

Propranolol Attenuates Hemorrhage and Accelerates Wound Healing in Severely Burned Adults

A severe burn injury is characterized by a profound increase in metabolism, that is mediated by a surge in stress hormones including catecholamines and glucocorticoids and may result in hyperdynamic changes associated with copious amounts of operative blood loss, and cardiac stress that is characterized by increased cardiac work, cardiac output, resting heart rate, and these changes lead to post burn morbidity and mortality. Additionally, as patients with burn injury undergo serial skin grafting procedures, limiting hemorrhage during these operations becomes paramount to early recovery ^[1].

Propranolol, a nonselective β -blocker, has widespread systemic effects following burn injury. Recently, they reported that administration of propranolol in children with severe burn injury for one year significantly improves body composition, resting energy expenditure, and cardiac function ^[2].

In a study published in 2015, they evaluated the role of propranolol and its activity on hemorrhage and wound healing and other hemodynamic changes in severely burned adult patients showed that administration of propranolol during the acute hospitalization period diminishes blood loss during skin grafting procedures and markedly improves wound healing in severely burned adults. ^[1]

In this prospective, randomized controlled-trial, 69 patients older than 18 years, burn wounds covering $\geq 30\%$ of the total body surface area, treatment with at least one surgical skin grafting procedure were enrolled in this study. Within 48 hours of hospital admission, patients received either standard burn care treatment (control; n = 34), or standard burn care treatment plus propranolol at a dose of 3.3 ± 3.0 mg/kg/day (propranolol; n = 35), which was administered throughout hospitalization to decrease baseline heart rates by approximately 20%. Thereafter, patients underwent serial skin grafting procedures once donor sites wounds healed. Patients were then discharged once wounds were deemed to be 95% healed. Wound healing was determined by comparing the time between grafting procedures. Blood loss was determined by comparing pre- and postoperative hematocrit levels that were obtained within 12 hours before or after skin grafting procedures. ^[1]

This study had resulted in many findings; first , it was found that the time between skin grafting procedures was lower in the propranolol group than in the control group (10 ± 5 days vs. 17 ± 12 days; $P = 0.02$) and this indicates that propranolol significantly improves donor site wound healing time compared to the control treatment. Second , Average blood loss (estimated) was similar between groups (control 0.37 ± 0.73 ml/cm² excised vs. propranolol 0.26 ± 0.21 ml/cm² excised; $P = 0.70$),and required a similar number of packed red blood cell transfusions as the control group to maintain perioperative hematocrit levels (propranolol 4.4 ± 3.1 units vs. control 5.3 ± 5.4 units; $P = 0.89$). But, Propranolol was associated with a 5 to 7% improvement in perioperative hematocrit during grafting procedures of 4,000 to 16,000 cm² compared to control ($P = 0.002$). ^[1]

Also, it was found that daily mean heart rate was significantly decreased in patients receiving propranolol compared to control ($P < 0.05$). Heart rates between post burn days 2 to 30 in propranolol patients were, on average, 11 ± 4 beats per minute lower than those in the control group. Finally, adverse events were comparable in both groups, and there was no significant difference in the incidence of bradycardia ($P=0.47$), bradypnea ($P=0.63$), hypotension ($P=1.00$), and ischemia ($P=0.23$). ^[1]

The mechanism by which propranolol works is direct inhibition of β -adrenergic receptors in the heart will decreases heart rate, blood flow, and cardiac output, also, angiogenesis may be attenuated via vasoconstriction, and decreased expression of matrix metalloproteinases, basic fibroblast growth factor, and vascular endothelial growth factor may limit operative hemorrhage. Similarly, propranolol enhances up-regulation of capillary endothelial cells and apoptosis, further limiting angiogenesis and blood loss ^[1].

In conclusion, administration of propranolol during acute hospitalization in severely burned adults diminishes blood loss during skin grafting procedures and speeds wound healing .The effect of propranolol on wound healing and hemorrhage in other injury/disease models deserves further investigation.

References:

- 1-** Ali A, Herndon DN, Mamachen A, Hasan S, Andersen CR, Grogans RJ.etal.Propranolol attenuates hemorrhage and accelerates wound healing in severely burned adults. Crit Care. 2015 May 4; 19:217. doi: 10.1186/s13054-015-0913-x.
- 2-** Herndon DN, Rodriguez NA, Diaz EC, Hegde S, Jennings K, Mlcak RP, et al. Long-term propranolol use in severely burned pediatric patients: a randomized controlled study. Ann Surg. 2012 Sep; 256(3):402-11.

Prepared by: Pharm D Hana'a M. Jaradat

Supervised by: Pharm D Eshraq Al-abweeny