devices

Introduction

Surgical procedures are associated with different complications. Some of these complications may occur in patients, despite their rare occurrence and major preventive measures applied by physicians. Similarly, complications associated with orthopedic surgeries are still reported, despite major improvements in this area. Overall, all surgical procedures, regardless of their scope, may cause insignificant to serious (e.g., fatal complications) complications in patients (1, 2).

Postoperative complications can be general or specific to the type of surgical procedure; management of these complications is dependent on the patient's medical history. Postoperative fever, atelectasis, embolism, wound infection, and deep vein thrombosis is the most common general complications in patients. The highest incidence of these complications is generally reported within 1 to 3 postoperative days. Nevertheless, specific complications may occur in the early postoperative period, a few days after surgery, during the

postoperative period, and in the late postoperative period, respectively (3, 4).

Considering the associated morbidities and pain among patients, dedicated surgeons are usually troubled by the development of postoperative complications. In fact, all surgical procedures, even the simplest ones, are associated with an unending list of complications. These complications can be due to the imprecise evaluation of patients, type of implant, or the surgeon's decisions and practice.

On the other hand, the causes of complications may be multifactorial or even unknown in some cases. Overall, infections are recognized as possible postoperative complications and are among the most serious complications associated with orthopedic surgeries. Moreover, tissue infections may occur at different ages among male and female patients (5). In addition, skin infections are prevalent occurrences, accounting for 5%-10% of complications in surgical settings (6).

Orthopedic surgery devices and materials are generally well tolerated by patients. Infections, mechanical problems, and allergic reactions (or hypersensitivity) are common patient complaints after orthopedic surgeries. The allergic reactions include cutaneous changes (such as eczema), pain, recurrent effusion, delay in wound healing, and implant loosening.

Unlike cutaneous metal contact allergies, which have high incidence rates, implant-associated allergies are quite rare. Nevertheless, there is little epidemiological information regarding the occurrence of these reactions (7). Such skin problems may not only result in the deterioration of patient's condition but also lead to reoperation and other side effects (8-10).

Post operation complication of orthopedic surgery (e.g. fever and surgical site infection) could occur in approximately 2%-5% of the patients especially in the young adult (11). Although there are not any reports regarding the prevalence of these complications among the Iranian patients and its cost on the health system, in the USA a financial cost of treatment is up to \$10 billion annually (12). In addition, surgical site infection after orthopedic surgeries leads to increased

morbidity, mortality, extended hospital in-patient stays, and economic burden to the hospital resources (13). Accordingly, it is better to prevent rather than treat infections and hypersensitivity reactions, resulting from orthopedic procedures and devices (14).

For this matter, knowledge of skin complications and contributing factors in orthopedic patients is important for the design and development of preventive approaches. Accordingly, the present study designed to assess these complications.

Methods

This retrospective descriptive study was conducted during 2013-2016. Among 1820 cases (including outpatient and hospitalized patients), referred to the orthopedic trauma centers of Rasoul Akram and Bahman Hospitals, Tehran, Iran; we selected 126 patients, subsequently referred to a dermatologist by an orthopedic surgeon due to skin complications.

The type of skin complications and contributing factors were assessed among patients. Skin complications were mostly diagnosed based on the clinical symptoms detected by a dermatologist; in few cases, definitive diagnosis was made by skin sampling. The exclusion criteria were incomplete data and known skin diseases. Well-trained and experienced specialists diagnosed the patients.

Written consents were obtained from the participants, and the local Ethics Committee approved the study.

Data collection was carried out, using the available medical records and data in the checklists. Fisher's exact test, independent sample t-test, and Chi-square were performed to assess the associations between skin complications and other variables. For statistical analysis, SPSS ver. 13.0 (Chicago, Illinois, USA) was used (significance level, $P < 0.05$).

Results

The mean age of the participants was 57.1 ± 12.6 yr. Moreover, 52 (41.2%) and 74 (58.7%) patients were female and male, respectively. Overall, 66 cases of fracture and 35 cases of cellulitis were

detected. The remaining cases included complications, such as disc herniation, nerve involvement, and osteoarthritis-related arthroplasty. The patients' conditions are shown in Table 1.

Skin complications in orthopedic patients included infections in 33 (26.1%) cases, hypersensitivity reactions in 88 (73.3%) cases, and 5 (4.1%) cases

with other complications. Local skin reactions were observed as irritant and allergic contact dermatitis with erythema, pruritus, and less frequently, bullous lesions (Table 2). Orthopedic implants and bandages were responsible for most cases of local contact dermatitis. Systemic skin reactions due to drugs are presented in Table 3.

Table 1: Demographic Data of patients

| <i>Variable</i> | <i>N(%)</i> |
|-------------------------------------|-------------|
| Gender | |
| Male | 74 (58.7) |
| Female | 52(41.2) |
| Site of hospital reference | |
| Orthopedic emergency room | 10 (8.3) |
| Orthopedic ward | 67 (55.8) |
| Intensive care unit | 5 (4.2) |
| Orthopedic clinic | 38 (31.7) |
| Underlining disease | |
| Fracture cases | 66 (52.3) |
| Arthroplasty | 28 (43) |
| Upper extremities | 16 (24) |
| Lower extremities | 14 (21) |
| Open fracture | 8 (12) |
| Cellulitis | 35 (27.7) |
| Disc herniation | 4 (3.1) |
| Tendonitis | 11 (8.7) |
| Osteoarthritis-related arthroplasty | 10 (7.9) |

Table 2: Local skin reaction to most common orthopaedic devices

| <i>Reaction</i> | <i>Percent</i> | <i>Number</i> |
|---|----------------|---------------|
| Surgical Tapes | 12.9 | 8 |
| Corn and callus removal tapes | 8 | 5 |
| Orthopedic Casts | 20.9 | 13 |
| Orthopedic Implants (plates and screws) | 22.5 | 14 |
| Topical Herbal Medicines | 8 | 5 |
| Wrist, knee bandages | 27.4 | 17 |

Table 3: Generalized Drug Reactions to most common orthopaedic drug prescription

| <i>Drug</i> | <i>Eruption</i> | | | | |
|---------------|----------------------|-------------------------|-----------------------------------|--------------------------------------|-----------------------|
| | <i>Urticaria (%)</i> | <i>Stevens /TEN (%)</i> | <i>Maculopapular Eruption (%)</i> | <i>Fixed Drug Eruption (FDE) (%)</i> | <i>Vasculitis (%)</i> |
| NSAID | 4(15.3) | 2(7.6) | 2(7.6) | 1(7.6) | 1(7.6) |
| Antibiotics | | | | | |
| Cephazolin | | 1(3.8) | 2(7.6) | | |
| Cephalexin | | 1(3.8%) | 3(11.5) | | |
| Ceftriaxone | | | 2(7.6) | | |
| Ciprofloxacin | | | | | 2(7.6) |
| Alendronate | 1(3.8) | | 1(3.8) | | |

Cartilage repair supplement 1(3.8)

1(3.8)

1(3.8)

Severe skin reactions, presenting as toxic epidermal necrolysis, were observed in 3 cases, 2 of whom died eventually. One patient was an 18-yr-old girl (with a prophylactic injection of cefazolin before ulnar fracture surgery), who died due to sepsis. The second patient was an 84-yr-old man (with diclofenac injection for discopathy pain relief), who died due to massive gastrointestinal bleeding, resulting from severe mucosal erosion. The third patient died due to the use of piroxicam for back pain relief. In addition, cephalexin for foot cellulitis led to Stevens-Johnson syndrome in 1 case. No significant correlation was observed between the underlying cause of admission and skin reactions ($P=0.6$).

Other complications included skin lacerations after implanting plates in 2 patients and depigmentation after intralesional corticosteroid injection for tendonitis in 3 patients. Cellulitis infection was observed in 33 (26.1%) patients. All these cases occurred in hospital-admitted patients. The most common site of laceration was the surgical site in 19 patients, with 8 patients experiencing intravenous catheter infections.

The most common causes of bacterial infection were *Staphylococcus* species (86%) and *Pseudomonas aeruginosa* (14%). Six patients had intertrigo with *Candida* and tinea infections in the inguinal region. All intertrigo patients underwent hip arthroplasty surgery. However, there was no significant correlation between the underlying cause of admission and infection rate ($P=0.7$). In addition, age and gender were not related to the type of skin complication in patients ($P=0.6$).

Discussion

In this study, skin complications were assessed in orthopedic patients. The skin complications of orthopedic procedures and devices are presented in 3 main categories, including infections, hypersensitivity reactions, and less common adverse effects. When the implants are located on the target site, successful biointegration requires colonization of a highly reactive implant surface by host cells (15).

Bacteria such as *Staphylococcus* species may attach to metallic or polymeric devices and colonize the implant surface instead of the host cells. Once attached, these bacteria can develop a biofilm and undergo phenotypic changes, which make them somewhat resistant to the host's immune responses and even antibiotics (15-17). Infections at or near surgical incisions within 30 d of an operative procedure are known as surgical site infections, which may present as skin infections (0.5%-2%) (18). The most common contributing bacteria are skin flora, such as coagulase-negative *Staphylococci* (19, 20).

Occasionally, other less common bacteria may be seen in some patients, especially those with immunodeficiency or underlying diseases (21-23). These infections are usually treatment-resistant, and responses to common antibiotics are less expected (24, 25). In more procedures complex, half of infected patients may require reoperation for wound debridement or sometimes skin flap closure (26).

Use of broad-spectrum antibiotics may be optionally indicated to reduce the resistance and recurrence of skin infections after orthopedic procedures (27, 28). In severe cases, removal of external devices may be necessary (29). In this study, the infections were the most common adverse effects and were more common in diabetic patients. Allergic reactions to implants, fixators, other orthopedic devices, or bone cement components are among other skin complications (30, 31). Nickel, chromium, and benzoyl peroxide are the major metallic etiologies for these allergic reactions (32, 33). Allergic reactions were the second most prevalent complication after infections in our study.

The common symptoms of skin complications include swelling, pain, inflammatory skin reactions, implant loosening, and occasionally fistula formation (33-35). These hypersensitivity reactions may cause orthopedic implant failure, leading to reoperation (29, 30). Hypersensitivity reactions may be seen in up to one-fourth of patients undergoing orthopedic surgeries (36, 37).

The need for reoperation and removal of orthopedic devices (or replacement with less allergenic devices) may be indicated in severe cases (38, 39). The effectiveness of local antiallergic components has not been evaluated yet. Trauma injuries, especially in pediatric patients and those requiring long-term casting, are other less common skin complications (40, 41, 42). However, skin can tolerate cast immobilization even for a prolonged duration (41). These types of skin complications are more preventable than the previously mentioned skin complications in orthopedic patients (43,45,46). In addition, spontaneous improvement is an expected consequence in the majority of cases.

Systemic drug reactions in orthopedic surgeries are similar to other surgeries. The most routinely prescribed drugs in orthopedic clinics are non-steroidal anti-inflammatory drugs (NSAIDs) (50). Although skin eruption due to NSAIDs is commonly mild, severe conditions, such as toxic epidermal necrolysis and Stevens-Johnson syndrome, may occur. In this study, the majority of negative reactions to NSAIDs were urticarial eruptions, although vasculitis (a rare skin reaction to NSAIDs) has been reported in the literature (51). Various bacteria have been observed in many studies to cause infection surgical site (44). Systemic antibiotic prophylaxis in orthopedic implant surgeries is the standard practice, used in the past 3 decades. Cephazolin is a commonly prescribed drug, and urticaria and maculopapular eruptions are the most common reactions; fatal reactions have been also reported in other studies (52). In this study, four patients had TEN; using this kind of drugs in any surgery can cause such side effects. Three per 10000 patients in orthopedic wards can experience such drug reactions, and careful attention must be paid to the high risk of TEN with NSAIDs and Antibiotics.

Generally, scattered and limited studies have been done in this area, whose results are mostly consistent with our study, though with certain differences due to the type of study, type of treatment, etc. The prophylactic use of antibiotics was evaluated, (47) or examined the difference between the upper and lower extremity infections

in Germany (48) and a study (49) investigated the difference between the position of the fracture and postoperative infection.

There are some other skin complications associated with orthopedic procedures, such as hypopigmentation after local corticosteroid injection to control the joint and tendon inflammation. Overall, this complication is quite rare (estimated risk, <1%), and steroid injections may result in skin atrophy or hypopigmentation (50). On the other hand, we can reduce the risk of subcutaneous fat atrophy and hypopigmentation by using soluble and potent steroids. Overall, low-solubility steroids (e.g., triamcinolone acetonide) are suggested for deep structures (e.g., knee), while high-solubility steroids (e.g., betamethasone and dexamethasone) are administered preferably in soft tissues (e.g., carpal tunnel and tendon sheath) (53).

Conclusion

However, there are skin complications that are not so common in orthopedic patients but remain important and life-threatening, and thus should be considered by physicians. Skin complications of orthopedic procedures and devices are common causes of operation failure. These may be more serious, such as skin infections, or less important, such as traumatic injuries. Knowledge of these adverse effects is essential to prevent them and improve the postoperative outcomes in patients.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

No fund was received for this study.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. <http://www.genou.com/anglais/complications.htm>
2. Chee YL, Crawford JC, Watson HG, Greaves M (2008). Guideline on the assessment of bleeding risk prior to surgery or invasive procedures; British Committee for Standards in Haematology. *Br J Haematol*, 140(5):496-504.
3. Thompson JS, Baxter BT, Allison JG et al (2003). Temporal patterns of postoperative complications. *Arch Surg*, 138(6):596-602.
4. Pile JC (2006). Evaluating postoperative fever: a focused approach. *Cleve Clin J Med*, 73 Suppl 1:S62-6.
5. Johnson KA (2012). Complications in orthopedic surgery. *Vet Comp Orthop Traumatol*, 25(5):III.
6. Kujath P, Kujath C (2010). Complicated skin, skin structure and soft tissue infections - are we threatened by multi-resistant pathogens? *Eur J Med Res*, 15(12):544-53.
7. Thomas P, Schuh A, Ring J et al (2008). [Orthopedic surgical implants and allergies. Joint statement by the Implant Allergy Working Group (AK 20) of the DGOOC (German Association of Orthopedics and Orthopedic Surgery), DKG (German Contact Dermatitis Research Group) and DGAKI (German Society for Allergology and Clinical Immunology)]. *Hautarzt*, 59(3):220-9.
8. Campoccia D, Montanaro L, Arciola CR (2006). The significance of infection related to orthopedic devices and issues of antibiotic resistance. *Biomaterials*, 27(11):2331-9.
9. Parvizi J, Antoci V Jr, Hickok NJ, Shapiro IM (2007). Selfprotective smart orthopedic implants. *Expert Rev Med Devices*, 4(1):55-64.
10. Difazio RL, Harris M, Feldman L, Mahan ST (2017). Reducing the Incidence of Cast-related Skin Complications in Children Treated with Cast Immobilization. *J Pediatr Orthop*, 37(8):526-531.
11. Chirca I, Marculescu C (2017). Prevention of Infection in Orthopedic Prosthetic Surgery. *Infect Dis Clin North Am*, 31(2):253-63.
12. Al-Mulhim FA, Baragbah MA, Sadat-Ali M et al (2014). Prevalence of Surgical Site Infection in Orthopedic Surgery: A 5-year Analysis. *Int Surg*, 99(3):264-8.
13. Weigelt JA, Lipsky BA, Tabak YP et al (2010). Surgical site infections: causative pathogens and associated outcomes. *Am J Infect Control*, 38(2):112-120.
14. Moriarty TF, Schlegel U, Perren S, Richards RG (2010). Infection in fracture fixation: can we influence infection rates through implant design? *J Mater Sci Mater Med*, 21(3):1031-5.
15. Schmidt AH, Swiontkowski MF (2000). Pathophysiology of infections after internal fixation of fractures. *J Am Acad Orthop Surg*, 8(5):285-91.
16. Wilson SE (2008). Microbial sealing: a new approach to reducing contamination. *J Hosp Infect*, 70 Suppl 2:11-4.
17. Dohmen PM (2008). Antibiotic resistance in common pathogens reinforces the need to minimise surgical site infections. *J Hosp Infect*, 70 Suppl 2:15-20.
18. Reichman DE, Greenberg JA (2009). Reducing surgical site infections: a review. *Rev Obstet Gynecol*, 2(4):212-21.
19. Song Z, Borgwardt L, Høiby N et al (2013). Prosthesis infections after orthopedic joint replacement: the possible role of bacterial biofilms. *Orthop Rev (Pavia)*, 5(2):65-71.
20. Geipel U, Herrmann M (2004). The infected implant. Part 1: bacteriology. *Der Orthopade*, 33(12):1411-26; 1427-8.
21. Zimmerli W (2006). Infection and musculoskeletal conditions: Prosthetic-joint-associated infections. *Best Pract Res Clin Rheumatol*, 20(6):1045-63.
22. Anguita-Alonso P, Hanssen AD, Patel R (2005). Prosthetic joint infection. *Expert Rev Anti Infect Ther*, 3(5):797-804.
23. Boutoille D, Leautez S, Maulaz D et al (2000). [Skin and osteoarticular bacterial infections of the diabetic foot. Treatment]. *Presse Med*, 29(7):396-400.
24. Esposito S, Leone S (2008). Prosthetic joint infections: microbiology, diagnosis, management and prevention. *Int J Antimicrob Agents*, 32(4):287-93.
25. Legout L, Senneville E (2013). Periprosthetic joint infections: clinical and bench research. *Scientific World Journal*, 2013:549091.

26. Barnes M, Liew S (2012). The incidence of infection after posterior cervical spine surgery: a 10 year review. *Global Spine J*, 2(1):3-6.
27. Giordano P, Weber K, Gesin G, Kubert J (2007). Skin and skin structure infections: treatment with newer generation fluoroquinolones. *Ther Clin Risk Manag*, 3(2):309-17.
28. Misiakos EP, Bagias G, Patapis P et al (2014). Current concepts in the management of necrotizing fasciitis. *Front Surg*, 1:36.
29. Madu KA, Enweani UN, Katchy AU et al (2011). Implant associated surgical site infection in orthopaedics: a regional hospital experience. *Niger J Med*, 20(4):435-40.
30. Sansone V, Pagani D, Melato M (2013). The effects on bone cells of metal ions released from orthopaedic implants. A review. *Clin Cases Miner Bone Metab*, 10(1):34-40.
31. Shang X, Wang L, Kou D, et al (2014). Metal hypersensitivity in patient with posterior lumbar spine fusion: a case report and its literature review. *BMC Musculoskelet Disord*, 15:314.
32. Krecisz B, Kieć-Swierczyńska M, Bakowicz-Mitura K (2006). Allergy to metals as a cause of orthopedic implant failure. *Int J Occup Med Environ Health*, 19(3):178-80.
33. Dudda M, Godau P, Al-Benna S et al (2013). Vitiligo and allergic complications from orthopaedic joint implants: the role of benzoyl peroxide. *Recent Pat Inflamm Allergy Drug Discov*, 7(2):176-82.
34. Thomas P (2014). Clinical and diagnostic challenges of metal implant allergy using the example of orthopaedic surgical implants: Part 15 of the Series Molecular Allergology. *Allergo J Int*, 23(6):179-185.
35. Bircher A, Friederich NF, Seelig W, Scherer K (2012). Allergic complications from orthopaedic joint implants: the role of delayed hypersensitivity to benzoyl peroxide in bone cement. *Contact Dermatitis*, 66(1):20-6.
36. Thomas P, Schuh A, Eben R, Thomsen M (2008). Allergy to bone cement components. *Orthopade*, 37(2):117-20.
37. Eben R, Dietrich KA, Nerz C, et al (2010). Contact allergy to metals and bone cement components in patients with intolerance of arthroplasty. *Dtsch Med Wochenschr*, 135(28-29):1418-22.
38. Schuh A, Lill C, Hönle W, Effenberger H (2008). Prevalence of allergic reactions to implant materials in total hip and knee arthroplasty. *Zentralbl Chir*, 133(3):292-6.
39. Thomas P, Schuh A, Ring J, Thomsen M (2008). [Orthopedic surgical implants and allergies: joint statement by the implant allergy working group (AK 20) of the DGOOC (German association of orthopedics and orthopedic surgery), DKG (German contact dermatitis research group) and dgaki (German society for allergology and clinical immunology)]. *Orthopade*, 37(1):75-88.
40. DiFazio R, Vessey J, Zurakowski D et al (2011). Incidence of skin complications and associated charges in children treated with hip spica casts for femur fractures. *J Pediatr Orthop*, 31(1):17-22.
41. Guo S (2011). Is Velband still a safe and cost effective skin protection beneath the tourniquet in hand surgery? *Hand Surg*, 16(1):5-8.
42. Ingoe H, Eastwood S, Elson DW, Young CF (2011). Removal of a below knee plaster cast worn for 28 months: a case report. *J Med Case Rep*, 5:74.
43. Vigier S, Casillas JM, Dulieu V et al (1999). Healing of open stump wounds after vascular below-knee amputation: plaster cast socket with silicone sleeve versus elastic compression. *Arch Phys Med Rehabil*, 80(10):1327-30.
44. Khan MS, ur Rehman S, Ali MA et al (2008). Infection in orthopedic implant surgery, its risk factors and outcome. *J Ayub Med Coll Abbottabad*, 20(1):23-5.
45. Swanson TV, Szabo RM, Anderson DD (1991). Open hand fractures: prognosis and classification. *J Hand Surg Am*, 16(1): 101-7.
46. Ruedi TP (2000). *AO principles of fracture management*. First edition, Thieme: 729-49
47. Sohrabi M, Fakhrtabatabaie SA (1998). Effective time of antibiotic therapy on surgical wound infection of back bone. *Pejohande Quarterby*, 3(12): 57-63 (In Persian).
48. Murray CK, Hau JR, Solomkin YS, et al (2008). Prevention and management of infection associated with combat - related extremity injuries. *J Trauma*, 64(3 Suppl):S239-51.
49. Mokurec m, Fristakova M (2008). Efficacy of antiseptic in the prevention of Post-operative infections of the proximal femur, hip and pelvis regions in orthopedic pediatric patients, Analysis of the first result. *Acta Chir Orthop Traumatol Cech*, 75(2):106-9.

50. Eyichukwu GO (2010). Non-Steroidal anti-inflammatory drugs usage in orthopaedics and trauma practice. A guide and review. *Niger J Med*, 19(4):374-81.
51. Roujeau JC (1987). Clinical aspects of skin reactions to NSAIDs. *Scand J Rheumatol Suppl*, 65:131-4.
52. Sirirat Tribuddharat, Thepakorn Sathitkarnmanee, Amnat Kitkhuandee et al (2016). A fatal adverse effect of cefazolin administration. *Drug Healthc Patient Saf*, 8: 9-12.
53. Sun-Kyung Park, Yun Suk Choi (2013). Hypopigmentation and subcutaneous fat, muscle atrophy after local corticosteroid injection. *Korean J Anesthesiol*, 65(6 Suppl): S59-S61.